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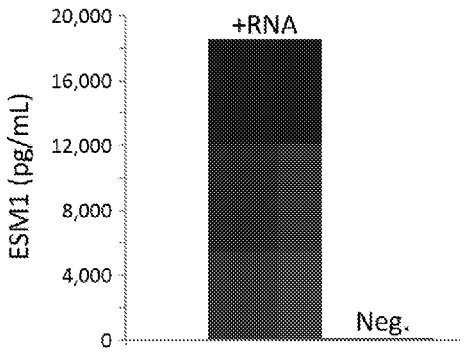
FIG. 60



(57) Abstract: The present invention relates in part to nucleic acids, including nucleic acids encoding proteins, therapeutics and cosmetics comprising nucleic acids, methods for delivering nucleic acids to cells, tissues, organs, and patients, methods for inducing cells to express proteins using nucleic acids, methods, kits and devices for transfecting, gene editing, and reprogramming cells, and cells, organisms, therapeutics, and cosmetics produced using these methods, kits, and devices.

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NUCLEIC ACID PRODUCTS AND METHODS OF ADMINISTRATION THEREOF

PRIORITY

This application claims priority to US Provisional Patent Application No. 62/376,209, filed August 17, 2016 and to US Provisional Patent Application No 62/509,350, filed May 22, 2017. The entire contents of the aforementioned patent applications are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates, in part, to methods, compositions, and products for producing and delivering nucleic acids to cells, tissues, organs, and patients, methods for expressing proteins in cells, tissues, organs, and patients, and cells, therapeutics, and cosmetics produced using these methods, compositions, and products.

DESCRIPTION OF THE TEXT FILE SUBMITTED ELECTRONICALLY

The instant application contains a Sequence Listing which has been submitted in ASCII format via EFS-Web and is hereby incorporated by reference in its entirety. Said ASCII copy, created on August 17, 2017, is named FAB-010PC_ST25 and is 2.32 MB in size.

BACKGROUND

Synthetic RNA and Nucleic-Acid Therapeutics

Ribonucleic acid (RNA) is ubiquitous in both prokaryotic and eukaryotic cells, where it encodes genetic information in the form of messenger RNA, binds and transports amino acids in the form of transfer RNA, assembles amino acids into proteins in the form of ribosomal RNA, and performs numerous other functions including gene expression regulation in the forms of microRNA and long non-coding RNA. RNA can be produced synthetically by methods including direct chemical synthesis and *in vitro* transcription, and can be administered to patients for therapeutic use. However, previously described synthetic RNA molecules are unstable and trigger a potent innate-immune response in human cells. In addition, methods for efficient non-viral delivery of nucleic acids to patients, organs, tissues, and cells *in vivo* have not been previously described. The many drawbacks of existing synthetic RNA technologies and methods for delivery of nucleic acids make them undesirable for therapeutic or cosmetic use.

Cell Reprogramming and Cell-Based Therapies

Cells can be reprogrammed by exposing them to specific extracellular cues and/or by ectopic expression of specific proteins, microRNAs, *etc.* While several reprogramming methods have been previously described, most that rely on ectopic expression require the introduction of exogenous DNA, which can carry mutation risks. DNA-free reprogramming methods based on direct delivery of reprogramming proteins have been reported. However, these methods are too inefficient and unreliable for commercial use. In addition, RNA-based reprogramming methods have been described (*see, e.g.*, Angel. MIT Thesis. 2008. 1-56; Angel *et al.* PLoS ONE. 2010. 5,107;

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Warren et al. Cell Stem Cell. 2010. 7,618-630; Angel. MIT Thesis. 2011. 1-89; and Lee et al. Cell. 2012. 151,547 558; the contents of all of which are hereby incorporated by reference). However, existing RNA-based reprogramming methods are slow, unreliable, and inefficient when performed on adult cells, require many transfections (resulting in significant expense and opportunity for error), can reprogram only a limited number of cell types, can reprogram cells to only a limited number of cell types, require the use of immunosuppressants, and require the use of multiple human-derived components, including blood-derived HSA and human fibroblast feeders. The many drawbacks of previously disclosed RNA-based reprogramming methods make them undesirable for research, therapeutic or cosmetic use.

Gene Editing

Several naturally occurring proteins contain DNA-binding domains that can recognize specific DNA sequences, for example, zinc fingers (ZFs) and transcription activator-like effectors (TALEs). Fusion proteins containing one or more of these DNA-binding domains and the cleavage domain of FokI endonuclease can be used to create a double-strand break in a desired region of DNA in a cell (see, e.g., US Patent Appl. Pub. No. US 2012/0064620, US Patent Appl. Pub. No. US 2011/0239315, US Patent No. 8,470,973, US Patent Appl. Pub. No. US 2013/0217119, US Patent No. 8,420,782, US Patent Appl. Pub. No. US 2011/0301073, US Patent Appl. Pub. No. US 2011/0145940, US Patent No. 8,450,471, US Patent No. 8,440,431, US Patent No. 8,440,432, and US Patent Appl. Pub. No. 2013/0122581, the contents of all of which are hereby incorporated by reference). Other gene-editing proteins include clustered regularly interspaced short palindromic repeat (CRISPR)-associated proteins. However, current methods for gene editing cells are inefficient and carry a risk of uncontrolled mutagenesis, making them undesirable for research, therapeutic or cosmetic use. Methods for DNA-free gene editing of somatic cells have not been previously explored, nor have methods for simultaneous or sequential gene editing and reprogramming of somatic cells. In addition, methods for directly gene editing cells in patients (i.e., in vivo) have not been previously explored, and the development of such methods has been limited by a lack of acceptable targets, inefficient delivery, inefficient expression of the gene-editing protein/proteins, inefficient gene editing by the expressed gene-editing protein/proteins, due in part to poor binding of DNA-binding domains, excessive off-target effects, due in part to non-directed dimerization of the FokI cleavage domain and poor specificity of DNA-binding domains, and other factors. Finally, the use of gene editing in anti-bacterial, anti viral, and anti-cancer treatments has not been previously explored.

Accordingly, there remains a need for improved methods and compositions for the production and delivery of nucleic acids to cells, tissues, organs, and patients.

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Any reference to or discussion of any document, act or item of knowledge in this specification is included solely for the purpose of providing a context for the present invention. It is not suggested or represented that any of these matters or any combination thereof formed at the priority date part of the common general knowledge, or was known to be relevant to an attempt to solve any problem with which this specification is concerned.

SUMMARY OF THE INVENTION

In a first aspect, the invention relates to an *in vivo* method to treat cancer in a subject comprising:

administering to a tumor cell in the subject a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-L1, PD-L2, and OX40L, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of the tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell in the subject, resulting in the stimulation or enhancement of an immune response in the subject,

thereby treating cancer in the subject.

In a second aspect, the invention relates to an *in vivo* method to treat cancer in a subject comprising:

administering to the subject by intratumoral injection a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a cell in the tumor, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell in the tumor of the subject, resulting in the stimulation or enhancement of an immune response in the subject;

thereby treating cancer in the subject.

In a third aspect, the inventio relates to an *in vivo* method for treating cancer in a subject comprising:

administering to a cell in the subject a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene

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is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of the cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell in the subject,

resulting in the stimulation or enhancement of an immune response in the subject, thereby treating cancer in the subject.

In a fourth aspect, the invention relates to use of a non-viral, cell-free composition in the manufacture of a medicament for an *in vivo* method of treating cancer in a subject, the medicament comprising:

a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-L1, PD-L2, and OX40L, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell, resulting in the stimulation or enhancement of an immune response in the subject.

In a fifth aspect, the invention relates to use of a non-viral, cell-free composition in the manufacture of a medicament for an *in vivo* method of treating cancer in a subject, the medicament comprising:

a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a cell in the tumor, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell in the tumor of the subject, resulting in the stimulation or enhancement of an immune response in the subject.

In a sixth aspect, the inventio relates to use of a non-viral, cell-free composition in the manufacture of a medicament for an *in vivo* method of treating cancer in a subject, the medicament comprising:

a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune

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checkpoint molecule gene is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a cell of the subject, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell,

resulting in the stimulation or enhancement of an immune response in the subject.

The present invention provides, in part, compositions, methods, articles, and devices for delivering nucleic acids to cells, tissues, organs, and patients, methods for inducing cells to express proteins, methods, articles, and devices for producing these compositions, methods, articles, and devices, and compositions and articles, including cells, organisms, cosmetics and therapeutics, produced using these compositions, methods, articles,

and devices. Unlike previously reported methods, certain embodiments of the present invention provide small doses of nucleic acids to achieve significant and lasting protein expression in humans.

In some aspects, the present invention relates to a method for treating a metabolic disorder. The method comprises a step of administering an effective amount of a synthetic RNA encoding growth differentiation factor 15 (GDF15) to a subject in need thereof or endothelial cell specific molecule 1 (ESM1), wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the metabolic disorder is selected from Type I diabetes, Type II diabetes, insulin resistance, obesity, dyslipidemia, hypercholesterolemia, hyperglycemia, hyperinsulinemia, hypertension, hepatosteaotosis such as non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty acid liver disease (NAFLD), cancer, a disease or disorder associated with impaired lipid metabolism, a disease or disorder associated with impaired renal function, a disease or disorder associated with impaired hepatic function, a disease or disorder associated with impaired lung function, a vascular or cardiovascular disease or disorder, muscle wasting, inflammation, and a respiratory disease.

In various embodiments, the disease or disorder associated with impaired renal function is selected from chronic kidney diseases, acute kidney injury, nephropathy, diabetic nephropathy, kidney failure, and kidney fibrosis.

In various embodiments, the vascular or cardiovascular disease or disorder is selected from coronary artery disease, cardiomyopathy, hypertension, atrial fibrillation, preeclampsia, peripheral artery disease, atherosclerosis, heart failure, acute myocardial infarction, acute coronary syndrome, muscle wasting, hypertensive ventricular hypertrophy, hypertensive cardiomyopathy, ischemic heart disease, myocardial infarction, abdominal aortic aneurysm, a blood clot, deep vein thrombosis, venous stasis disease, phlebitis, and varicose veins.

In various embodiments, the treatment results in reduction in one or more of aspartate transaminase (AST), alanine transaminase (ALT), or glucose levels in the subject, as compared to untreated subjects.

In various embodiments, the treatment results in increased lipid mobilization in the subject, as compared to untreated subjects.

In various embodiments, the administration is intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intracerebral, intravaginal, transdermal, intraportal, rectally, by inhalation, or topically.

In some aspects, the present invention relates to a method for modulating GDF15. The method comprises a step of administering an effective amount of a synthetic RNA encoding GDF15 to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the modulating results in reduction in one or more of ALT, AST, or glucose levels in the subject, as compared to untreated subjects.

In various embodiments, the modulating results in increased lipid mobilization in the subject, as compared to untreated subjects.

In various embodiments, the administration is intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intracerebral, intravaginal, transdermal, intraportal, rectally, by inhalation, or topically.

In various embodiments, the modulating results in an increase in the quantity of GDF15 in the subject.

In various embodiments, the modulating results in a decrease in the quantity of GDF15 in the subject.

In some aspects, the present invention relates to a method for modulating ESM1. The method comprises a step of administering an effective amount of a synthetic RNA encoding ESM1 to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the modulating results in one or more of reduced ALT, AST, or glucose levels in the subject, as compared to untreated subjects.

In various embodiments, the modulating results in increased lipid mobilization in the subject, as compared to untreated subjects.

In various embodiments, the administration is intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intracerebral, intravaginal, transdermal, intraportal, rectally, by inhalation, or topically.

In various embodiments, the modulating results in an increase in the quantity of ESM1 in the subject.

In various embodiments, the modulating results in a decrease in the quantity of ESM1 in the subject.

In some aspects, the present invention relates to a method for treating a liver disorder. The method comprises a step of administering an effective amount of a synthetic RNA encoding growth differentiation factor 15 (GDF15) or endothelial cell specific molecule 1 (ESM1) to a subject in need thereof, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity; and the treatment reduces one or more of fatty liver, NAFLD, NASH, inflammation, hepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma in the subject.

In various embodiments, the treatment results in reduction in one or more of AST, ALT, or glucose levels in the subject, as compared to untreated subjects.

In various embodiments, the treatment results in increased lipid mobilization in the subject, as compared to untreated subjects.

In various embodiments, the administration is directed to the liver.

In various embodiments, the administration is intraportal injection.

In some aspects, the present invention relates to a method for treating Friedrich's Ataxia. The method comprises a step of administering to a subject in need thereof an effective amount of (a) a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in FXNA (SEQ ID NO: 582), and/or (b) a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in FXNB (SEQ ID NO: 583), wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity. In various embodiments, the treatment comprises administering to a subject in need thereof an effective amount of (a) the synthetic RNA encoding the gene-editing protein capable of creating a double strand break in FXNA (SEQ ID NO: 582), and (b) the synthetic RNA encoding the gene-editing protein capable of creating a double strand break in FXNB (SEQ ID NO: 583).

In various embodiments, the administration is directed to the heart.

In various embodiments, the administration is via a catheter.

In various embodiments, the treatment ameliorates one or more of muscle weakness, loss of coordination, vision impairment, hearing impairment, slurred speech, scoliosis, pes cavus deformity of the foot, diabetes, and heart disorders, selected from one or more atrial fibrillation, tachycardia and hypertrophic cardiomyopathy.

In various embodiments, the gene-editing protein is selected from a CRISPR/Cas9, TALEN and a zinc finger nuclease.

In various embodiments, the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain. The DNA-binding domain comprises a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 629) and is between 36 and 39 amino acids long, wherein:"v" is Q, D or E; "w" is S or N; "x" is H, N, or I; "y" is D, A, I, N, G, H, K, S, or null; and "z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 630) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 631). The nuclease domain comprises a catalytic domain of a nuclease.

In various embodiments, the nuclease domain is capable of forming a dimer with another nuclease domain.

In various embodiments, the nuclease domain comprises the catalytic domain of a protein comprising the amino acid sequence of SEQ ID NO: 632.

In some aspects, the present invention relates to a method for reducing inflammation. The method comprises a step of administering an effective amount of a synthetic RNA encoding superoxide dismutase 3 (SOD3) or IFκB, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity to a subject in need thereof.

In various embodiments, the inflammation is associated with a lung disease or disorder.

In various embodiments, the lung disease or disorder is selected from Asbestosis, Asthma, Bronchiectasis, Bronchitis, Chronic Cough, Chronic Obstructive Pulmonary Disease (COPD), Common Cold, Croup, Cystic Fibrosis, Hantavirus, Idiopathic Pulmonary Fibrosis, Influenza, Lung Cancer, Pandemic Flu, Pertussis, Pleurisy,

Pneumonia, Pulmonary Embolism, Pulmonary Hypertension, Respiratory Syncytial Virus (RSV), Sarcoidosis, Sleep Apnea, Spirometry, Sudden Infant Death Syndrome (SIDS), and Tuberculosis.

In various embodiments, the inflammation is associated with a lung infection.

In various embodiments, the lung infection is cause by a bacterium, a fungus, a protozoa, a multi-cellular organism, a particulate, or a virus.

In various embodiments, the synthetic RNA is administered by inhalation.

In various embodiments, the inflammation is associated with sepsis.

In some aspects, the present invention relates to a method for treating alpha-1 antitrypsin (A1AT) deficiency. The method comprises a step of administering to a subject in need thereof an effective amount of (a) a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in A1AT_A (SEQ ID NO: 584) and/or (b) a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in A1AT_B (SEQ ID NO: 585), wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity. In various embodiments, the treatment comprises administering to a subject in need thereof an effective amount of (a) the synthetic RNA encoding the gene-editing protein capable of creating a double strand break in A1AT_A (SEQ ID NO: 584) and (b) the synthetic RNA encoding the a gene-editing protein capable of creating a double strand break in A1AT_B (SEQ ID NO: 585).

In various embodiments, the administration is directed to the liver.

In various embodiments, the administration is intraportal injection.

In various embodiments, the treatment corrects the Z mutation in the subject's liver cells.

In various embodiments, the treatment reduces polymerized Z protein accumulation in the subject's liver cells.

In various embodiments, the treatment increases secretion and/or serum levels of functional A1AT.

In various embodiments, the treatment ameliorates one or more of chronic cough, emphysema, COPD, liver failure, hepatitis, hepatomegaly, jaundice, and cirrhosis.

In various embodiments, the gene-editing protein is selected from a CRISPR/Cas9, TALEN, and a zinc finger nuclease.

In various embodiments, the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain. The DNA-binding domain comprises a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 629) and is between 36 and 39 amino acids long, wherein: "v" is Q, D or E; "w" is S or N; "x" is H, N, or I; "y" is D, A, I, N, G, H, K, S, or null; and "z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 630) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 631). The nuclease domain comprises a catalytic domain of a nuclease.

In various embodiments, the nuclease domain is capable of forming a dimer with another nuclease domain.

In various embodiments, the nuclease domain comprises the catalytic domain of a protein comprising the amino acid sequence of SEQ ID NO: 632.

In some aspects, the present invention relates to a method for treating alpha-1 antitrypsin (A1AT) deficiency. The method comprises a step of administering an effective amount of a synthetic RNA encoding A1AT to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the administration is directed to the liver.

In various embodiments, the administration is intraportal injection.

In various embodiments, the treatment corrects the Z mutation in the subject's liver cells.

In various embodiments, the treatment reduces polymerized Z protein accumulation in the subject's liver cells.

In various embodiments, the treatment increases secretion and/or serum levels of functional A1AT.

In various embodiments, the treatment ameliorates one or more of the subject's symptoms.

In some aspects, the present invention relates to a method for reversing an alpha-1 antitrypsin (A1AT) deficiency in a cell. The method comprises steps of (a) obtaining a cell comprising a defective A1AT gene and (b) contacting the cell with a synthetic RNA encoding A1AT, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the method further comprises steps of (c) obtaining the cell contacted in step (b); and (d) administering the cell to a subject in need thereof.

In various embodiments, the administration is directed to the liver.

In various embodiments, the administration is intraportal injection.

In some aspects, the present invention relates to a method for reversing an alpha-1 antitrypsin (A1AT) deficiency in a cell. The method comprises steps of (a) obtaining a cell comprising a defective A1AT gene and (b) contacting the cell with one or both of a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in A1AT_A (SEQ ID NO: 584) and a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in A1AT_B (SEQ ID NO: 585), wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the method further comprises steps of (c) obtaining the cell contacted in step (b); and (d) administering the cell to a subject in need thereof.

In various embodiments, the administration is directed to the liver.

In various embodiments, the administration is intraportal injection.

In various embodiments, the gene-editing protein is selected from a CRISPR/Cas9, TALEN and a zinc finger nuclease.

In various embodiments, the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain. The DNA-binding domain comprises a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 629) and is between 36 and 39 amino acids long, wherein: "v" is Q, D or E; "w" is S or N; "x" is H, N, or I; "y" is D, A, I, N, G, H, K, S, or null; and "z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 630) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 631). The nuclease domain comprises a catalytic domain of a nuclease.

In various embodiments, the nuclease domain is capable of forming a dimer with another nuclease domain.

In various embodiments, the nuclease domain comprises the catalytic domain of a protein comprising the amino acid sequence of SEQ ID NO: 632.

In some aspects, the present invention relates to a method for modulating BMP7. The method comprises a step of administering an effective amount of a synthetic RNA encoding BMP7 to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the modulating results in an increase in the quantity of BMP7 in the subject.

In various embodiments, the modulating results in a decrease in the quantity of BMP7 in the subject.

In various embodiments, the modulating results in an increase in intracellular alkaline phosphatase activity.

In various embodiments, the synthetic RNA encoding BMP7 comprises a sequence encoding the BMP7 signal peptide.

In various embodiments, the BMP7 signal peptide comprises the sequence of SEQ ID NO: 597.

In various embodiments, the administration is directed to the liver.

In various embodiments, the administration is intraportal injection.

In various embodiments, the administration treats diabetic nephropathy.

In various embodiments, the administration treats liver fibrosis.

In various embodiments, the administration is directed to the kidney.

In various embodiments, the administration is intravenous or intradermal.

In various embodiments, the administration treats kidney disease.

In various embodiments, the kidney disease is diabetic nephropathy.

In various embodiments, the modulating results in reduced levels of urine albumin in the subject.

In some aspects, the present invention relates to a method for modulating an immune checkpoint molecule. The method comprises a step of administering an effective amount of a synthetic RNA encoding the immune checkpoint molecule to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In some aspects, the present invention relates to a method for treating a subject comprising administering a step of a synthetic RNA encoding a gene-editing protein targeting an immune checkpoint molecule gene.

In some aspects, the present invention relates to a method for treating a subject comprising steps of (a) obtaining a cell comprising an immune checkpoint molecule gene and (b) contacting the cell with a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in the immune checkpoint molecule gene, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the method further comprises steps of (c) obtaining the cell contacted in step (b); and (d) administering the cell to a subject in need thereof.

In various embodiments, the gene-editing protein is selected from a CRISPR/Cas9, TALEN and a zinc finger nuclease.

In various embodiments, the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain. The DNA-binding domain comprises a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 629) and is between 36 and 39 amino acids long, wherein:

"v" is Q, D or E; "w" is S or N; "x" is H, N, or I; "y" is D, A, I, N, G, H, K, S, or null; and "z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 630) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 631). The nuclease domain comprises a catalytic domain of a nuclease.

In various embodiments, the nuclease domain is capable of forming a dimer with another nuclease domain.

In various embodiments, the nuclease domain comprises the catalytic domain of a protein comprising the amino acid sequence of SEQ ID NO: 632.

In various embodiments, the immune checkpoint molecule is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3.

In various embodiments, the immune checkpoint molecule is PD-1.

In various embodiments, the administering stimulates or enhances an immune response in the subject.

In various embodiments, the administering inhibits or reduces an immune response in the subject.

In various embodiments, the subject is afflicted with a cancer.

In various embodiments, the subject is afflicted with an autoimmune disease.

In various embodiments, the administration is intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intracerebral, intravaginal, transdermal, intraportal, rectally, by inhalation, or topically.

In various embodiments, the modulating results in an increase in the quantity of PD-1 in the subject.

In various embodiments, the modulating results in a decrease in the quantity of PD-1 in the subject.

In some aspects, the present invention relates to a method for treating a cancer comprising steps of (a) isolating an cell from a subject, the cell being an immune cell or hematopoietic cell; (b) contacting the isolated cell with an effective amount of a synthetic RNA encoding a chimeric antigen receptor (CAR), wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity; and (c) administering the cell to the subject.

In various embodiments, the immune cell is a T cell.

In some aspects, the present invention relates to a method for making a chimeric antigen receptor (CAR) T cell comprising steps of (a) obtaining a cell from a subject and (b) contacting the cell with a synthetic RNA encoding a gene-editing protein capable of creating a double strand break to yield a safe harbor locus for CAR insertion, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the wherein the gene-editing protein is selected from a CRISPR/Cas9, TALEN and a zinc finger nuclease.

In various embodiments, the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain. The DNA-binding domain comprises a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 629) and is between 36 and 39 amino acids long, wherein: “v” is Q, D or E; “w” is S or N; “x” is H, N, or I; “y” is D, A, I, N, G, H, K, S, or null; and “z” is GGKQALETVQRLLPVLCQD (SEQ ID NO: 630) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 631). The nuclease domain comprises a catalytic domain of a nuclease.

In various embodiments, the nuclease domain is capable of forming a dimer with another nuclease domain.

In various embodiments, the nuclease domain comprises the catalytic domain of a protein comprising the amino acid sequence of SEQ ID NO: 632.

In some aspects, the present invention relates to a method for increasing the persistence of a chimeric antigen receptor (CAR) T cell, comprising a step of contacting the chimeric antigen receptor (CAR) T cell with a synthetic RNA encoding a encoding a telomerase, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In some aspects, the present invention relates to a method for treating a skin wound, comprising a step of administering an effective amount of a synthetic RNA encoding interleukin 22 (IL22) to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the administration is directed to a population of cells of the integumentary system.

In various embodiments, the population of cells comprises one or more of cells of the epidermis, cells of the basement membrane, cells of the dermis, and/or cells of the subcutis.

In various embodiments, the population of cells is cells of the epidermis, and comprises one more of cells of the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and/or stratum germinativum.

In various embodiments, the population of cells is cells of the dermis, and comprises one or more of cells from the papillary region and the reticular region.

In various embodiments, the administration is by subcutaneous injection, intradermal injection, subdermal injection, intramuscular injection, or topical administration.

In various embodiments, the administration is intradermal injection to one or more of the dermis or epidermis.

In various embodiments, the an effective amount is from about 10 ng to about 5000 ng per treatment area of about 10 cm^2 or less, or about 5 cm^2 or less, or about 1 cm^2 or less, or about 0.5 cm^2 or less, or about 0.2 cm^2 or less.

In various embodiments, about 10 ng, or about 20 ng, or about 50 ng, or about 100 ng, or about 200 ng, or about 300 ng, or about 400 ng, or about 500 ng, or about 600 ng, or about 700 ng, or about 800 ng, or about 900 ng, or about 1000 ng, or about 1100 ng, or about 1200 ng, or about 1300 ng, or about 1400 ng, or about 1500 ng, or about 1600 ng, or about 1700 ng, or about 1800 ng, or about 1900 ng, or about 2000 ng, or about 3000 ng, or about 4000 ng, or about 5000 ng of the synthetic RNA is administered per treatment area of about 10 cm^2 or less, or about 5 cm^2 or less, or about 1 cm^2 or less, or about 0.5 cm^2 or less, or about 0.2 cm^2 or less.

In various embodiments, the modulating results in an increase in the quantity of IL22 in the subject.

In various embodiments, the modulating results in a decrease in the quantity of IL22 in the subject.

In various embodiments, the effective amount of synthetic RNA is administered using an array of needles covering an affected area of the subject.

In various embodiments, the treatment area is mechanically massaged after administration.

In various embodiments, the treatment area is exposed to electric pulses after administration.

In various embodiments, the electric pulses are between about 10V and about 200V for from about 50 microseconds to about 1 second.

In various embodiments, the electric pulses are generated around the treatment area by a multielectrode array.

In some aspects, the present invention relates to a method for treating a metabolic disorder, comprising a step of administering a synthetic RNA encoding a gene-editing protein targeting a defective gene, wherein the administration is by intraportal injection.

In some aspects, the present invention relates to a method for treating a metabolic disorder comprising a step of (a) obtaining a cell comprising a defective gene and (b) contacting the cell with a synthetic RNA encoding a gene-editing protein capable of creating a double strand break in the defective gene, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity. In various embodiments,

the method further comprises steps of (c) obtaining the cell contacted in step (b); and (d) administering the cell to a subject in need thereof by intraportal injection.

In various embodiments, the gene-editing protein is selected from a CRISPR/Cas9, TALEN and a zinc finger nuclease.

In various embodiments, the gene-editing protein comprises: (a) a DNA-binding domain and (b) a nuclease domain. The DNA-binding domain comprises a plurality of repeat sequences and at least one of the repeat sequences comprises the amino acid sequence: LTPvQVVAIAwxyzGHGG (SEQ ID NO: 629) and is between 36 and 39 amino acids long, wherein: "v" is Q, D or E; "w" is S or N; "x" is H, N, or I; "y" is D, A, I, N, G, H, K, S, or null; and "z" is GGKQALETVQRLLPVLCQD (SEQ ID NO: 630) or GGKQALETVQRLLPVLCQA (SEQ ID NO: 631). The nuclease domain comprises a catalytic domain of a nuclease.

In various embodiments, the nuclease domain is capable of forming a dimer with another nuclease domain.

In various embodiments, the nuclease domain comprises the catalytic domain of a protein comprising the amino acid sequence of SEQ ID NO: 632.

In various embodiments, the metabolic disorder is selected from a disorder of carbohydrate metabolism, a disorder of amino acid metabolism, a disorder of the urea cycle, a disorder of fatty acid metabolism, a disorder of porphyrin metabolism, a disorder of lysosomal storage, a disorder of peroxisome biogenesis, and a disorder of purine or pyrimidine metabolism.

In various embodiments, the metabolic disorder is a disorder of carbohydrate metabolism and wherein the disease is galactosemia and the defective gene is optionally GALT, GALK1, or GALE; wherein the disease is essential fructosuria and the defective gene is optionally KHK; wherein the disease is Hereditary fructose intolerance and the defective gene is optionally ALDOB; wherein the disease is glycogen storage disease type I and the defective gene is optionally G6PC, SLC37A4, or SLC17A3; wherein the disease is glycogen storage disease type II and the defective gene is optionally GAA; wherein the disease is glycogen storage disease type III and the defective gene is optionally AGL; wherein the disease is glycogen storage disease type IV and the defective gene is optionally GBE1; wherein the disease is glycogen storage disease type V and the defective gene is optionally PYGM; wherein the disease is glycogen storage disease type VI and the defective gene is optionally PYGL; wherein the disease is glycogen storage disease type VII and the defective gene is optionally PYGM; wherein the disease is glycogen storage disease type IX and the defective gene is optionally PHKA1, PHKA2, PHKB, PHKG1, or PHKG2; wherein the disease is glycogen storage disease type XI and the defective gene is optionally SLC2A2; wherein the disease is glycogen storage disease type XII and the defective gene is optionally ALDOA; wherein the disease is glycogen storage disease type XIII and the defective gene is optionally ENO1, ENO2, or ENO3; wherein the disease is glycogen storage disease type 0 and the defective gene is optionally GYS1 or GYS2; wherein the disease is pyruvate carboxylase deficiency and the defective gene is optionally PC; wherein the disease is pyruvate kinase deficiency and the defective gene is optionally PKLR; wherein the disease is transaldolase deficiency and the defective gene is optionally TALDO1; wherein the

disease is triosephosphate isomerase deficiency and the defective gene is optionally TPI1; wherein the disease is fructose bisphosphatase deficiency and the defective gene is optionally FBP1; wherein the disease is hyperoxaluria and the defective gene is optionally AGXT or GRHPR; wherein the disease is hexokinase deficiency and the defective gene is optionally HK1; wherein the disease is glucose-galactose malabsorption and the defective gene is optionally SLC5A1; or wherein the disease is glucose-6-phosphate dehydrogenase deficiency and the defective gene is optionally G6PD.

In various embodiments, the metabolic disorder is a disorder of amino acid metabolism wherein the disease is alkaptonuria and the defective gene is optionally HGD; wherein the disease is aspartylglucosaminuria and the defective gene is optionally AGA; wherein the disease is methylmalonic acidemia and the defective gene is optionally MUT, MCEE, MMAA, MMAB, MMACHC, MMADHC, or LMBRD1; wherein the disease is maple syrup urine disease and the defective gene is optionally BCKDHA, BCKDHB, DBT, or DLD; wherein the disease is homocystinuria and the defective gene is optionally CBS; wherein the disease is tyrosinemia and the defective gene is optionally FAH, TAT, or HPD; wherein the disease is trimethylaminuria and the defective gene is optionally FMO3; wherein the disease is Hartnup disease and the defective gene is optionally SLC6A19; wherein the disease is biotinidase deficiency and the defective gene is optionally BTD; wherein the disease is ornithine carbamoyltransferase deficiency and the defective gene is optionally OTC; wherein the disease is carbamoyl-phosphate synthase I deficiency disease and the defective gene is optionally CPS1; wherein the disease is citrullinemia and the defective gene is optionally ASS or SLC25A13; wherein the disease is hyperargininemia and the defective gene is optionally ARG1; wherein the disease is hyperhomocysteinemia and the defective gene is optionally MTHFR; wherein the disease is hypermethioninemia and the defective gene is optionally MAT1A, GNMT, or AHCY; wherein the disease is hyperlysinemias and the defective gene is optionally AASS; wherein the disease is nonketotic hyperglycinemia and the defective gene is optionally GLDC, AMT, or GCSH; wherein the disease is Propionic acidemia and the defective gene is optionally PCCA or PCCB; wherein the disease is hyperprolinemia and the defective gene is optionally ALDH4A1 or PRODH; wherein the disease is cystinuria and the defective gene is optionally SLC3A1 or SLC7A9; wherein the disease is dicarboxylic aminoaciduria and the defective gene is optionally SLC1A1; wherein the disease is glutaric acidemia type 2 and the defective gene is optionally ETFA, ETFB, or ETFDH; wherein the disease is isovaleric acidemia and the defective gene is optionally IVD; or wherein the disease is 2-hydroxyglutaric aciduria and the defective gene is optionally L2HGDH or D2HGDH.

In various embodiments, the metabolic disorder is a disorder of the urea cycle wherein the disease is N-acetylglutamate synthase deficiency and the defective gene is optionally NAGS; wherein the disease is argininosuccinic aciduria and the defective gene is optionally ASL; or wherein the disease is argininemia and the defective gene is optionally ARG1.

In various embodiments, the metabolic disorder is a disorder of fatty acid metabolism wherein the disease is very long-chain acyl-coenzyme A dehydrogenase deficiency and the defective gene is optionally ACADVL; wherein the disease is long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency and the defective gene is

optionally HADHA; wherein the disease is medium-chain acyl-coenzyme A dehydrogenase deficiency and the defective gene is optionally ACADM; wherein the disease is short-chain acyl-coenzyme A dehydrogenase deficiency and the defective gene is optionally ACADS; wherein the disease is 3-hydroxyacyl-coenzyme A dehydrogenase deficiency and the defective gene is optionally HADH; wherein the disease is 2,4 dienoyl-CoA reductase deficiency and the defective gene is optionally NADK2; wherein the disease is 3-hydroxy-3-methylglutaryl-CoA lyase deficiency and the defective gene is optionally HMGCL; wherein the disease is malonyl-CoA decarboxylase deficiency and the defective gene is optionally MLYCD; wherein the disease is systemic primary carnitine deficiency and the defective gene is optionally SLC22A5; wherein the disease is carnitine-acylcarnitine translocase deficiency and the defective gene is optionally SLC25A20; wherein the disease is carnitine palmitoyltransferase I deficiency and the defective gene is optionally CPT1A; wherein the disease is carnitine palmitoyltransferase II deficiency and the defective gene is optionally CPT2; wherein the disease is lysosomal acid lipase deficiency and the defective gene is optionally LIPA; or wherein the disease is Gaucher's disease and the defective gene is optionally GBA.

In various embodiments, the metabolic disorder is a disorder of porphyrin metabolism wherein the disease is acute intermittent porphyria and the defective gene is optionally HMBS; wherein the disease is Gunther disease and the defective gene is optionally UROS; wherein the disease is porphyria cutanea tarda and the defective gene is optionally UROD; wherein the disease is hepatoerythropoietic porphyria and the defective gene is optionally UROD; wherein the disease is hereditary coproporphyria and the defective gene is optionally CPOX; wherein the disease is variegate porphyria and the defective gene is optionally PPOX; wherein the disease is erythropoietic protoporphyria and the defective gene is optionally FECH; or wherein the disease is aminolevulinic acid dehydratase deficiency porphyria and the defective gene is optionally ALAD.

In various embodiments, the metabolic disorder is a disorder of lysosomal storage wherein the disease is Farber disease and the defective gene is optionally ASAH1; wherein the disease is Krabbe disease and the defective gene is optionally GALC; wherein the disease is galactosialidosis and the defective gene is optionally CTSA; wherein the disease is fabry disease and the defective gene is optionally GLA; wherein the disease is Schindler disease and the defective gene is optionally NAGA; wherein the disease is GM1 gangliosidosis and the defective gene is optionally GLB1; wherein the disease is Tay–Sachs disease and the defective gene is optionally HEXA; wherein the disease is Sandhoff disease and the defective gene is optionally HEXB; wherein the disease is GM2-gangliosidosis, AB variant and the defective gene is optionally GM2A; wherein the disease is Niemann–Pick disease and the defective gene is optionally SMPD1, NPC1, or NPC2; wherein the disease is metachromatic leukodystrophy and the defective gene is optionally ARSA or PSAP; wherein the disease is multiple sulfatase deficiency and the defective gene is optionally SUMF1; wherein the disease is Hurler syndrome and the defective gene is optionally IDUA; wherein the disease is Hunter syndrome and the defective gene is optionally IDS; wherein the disease is Sanfilippo syndrome and the defective gene is optionally SGSH, NAGLU, HGSNAT, or GNS; wherein the disease is Morquio syndrome and the defective gene is optionally GALNS or GLB1; wherein the disease is Maroteaux–Lamy syndrome and the defective gene is optionally ARSB; wherein the disease is Sly

syndrome and the defective gene is optionally GUSB; wherein the disease is sialidosis and the defective gene is optionally NEU1, NEU2, NEU3, or NEU4; wherein the disease is I-cell disease and the defective gene is optionally GNPTAB or GNPTG; wherein the disease is mucolipidosis type IV and the defective gene is optionally MCOLN1; wherein the disease is infantile neuronal ceroid lipofuscinosis and the defective gene is optionally PPT1 or PPT2; wherein the disease is Jansky–Bielschowsky disease and the defective gene is optionally TPP1; wherein the disease is Batten disease and the defective gene is optionally CLN1, CLN2, CLN3, CLN5, CLN6, MFSD8, CLN8, or CTSD; wherein the disease is Kufs disease, Type A and the defective gene is optionally CLN6 or PPT1; wherein the disease is Kufs disease, Type B and the defective gene is optionally DNAJC5 or CTSF; wherein the disease is alpha-mannosidosis and the defective gene is optionally MAN2B1, MAN2B2, or MAN2C1; wherein the disease is beta-mannosidosis and the defective gene is optionally MANBA; wherein the disease is fucosidosis and the defective gene is optionally FUCA1; wherein the disease is cystinosis and the defective gene is optionally CTNS; wherein the disease is pycnodysostosis and the defective gene is optionally CTSK; wherein the disease is Salla disease and the defective gene is optionally SLC17A5; wherein the disease is Infantile free sialic acid storage disease and the defective gene is optionally SLC17A5; or wherein the disease is Danon disease and the defective gene is optionally LAMP2.

In various embodiments, the metabolic disorder is a disorder of peroxisome biogenesis wherein the disease is Zellweger syndrome and the defective gene is optionally PEX1, PEX2, PEX3, PEX5, PEX6, PEX12, PEX14, or PEX26; wherein the disease is Infantile Refsum disease and the defective gene is optionally PEX1, PEX2, or PEX26; wherein the disease is neonatal adrenoleukodystrophy and the defective gene is optionally PEX5, PEX1, PEX10, PEX13, or PEX26; wherein the disease is RCDP Type 1 and the defective gene is optionally PEX7; wherein the disease is pipecolic acidemia and the defective gene is optionally PAHX; wherein the disease is acatalasia and the defective gene is optionally CAT; wherein the disease is hyperoxaluria type 1 and the defective gene is optionally AGXT; wherein the disease is Acyl-CoA oxidase deficiency and the defective gene is optionally ACOX1; wherein the disease is D-bifunctional protein deficiency and the defective gene is optionally HSD17B4; wherein the disease is dihydroxyacetonephosphate acyltransferase deficiency and the defective gene is optionally GNPAT; wherein the disease is X-linked adrenoleukodystrophy and the defective gene is optionally ABCD1; wherein the disease is α-methylacyl-CoA racemase deficiency and the defective gene is optionally AMACR; wherein the disease is RCDP Type 2 and the defective gene is optionally DHAPAT; wherein the disease is RCDP Type 3 and the defective gene is optionally AGPS; wherein the disease is adult refsum disease-1 and the defective gene is optionally PHYH; or wherein the disease is mulibrey nanism and the defective gene is optionally TRIM37.

In various embodiments, the metabolic disorder is a disorder of purine or pyrimidine metabolism wherein the disease is Lesch–Nyhan syndrome and the defective gene is optionally HPRT; wherein the disease is adenine phosphoribosyltransferase deficiency and the defective gene is optionally APRT; wherein the disease is adenosine deaminase deficiency and the defective gene is optionally ADA; wherein the disease is Adenosine monophosphate deaminase deficiency type 1 and the defective gene is optionally AMPD1; wherein the disease

is adenylosuccinate lyase deficiency and the defective gene is optionally ADSL; wherein the disease is dihydropyrimidine dehydrogenase deficiency and the defective gene is optionally DPYD; wherein the disease is Miller syndrome and the defective gene is optionally DHODH; wherein the disease is orotic aciduria and the defective gene is optionally UMPS; wherein the disease is purine nucleoside phosphorylase deficiency and the defective gene is optionally PNP; or wherein the disease is xanthinuria and the defective gene is optionally XDH, MOCS1, or MOCS2, GEPH.

In some aspects, the present invention relates to a method for modulating transthyretin (TTR). The method comprising a step of administering an effective amount of a synthetic RNA encoding TTR to a subject, wherein the synthetic RNA comprises one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In various embodiments, the modulating results in an increase in the quantity of TTR in the subject.

In various embodiments, the modulating results in a decrease in the quantity of TTR in the subject.

In various embodiments, the modulating results in treatment of one or more of an amyloid disease, senile systemic amyloidosis (SSA), familial amyloid polyneuropathy (FAP), and familial amyloid cardiomyopathy (FAC).

In various embodiments, the non-canonical nucleotides have one or more substitutions at positions selected from the 2C, 4C, and 5C positions for a pyrimidine, or selected from the 6C, 7N and 8C positions for a purine.

In various embodiments, the non-canonical nucleotides comprise one or more of 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine, pseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine, optionally at an amount of at least 50%, or at least 60%, or at least 70%, or at least 80%, or at least 90%, or 100% of the non-canonical nucleotides.

In various embodiments, the at least about 50% of cytidine residues are non-canonical nucleotides, and which are selected from 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, and 5-methoxycytidine.

In various embodiments, the at least about 75% or at least about 90% of cytidine residues are non-canonical nucleotides, and the non-canonical nucleotides are selected from 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, and 5-methoxycytidine.

In various embodiments, the at least about 20% of uridine, or at least about 40%, or at least about 50%, or at least about 75%, or at about least 90% of uridine residues are non-canonical nucleotides, and the non-canonical are selected from pseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine.

In various embodiments, the at least about 40%, or at least about 50%, or at least about 75%, or at about least 90% of uridine residues are non-canonical nucleotides, and the non-canonical nucleotides are selected from

pseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine.

In various embodiments, the at least about 10% of guanine residues are non-canonical nucleotides, and the non-canonical nucleotide is optionally 7-deazaguanosine.

In various embodiments, the synthetic RNA contains no more than about 50% 7-deazaguanosine in place of guanosine residues.

In various embodiments, the synthetic RNA does not contain non-canonical nucleotides in place of adenosine residues.

In various embodiments, the synthetic RNA comprises a 5' cap structure.

In various embodiments, the synthetic RNA 5'-UTR comprises a Kozak consensus sequence.

In various embodiments, the synthetic RNA 5'-UTR comprises a sequence that increases RNA stability in vivo, and the 5'-UTR may comprise an alpha-globin or beta-globin 5'-UTR.

In various embodiments, the synthetic RNA 3'-UTR comprises a sequence that increases RNA stability in vivo, and the 3'-UTR may comprise an alpha-globin or beta-globin 3'-UTR.

In various embodiments, the synthetic RNA comprises a 3' poly(A) tail.

In various embodiments, the synthetic RNA 3' poly(A) tail is from about 20 nucleotides to about 250 nucleotides in length.

In various embodiments, the synthetic RNA is from about 200 nucleotides to about 5000 nucleotides in length.

In various embodiments, the synthetic RNA is from about 500 to about 2000 nucleotides in length, or about 500 to about 1500 nucleotides in length, or about 500 to about 1000 nucleotides in length.

In various embodiments, the synthetic RNA is prepared by in vitro transcription.

In various embodiments, the effective amount of the synthetic RNA is administered as one or more injections containing about 10 ng to about 5000 ng of RNA.

In various embodiments, the effective amount of the synthetic RNA is administered as one or more injections each containing no more than about 10 ng, or no more than about 20 ng, or no more than about 50 ng, or no more than about 100 ng, or no more than about 200 ng, or no more than about 300 ng, or no more than about 400 ng, or no more than about 500 ng, or no more than about 600 ng, or no more than about 700 ng, or no more than about 800 ng, or no more than about 900 ng, or no more than about 1000 ng, or no more than about 1100 ng, or no more than about 1200 ng, or no more than about 1300 ng, or no more than about 1400 ng, or no more than about 1500 ng, or no more than about 1600 ng, or no more than about 1700 ng, or no more than about

1800 ng, or no more than about 1900 ng, or no more than about 2000 ng, or no more than about 3000 ng, or no more than about 4000 ng, or no more than about 5000 ng.

In various embodiments, the effective amount of the synthetic RNA is administered as one or more injections each containing about 10 ng, or about 20 ng, or about 50 ng, or about 100 ng, or about 200 ng, or about 300 ng, or about 400 ng, or about 500 ng, or about 600 ng, or about 700 ng, or about 800 ng, or about 900 ng, or about 1000 ng, or about 1 100 ng, or about 1200 ng, or about 1300 ng, or about 1400 ng, or about 1500 ng, or about 1600 ng, or about 1700 ng, or about 1800 ng, or about 1900 ng, or about 2000 ng, or about 3000 ng, or about 4000 ng, or about 5000 ng.

In various embodiments, the effective amount of the synthetic RNA comprises one or more lipids to enhance uptake of RNA by cells.

In various embodiments, the effective amount of the synthetic RNA comprises a cationic liposome formulation and the lipids are optionally selected from **Table 1.**

In various embodiments, the subject is a human.

In various embodiments, the effective amount of the synthetic RNA is administered about weekly, for at least 2 weeks.

In various embodiments, the effective amount of the synthetic RNA is administered about every other week for at least one month.

In various embodiments, the effective amount of the synthetic RNA is administered monthly or about every other month.

In various embodiments, the effective amount of the synthetic RNA is administered for at least two months, or at least 4 months, or at least 6 months, or at least 9 months, or at least one year.

In some aspects, the present invention relates to a composition comprising an effective amount of the synthetic RNA used in any herein-disclosed aspect or embodiment.

In some aspects, the present invention relates to a pharmaceutical composition, comprising the composition of any herein-disclosed aspect or embodiment and a pharmaceutically acceptable excipient.

In one aspect, the present invention relates to an *in vivo* method to treat cancer in a subject comprising: administering to a tumor cell in the subject a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the synthetic mRNA comprises 5-

methoxyuridine, and causing a single-strand or double-strand break in the DNA of the tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell in the subject, resulting in the stimulation or enhancement of an immune response in the subject, thereby treating cancer in the subject.

In another aspect, the present invention relates to an *in vivo* method to treat cancer in a subject comprising: administering to the subject by intratumoral injection a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, and causing a single-strand or double-strand break in the DNA of a tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell in the subject, resulting in the stimulation or enhancement of an immune response in the subject; thereby treating cancer in the subject.

In yet a further aspect, the present invention relates to an *in vivo* method for treating cancer in a subject comprising: administering to a tumor cell in the subject a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, and causing a single-strand or double-strand break in the DNA of the tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell in the subject, resulting in the stimulation or enhancement of an immune response in the subject, thereby treating cancer in the subject.

In another aspect, the present invention relates to a method to treat cancer comprising: contacting a tumor cell with a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, and causing a single-strand or double-strand break in the DNA of the tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell, resulting in the stimulation or enhancement of an immune response, thereby treating cancer in the subject.

In one aspect, the present invention relates to the use of a non-viral, cell-free composition for the manufacture of a medicament for an *in vivo* method to treat cancer in a subject, the composition comprising: a synthetic messenger RNA (mRNA)

encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the synthetic mRNA comprises 5-methoxyuridine, wherein the non-viral, cell-free composition is capable of causing a single-strand or double-strand break in the DNA of the tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell in the subject, resulting in the stimulation or enhancement of an immune response in the subject, thereby treating cancer in the subject.

In some aspects, the present invention relates to the use of a composition or pharmaceutical composition of any herein-disclosed aspect or embodiment in the treatment of a disease or disorder described herein.

In some aspects, the present invention relates to the use of a composition or pharmaceutical composition of any herein-disclosed aspect or embodiment in the manufacture of a medicament for the treatment of a disease or disorder described herein.

In various aspects, the present invention is based on the surprising discovery of safe and effective doses and administration parameters for nucleic acid drugs in human subjects. In some aspects, there is provided a method for delivering a nucleic acid drug, comprising administering an effective dose of a nucleic acid drug to a human

subject in need thereof. In various embodiments, the nucleic acid drug comprises a RNA comprising one or more non-canonical nucleotides (a/k/a "modified RNA"). In other embodiments, the effective dose is an amount sufficient to substantially increase an amount of a protein encoded by the nucleic acid drug in the human subject and/or substantially avoid an immune reaction in a human subject, wherein the immune reaction is optionally mediated by the innate immune system.

In some aspects, there is provided a method for expressing a protein of interest in a population of cells in a mammalian subject, comprising administering a non-viral transfection composition comprising an effective dose of a RNA encoding the protein of interest to said cells, where the transfection composition is administered in an amount that allows for expression of said protein in said cells for at least about six hours to about five days without substantial cellular toxicity. In some embodiments, the RNA contains one or more non-canonical nucleotides that avoid substantial cellular toxicity.

In some embodiments, the effective dose is about 100 ng to about 5000 ng (*e.g.,* about, or no more than about, 100 ng, or 200 ng, or 300 ng, or 400 ng, or 500 ng, or 600 ng, or 700 ng, or 800 ng, or 900 ng, or 1000 ng, or 1100 ng, or 1200 ng, or 1300 ng, or 1400 ng, or 1500 ng, or 1600 ng, or 1700 ng, or 1800 ng, or 1900 ng, or 2000 ng, or 3000 ng, or 4000 ng, or 5000 ng). In other embodiments, the effective dose is less than about 100 ng. In certain embodiments, the effective dose is about 10 ng to about 100 ng (*e.g.*, about, or no more than about, 10 ng, or 20 ng, or 30 ng, or 40 ng, or 50 ng, or 60 ng, or 70 ng, or 80 ng, or 90 ng, or 100 ng).

In some embodiments, the effective dose is about 1.4 ng/kg to about 30 ng/kg (*e.g.,* about, or no more than about, 1.4 ng/kg, or 2.5 ng/kg, or 5 ng/kg, or 10 ng/kg, or 15 ng/kg, or 20 ng/kg, or 25 ng/kg, or 30 ng/kg. In other embodiments, the effective dose is less than about 1.5 ng/kg. In certain embodiments, the effective dose is about 0.14 ng/kg to about 1.4 ng/kg (*e.g.*, about, or no more than about, 0.14 ng/kg, or 0.25 ng/kg, or 0.5 ng/kg, or 0.75 ng/kg, or 1 ng/kg, or 1.25 ng/kg, or 1.4 ng/kg).

In some embodiments, the effective dose is about 350 ng/cm^2 to about 7000 ng/cm^2 (*e.g.*, about, or no more than about, 350 ng/cm^2, or 500 ng/cm^2, or 750 ng/cm^2, or 1000 ng/cm^2, or 2000 ng/cm^2, or 3000 ng/cm^2, or 4000 ng/cm^2, or 5000 ng/cm^2, or 6000 ng/cm^2, or 7000 ng/cm^2). In other embodiments, the effective dose is less than about 350 ng/cm^2. In certain embodiments, the effective dose is about 35 ng/cm^2 to about 350 ng/cm^2 (*e.g.*, about, or no more than about, 35 ng/cm^2, or 50 ng/cm^2, or 75 ng/cm^2, or 100 ng/cm^2, or 150 ng/cm^2, or 200 ng/cm^2, or 250 ng/cm^2, or 300 ng/cm^2, or 350 ng/cm^2.

In some embodiments, the effective dose is about 0.28 picomoles to about 5.7 picomoles (*e.g.*, about, or no more than about, 0.28 picomoles, or 0.5 picomoles, or 0.75 picomoles, or 1 picomole, or 2 picomoles, or 3 picomoles, or 4 picomoles, or 5 picomoles, or 5.7 picomoles). In other embodiments, the effective dose is less than about 0.28 picomoles. In certain embodiments, the effective dose is about 0.028 picomoles to about 0.28 picomoles (*e.g.*, about, or no more than about, 0.028 picomoles, or 0.05 picomoles, or 0.075 picomoles, or 0.1 picomoles, or 0.15 picomoles, or 0.2 picomoles, or 0.25 picomoles, or 0.28 picomoles).

In some embodiments, the effective dose is about 0.004 picomoles/kg to about 0.082 picomoles/kg (*e.g.*, about, or no more than about, 0.004 picomoles/kg, or 0.01 picomoles/kg, or 0.02 picomoles/kg, or 0.03 picomoles/kg, or 0.04 picomoles/kg, or 0.05 picomoles/kg, or 0.06 picomoles/kg, or 0.07 picomoles/kg, or 0.08 picomoles/kg, or 0.082 picomoles/kg). In other embodiments, the effective dose is less than about 0.004 picomoles/kg. In certain embodiments, the effective dose is about 0.0004 picomoles/kg to about 0.004 picomoles/kg (*e.g.*, about, or no more than about, 0.0004 picomoles/kg, or 0.001 picomoles/kg, or 0.002 picomoles/kg, or 0.003 picomoles/kg, or 0.004 picomoles/kg).

In some embodiments, the effective dose is about 1 picomole/cm^2 to about 20 picomoles/cm^2 (*e.g.*, about, or no more than about, 1 picomole/cm^2, or 2 picomoles/cm^2, or 3 picomoles/cm^2, or 4 picomoles/cm^2, or 5 picomoles/cm^2, or 6 picomoles/cm^2, or 7 picomoles/cm^2, or 8 picomoles/cm^2, or 9 picomoles/cm^2, or 10 picomoles/cm^2, or 12 picomoles/cm^2, or 14 picomoles/cm^2, or 16 picomoles/cm^2, or 18 picomoles/cm^2, or 20 picomoles/cm^2). In other embodiments, the effective dose is less than about 1 picomole/cm^2. In certain embodiments, the effective dose is about 0.1 picomoles/cm^2 to about 1 picomole/cm^2 (*e.g.*, about, or no more than about, 0.1 picomoles/cm^2, or 0.2 picomoles/cm^2, or 0.3 picomoles/cm^2, or 0.4 picomoles/cm^2, or 0.5 picomoles/cm^2, or 0.6 picomoles/cm^2, or 0.7 picomoles/cm^2, or 0.8 picomoles/cm^2, or 0.9 picomoles/cm^2, or 1 picomole/cm^2).

In various embodiments, the nucleic acid drug is administered in a pharmaceutically acceptable formulation, including a formulation suitable for one or more of injection (*e.g.* subcutaneous injection, intradermal injection (including to the dermis or epidermis), subdermal injection, intramuscular injection, intraocular injection, intravitreal injection, intra-articular injection, intracardiac injection, intravenous injection, epidural injection, intrathecal injection, intraportal injection, intratumoral injection) and topical administration and/or for administration to the integumentary system (*e.g.* to one or more of the epidermis (optionally selected from the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum germinativum), basement membrane, dermis (optionally selected from the papillary region and the reticular region), subcutis, and conjunctiva) and/or for administration to the eye (*e.g.*, to one or more of the cornea, sclera, iris, lens, corneal limbus, optic nerve, choroid, ciliary body, anterior segment, anterior chamber, and retina).

In various embodiments, the nucleic acid drug is formulated with one or more lipids to enhance uptake of the nucleic acid drug by cells, the lipids optionally selected from **Table 1**. In other embodiments, the nucleic acid drug is formulated with one or more nanoparticles, optionally lipid or polymeric nanoparticles, to enhance uptake of the nucleic acid drug by cells, to enhance duration of protein expression, or to otherwise enhance the safety and/or efficacy of the nucleic acid drug.

In various embodiments, the nucleic acid drug is administered locally, optionally by one or more of subcutaneous injection, intradermal injection, subdermal injection and intramuscular injection, and the effective dose is administered to a surface area of about 4 mm^2 to about 1000 mm^2 (*e.g.* about, or no more than about, 4 mm^2, or

5 mm^2, or 10 mm^2, or 25 mm^2, or 50 mm^2, or 75 mm^2, or 100 mm^2, or 125 mm^2, or 150 mm^2, or 200 mm^2, or 500 mm^2, or 1000 mm^2).

In various embodiments, the nucleic acid drug is administered in a treatment regimen, optionally with an additional agent or adjuvant therapy described herein, and the administration is about weekly to about once every 24 weeks (*e.g.* about, or not more than about, weekly, or once every 2 weeks, or once every 3 weeks, or once every 4 weeks, or once every 5 weeks, or once every 6 weeks, or once every 7 weeks, or once every 8 weeks, or once every 9 weeks, or once every 9 weeks, or once every 9 weeks, or once every 9 weeks, or once every 10 weeks, or once every 11 weeks, or once every 12 weeks, or once every 13 weeks, or once every 14 weeks, or once every 15 weeks, or once every 20 weeks, or once every 24 weeks). In other embodiments, the nucleic acid drug is administered in a treatment regimen, optionally with an additional agent or adjuvant therapy described herein, and the administration is about daily to about weekly (*e.g.*, about, or not more than about, daily, or once every 2 days, or once every 3 days, or once every 4 days, or once every 5 days, or once every 6 days, or weekly).

In various embodiments the nucleic acid drug comprises RNA comprising one or more non-canonical nucleotides, optionally having one or more substitutions at the 2C and/or 4C and/or 5C positions for a pyrimidine or the 6C and/or 7N and/or 8C positions for a purine. In various embodiments, the non-canonical nucleotide is one or more of the non-canonical nucleotides described herein, including, for example, 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine, pseudouridine, 5-hydroxyuridine, 5-hydroxypseudouridine, 5-methyluridine, 5-methylpseudouridine, 5-hydroxymethyluridine, 5-hydroxymethylpseudouridine, 5-carboxyuridine, 5-carboxypseudouridine, 5-formyluridine, 5-formylpseudouridine, 5-methoxyuridine, and 5-methoxypseudouridine. Further, the RNA comprising one or more non-canonical nucleotides may have one or more of a 5'-UTR comprising a Kozak consensus sequence, a 5'-UTR or 3'-UTR comprising a sequence that increases RNA stability *in vivo* (*e.g.* an alpha-globin or beta-globin 5'-UTR or an alpha-globin or beta-globin 3'-UTR), and a 3' poly(A) tail from about 20 nucleotides to about 250 nucleotides in length (*e.g.* about 20, or about 30, or about 40, or about 50, or about 60, or about 70, or about 80, or about 90, or about 100, or about 110, or about 120, or about 130, or about 140, or about 150, or about 160, or about 170, or about 180, or about 190, or about 200, or about 210, or about 220, or about 230, or about 240, or about 250 nucleotides in length).

Further, some aspects of the methods described herein find use in various medical treatments, including, by way of illustration, treating a disease, disorder and/or condition of the integumentary system or altering, modifying and/or changing the integumentary system (*e.g.* cosmetically).

Also contemplated are kits suitable for use in human therapy, comprising the nucleic acid drug described herein in a unit dosage form of about 10 ng to about 5000 ng (*e.g.* about, or no more than about, 10 ng, or 20 ng, or 50 ng, or 100 ng, or 200 ng, or 300 ng, or 400 ng, or 500 ng, or 600 ng, or 700 ng, or 800 ng, or 900 ng, or 1000 ng,

or 1100 ng, or 1200 ng, or 1300 ng, or 1400 ng, or 1500 ng, or 1600 ng, or 1700 ng, or 1800 ng, or 1900 ng, or 2000 ng, or 3000 ng, or 4000 ng, or 5000 ng) and an injection needle.

Further, in some aspects, the present invention provides a pharmaceutical formulation comprising the nucleic acid drug described herein and one or more of the vehicles (a/k/a "transfection reagents", *e.g.*, lipids) described herein, the formulation optionally being suitable for one or more of subcutaneous injection, intradermal injection, subdermal injection, intramuscular injection, intraocular injection, intravitreal injection, intra-articular injection, intracardiac injection, intravenous injection, epidural injection, intrathecal injection, intraportal injection, intratumoral injection, and topical administration. As used herein, the term "injection" can refer to injection, for example, with a syringe, and to other methods of administering liquids, for example, infusion, perfusion, administration using a pen injector, cartridge system needle-array or patch and/or administration by a catheter system.

In some aspects, nucleic acid delivery patches are provided. In one aspect, devices for delivering nucleic acids using electric fields are provided. Other aspects pertain to methods and compositions for delivery of nucleic acids to the skin. Still further aspects pertain to methods and compositions for expression of proteins in the skin.

In one aspect, the invention provides methods and compositions for treating diseases and conditions in humans, including, but not limited to, prophylactic treatments, treatments for rare diseases, including, but not limited to, dermatologic rare diseases, and treatments for use in medical dermatology and aesthetic medicine. In another aspect, the invention provides cosmetics comprising nucleic acids. Still further aspects relate to methods and compositions for altering pigmentation, for example, for the treatment of pigmentation disorders. Still further aspects relate to methods and compositions for enhancing healing, including, but not limited to, healing in response to a wound or surgery. The compositions of the present invention may alter, modify and/or change the appearance of a member of the integumentary system of a subject such as, but not limited, to skin, hair and nails. Such alteration, modification and/or change may be in the context of treatment methods and/or therapeutic uses as described herein including, by way of non-limiting example, dermatological treatments and cosmetics procedures.

Further, in various embodiments, the present invention relates to the targeting of various therapeutic proteins that are not limited to dermatological applications. For example, in various embodiments, the present compositions and methods find use in methods of treatment that are mediated by the increased expression of, for example, various soluble proteins as illustrated herein. In various embodiments, the nucleic acid drug encodes and/or increases the expression of one or more of a circulating protein, an extracellular matrix protein, an engineered protein, a gene-editing protein, a protein or peptide hormone, an enzyme, erythropoietin, darbepoetin alfa, NOVEPOETIN, elastin, collagen, an antibody or antibody fragment (*e.g.*, a neutralizing antibody or antibody fragment), an intracellular protein, telomerase reverse transcriptase, a membrane protein, a fusion protein, a receptor, a ligand binding domain, a protein inhibitor, or a biologically active fragment, analogue or variant thereof. In other embodiments, administration of the nucleic acid drug results in one or more of an increase in

hematocrit, an increase in tissue elasticity, an increase in tissue strength, and increase in skin hydration and/or water retention, hair growth, fat reduction, an insertion, deletion or mutation in DNA, conversion of a prodrug to an active drug, a decrease in tumor size and/or number, a decrease in plaque size and/or number, an increase in vascularization, a decrease in vascularization, an increase in visual acuity, a decrease in pain, an increase in cardiac output (*e.g.*, ejection fraction and stroke volume), a decrease in abnormal heart rhythm, a decrease in fibrosis, a decrease in one or more adverse neurological symptoms, conditions, or disorders (*e.g.*, depression, dysregulation of appetite, polyphagia, anorexia, dementia, headache, fatigue, numbness, tremors, and dizziness), a decrease in erectile dysfunction, an increase in vitality, an increase in pulmonary function, an increase in kidney function, an increase in liver function, an increase in insulin sensitivity, a decrease in insulin sensitivity, a decrease in inflammation, an increase in tear production, an improvement in hearing, an increase in auditory perception, a decrease in tinnitus, a reduction in perspiration, partial or total clearance of an infection, an increase in fertility, a decrease in fertility, inhibition or neutralization of a protein, recruitment or stimulation of one or more components of the immune system, lengthening of telomeres, inhibition of cellular senescence, an increase in replicative potential, reprogramming, proliferation, differentiation, and an increase in differentiation potential.

In some aspects, RNA molecules with low toxicity and high translation efficiency are provided. In one aspect, a cell-culture medium for high-efficiency *in vivo* transfection, reprogramming, and gene editing of cells is provided. Other aspects pertain to methods for producing RNA molecules encoding reprogramming proteins. Still further aspects pertain to methods for producing RNA molecules encoding gene-editing proteins.

In one aspect, the invention provides high-efficiency gene-editing proteins comprising engineered nuclease cleavage domains. In another aspect, the invention provides high-fidelity gene-editing proteins comprising engineered nuclease cleavage domains. Other aspects relate to high-efficiency gene-editing proteins comprising engineered DNA-binding domains. Still further aspects pertain to high-fidelity gene-editing proteins comprising engineered DNA-binding domains. Still further aspects relate to gene-editing proteins comprising engineered repeat sequences. Still further aspects relate to gene-editing proteins comprising DNA-modification domains. Some aspects relate to methods for altering the DNA sequence of a cell by transfecting the cell with or inducing the cell to express a gene-editing protein. Other aspects relate to methods for altering the DNA sequence of a cell that is present in an *in vitro* culture. Still further aspects relate to methods for altering the DNA sequence of a cell that is present *in vivo*.

In some aspects, the invention provides methods for treating cancer comprising administering to a patient a therapeutically effective amount of a gene-editing protein or a nucleic-acid encoding a gene-editing protein. In one aspect, the gene-editing protein is capable of altering the DNA sequence of a cancer associated gene. In another aspect, the cancer-associated gene is the BIRC5 gene. In other aspects, the gene-editing protein is capable of altering the DNA sequence of a cell to cause the cell to express an antigen or antigen receptor. In one aspect, the antigen is a tumor antigen. In another aspect, the antigen receptor binds to a tumor antigen. In yet another aspect, the antigen receptor is a chimeric antigen receptor. Still other aspects relate to therapeutics

comprising nucleic acids and/or cells and methods of using therapeutics comprising nucleic acids and/or cells for the treatment of, for example, type 1 diabetes, heart disease, including ischemic and dilated cardiomyopathy, macular degeneration, Parkinson's disease, cystic fibrosis, sickle-cell anemia, thalassemia, Fanconi anemia, severe combined immunodeficiency, hereditary sensory neuropathy, xeroderma pigmentosum, Huntington's disease, muscular dystrophy, amyotrophic lateral sclerosis, Alzheimer's disease, cancer, and infectious diseases including hepatitis and HIV/AIDS. In some aspects, the nucleic acids comprise RNA. In other aspects, the RNA comprises one or more non-canonical nucleotides. In still other aspects, the nucleic acids are delivered to cells using a virus. In some aspects, the virus is a replication-competent virus. In other aspects, the virus is a replication-incompetent virus.

The details of the invention are set forth in the accompanying description below. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, illustrative methods and materials are now described. Other features, objects, and advantages of the invention will be apparent from the description and from the claims. In the specification and the appended claims, the singular forms also include the plural unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs.

Any aspect or embodiment disclosed herein can be combined with any other aspect or embodiment as disclosed herein.

DETAILED DESCRIPTION OF THE FIGURES

FIG. 1 depicts primary adult human dermal fibroblasts transfected with RNA encoding green fluorescent protein ("GFP") and comprising the indicated nucleotides.

FIG. 2 depicts the result of a gene-expression analysis of the primary adult human dermal fibroblasts of **FIG. 1** using a one-step real-time RT-PCR and primers designed to amplify human interferon beta mRNA. Data were normalized to the untransfected sample ("Neg."). GAPDH was used as a loading control.

FIG. 3 depicts the results of a gene-expression analysis of cells transfected with RNA comprising the indicated nucleotides, conducted as in **FIG. 2**. Data were normalized to the untransfected sample ("Neg."). GAPDH was used as a loading control.

FIG. 4 depicts the results of a gene-expression analysis of cells transfected with RNA comprising the indicated nucleotides, conducted as in **FIG. 2**, and using primers designed to amplify the indicated transcripts. Data were normalized to the untransfected sample ("Neg."). GAPDH was used as a loading control.

FIG. 5 depicts the results of a gene-expression analysis of primary human epidermal keratinocytes transfected with RNA encoding NOVEPOETIN, and comprising the indicated nucleotides, conducted as in **FIG. 2**. Data were normalized to the untransfected sample ("Neg."). GAPDH was used as a loading control.

FIG. 6 depicts intradermal injection of a solution comprising RNA encoding GFP into the ventral forearm of a healthy, 33 year-old, 70 kg, male human subject.

FIG. 7 depicts a region of the ventral forearm of the subject shown in **FIG. 6** after treatment with RNA comprising 5-methoxyuridine and encoding GFP (injection sites 1-3) or COL7 (injection site 4). The image was taken immediately following the final injection.

FIG. 8 depicts the region of **FIG. 7**, 24 hours after injection.

FIG. 9 depicts the results of fluorescent imaging of the region of **FIG. 7**, using the indicated fluorescent channels. The dose at each injection site is also indicated. Images were taken 24 hours after injection.

FIG. 10 depicts the results of fluorescent imaging of the region of **FIG. 7**, using the FITC fluorescent channel. The dose at each injection site is indicated. Images were taken 48 hours after injection.

FIG. 11 depicts the results of quantitative fluorescent imaging of the region of **FIG. 7**, using the FITC fluorescent channel. The horizontal axis indicates time after injection.

FIG. 12 depicts the results of fluorescent imaging of an independent experiment in which a region of the ventral forearm of as the subject shown in **FIG. 6** treated with RNA comprising 5-methoxyuridine and encoding GFP. The image was taken 24 hours after injection.

FIG. 13 depicts the results of an ELISA designed to detect darbepoetin alfa in culture media of primary human epidermal keratinocytes transfected with RNA comprising the indicated nucleotides and encoding NOVEPOETIN.

FIG. 14 depicts the results of an ELISA designed to detect darbepoetin alfa in culture media of primary human epidermal keratinocytes transfected with RNA comprising the indicated nucleotides and encoding NOVEPOETIN.

FIG. 15 depicts the results of an ELISA designed to detect darbepoetin alfa in culture media of primary human epidermal keratinocytes transfected with RNA comprising the indicated nucleotides and encoding NOVEPOETIN.

FIG. 16 depicts primary human dermal fibroblasts transfected with RNA comprising 5-methoxyuridine and encoding hTERT. Cells were fixed and stained using an antibody targeting hTERT 24 hours after transfection.

FIG. 17 depicts primary adult human dermal fibroblasts transfected with RNA encoding green fluorescent protein ("GFP"), prepared and stored as indicated.

FIG. 18 depicts single administration of NOVECRIT induced a rapid increase and sustained level of NOVEPOIETIN in serum. The Y axis shows concentration of NOVEPOIETIN protein (mU/mL).

FIG. 19 depicts a single administration of NOVECRIT stimulated erythropoiesis, yielding elevated hematocrit for at least 14 days. The left panel shows % hematocrit on the Y axis, while the right panel shows % reticulocytes.

FIG. 20 depicts a table summarizing TNFα, IL-6, and IFNα cytokine levels in plasma samples collected from a maximum tolerated dose of NOVECRIT in male Sprague Dawley rats study of Example 35.

FIG. 21 depicts a SURVEYOR assay using the DNA of primary adult human dermal fibroblasts transfected with RNA TALENs targeting the sequence TGAGCAGAAGTGGCTCAGTG (SEQ ID NO: 467) and TGGCTGTACAGCTACACCCC (SEQ ID NO: 468), located within the COL7A1 gene. The bands present in the +RNA lane indicate editing of a region of the gene that is frequently involved in dystrophic epidermolysis bullosa.

FIG. 22 depicts a SURVEYOR assay using the DNA of primary adult human dermal fibroblasts transfected with RNA TALENs targeting the sequence TTCCACTCCTGCAGGGCCCC (SEQ ID NO: 469) and TCGCCCTTCAGCCCGCGTTC (SEQ ID NO:470), located within the COL7A1 gene. The bands present in the +RNA lane indicate editing of a region of the gene that is frequently involved in dystrophic epidermolysis bullosa.

FIG. 23 shows the immunogenicity of various synthetic RNA constructs in the context of a gene-editing (*i.e.* unmodified nucleotides "A,G,U,C"; pseudouridine only "psU"; 5-methylcytidine only "5mC"; both pseudouridine and 5-methylcytidine "psU+5mC"; and a negative control "neg").

FIG. 24 shows the gene-editing activity in cells transfected with various synthetic RNA constructs (*i.e.* unmodified nucleotides "A,G,U,C"; psuedouridine only "psU"; 5-methylcytidine only "5mC"; both psuedouridine and 5-methylcytidine "psU+5mC"; and a negative control "neg").

FIG. 25 depicts gene editing of the COL7A1 gene in primary human epidermal keratinocytes transfected with RNA encoding TALENs and a single-stranded DNA repair template ("RT") of the indicated length. The presence of bands at the locations shown by asterisks ("*") indicates successful gene editing.

FIG. 26 depicts gene editing of the COL7A1 gene in primary human epidermal keratinocytes transfected with RNA encoding TALENs and an 80 nt single-stranded DNA repair template ("RT") at the indicated ratios of RNA to repair template. The presence of bands at the locations shown by asterisks ("*") indicates successful gene editing.

FIG. 27 depicts gene correction of the COL7A1 gene in primary human epidermal keratinocytes transfected with RNA encoding TALENs and a single-stranded DNA repair template ("RT") of the indicated length. The presence of bands at the locations shown by asterisks ("*") indicates successful gene correction.

FIG. 28 depicts gene correction of the COL7A1 gene in primary human epidermal keratinocytes transfected with RNA encoding TALENs and an 80 nt single-stranded DNA repair template ("RT") at the indicated ratios of RNA to repair template. The presence of bands at the locations shown by asterisks ("*") indicates successful gene correction.

FIG. 29 depicts gene editing ("T7E1") and correction ("Digestion") of the COL7A1 gene in primary human epidermal keratinocytes transfected with RNA encoding TALENs and an 80 nt single-stranded DNA repair template ("RT"). The presence of bands at the locations shown by asterisks ("*") indicates successful gene editing ("T7E1") and correction ("Digestion").

FIG. 30 depicts the amount of BMP7 protein secreted by primary human dermal fibroblasts and primary human epidermal keratinocytes transfected with RNA encoding the indicated BMP7 variant, measured by ELISA. Asterisks ("*") indicate saturation of the ELISA assay.

FIG. 31 depicts the amount of parathyroid hormone secreted by primary human epidermal keratinocytes transfected with RNA encoding PTH, measured by ELISA.

FIG. 32 demonstrates that repeated administration of NOVECRIT stimulated erythropoiesis, yielding elevated hematocrit for at least 14 days. For each data set, the order of histograms from left to right is: Group 1, Group 2, Group 3, Group 4, and Group 5.

FIG. 33 provides an illustrative experimental design for studying the effects of RNAs encoding BMP7 variants for the prevention and treatment of diabetic nephropathy.

FIG. 34 depicts BMP7 protein levels in rats treated with RNAs encoding BMP7 variants as described in Example 42. Error bars indicate SEM (n=6).

FIG. 35 depicts the urine volume, urine albumin, and urine creatinine levels in rats treated with RNAs encoding BMP7 variants as described in Example 42. For each data set, the order of histograms from left to right is: urine volume, urine creatinine, and urine albumin.

FIG. 36 depicts the effect of RNAs encoding BMP7 variants in treating diabetic nephropathy as described in Example 42. For each data set, the order of histograms from left to right is: Group 6 – vehicle and Group 7 – FTB-2 (BMP7 variant A).

FIG. 37, panels A-I, depict the results of gene-expression analysis of human epidermal keratinocytes transfected with RNA encoding BDNF, BMP-2, BMP-6, IL-2, IL-6, IL-15, IL-22, LIF or FGF-21.

FIG. 38 depicts the results of gene-expression analysis of human epidermal keratinocytes transfected with RNA encoding IL-15 or IL-15 and IL-15RA.

FIG. 39 depicts the serum levels of FGF21, IL15, IL6, IL22, and Novepoietin following a single intradermal injection of various RNAs encoding these proteins as described in Example 45. Three rats were analyzed for each RNA tested.

FIG. 40 depicts the results of the wound-healing assay described in Example 46. Four scratch locations were measured for each well, and two wells were measured for each condition. Error bars indicate standard deviation.

FIG. 41 depicts gene editing of primary human epidermal keratinocytes, as described in Example 47.

FIG. 42 depicts gene correction of primary human epidermal keratinocytes, as described in Example 47.

FIG. 43 depicts gene editing of primary human epidermal keratinocytes, as described in Example 47.

FIG. 44 depicts IL10 production in COLO 205 human colorectal adenocarcinoma cells. COLO 205 cells were plated at a density of 20,000 cells / well in a 24 well plate in 0.5 mL RPMI1640 + 10% FBS per well. The next

day, cells were either (i) transfected with 0.4 µg RNA encoding GFP, as described in example (Example 3), (ii) transfected with 0.4 µg RNA encoding IL22, as described in example (Example 3), (iii) exposed to cell culture medium taken from human epidermal keratinocytes transfected with RNA encoding IL22, (iv) exposed to cell culture medium taken from untransfected human epidermal keratinocytes, (v) exposed to recombinant human IL22 (782-IL-010; R&D Systems). 48h later, IL10 levels in the culture medium were measured via ELISA (D1000B; R&D Systems). IL22 levels for sample (iii) were determined via ELISA (D2200; R&D Systems) prior to the experiment, and the same volumes of medium were used for condition (iv).

FIG. 45 depicts a BMP7 activity assay involving the measurement of alkaline phosphatase activity in ATDC 5 cells following transfection with RNA encoding BMP7 (variant A) or exposure to recombinant human BMP7. ATDC 5 cells were plated at a density of 20,000 cells/well in a 24 well plate in DMEM/F12 + 5% FBS. The next day, the cells were serum starved by changing the medium to DMEM/F12 + 2% FBS. The following day, the cells were either (i) transfected with RNA encoding BMP7 or (ii) exposed to recombinant human BMP7 (54-BP-010, R&D Systems). Three days later, intracellular alkaline phosphatase activity was measured (ab83369; Abcam).

FIG. 46 depicts the results of an experiment in which 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) were transfected with 2 µg RNA encoding the indicated gene-editing proteins (1 µg L and 1 µg R). DNA was harvested after 48h and analyzed for gene editing (A/B indicates RIBOSLICE_A L, RIBOSLICE_B R; RIBOSLICE A indicates repeat sequences comprising the sequence: GHGG, HG, GHGG, HG, etc.; RIBOSLICE B indicates repeat sequences comprising the sequence: HG, GHGG, HG, GHGG, etc.; L targets the sequence: TGCCTGGTCCCTGTCTCCCT (SEQ ID NO: 615); R targets the sequence: TGTCTTCTGGGCAGCATCTC (SEQ ID NO: 616); a target sequence is approximately 75 bp from A1AT [SERPINA1] start codon). “TAL” indicates a control TALEN directed to the target sequence.

FIG. 47 depicts the results of an experiment in which 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) were transfected with 2 µg RNA encoding the indicated gene-editing proteins (1 µg L and 1 µg R). DNA was harvested after 48h and analyzed for gene editing (A/B indicates RIBOSLICE_A L, RIBOSLICE_B R; RIBOSLICE A indicates repeat sequences comprising the sequence: GHGG, HG, GHGG, HG, etc.; RIBOSLICE B indicates repeat sequences comprising the sequence: HG, GHGG, HG, GHGG, etc.; L targets the sequence: TATTCCCGGGCTCCCAGGCA (SEQ ID NO: 622); R targets the sequence: TCTCCTGGCCTTCCTGCCTC (SEQ ID NO: 612); a target sequence is near the end of exon 73 of COL7A1). “TAL” indicates a control TALEN directed to the target sequence.

FIG. 48 depicts the results of an experiment in which 50,000 primary human neonatal epidermal keratinocytes (HEKn) (animal-protein free) were transfected with 2 µg RNA encoding the indicated gene-editing proteins. DNA was harvested after 48h and analyzed for gene editing (“Neg” indicates untreated HEKn DNA; “WT” indicates wild type FokI; “EA” indicates enhanced activity FokI (S35P and K58E); “Het” indicates heterodimer (L: Q103E, N113D, I116L, R: E107K, H154R, I155K); “EA/Het” indicates both EA and Het; L targets the sequence: TATTCCCGGGCTCCCAGGCA (SEQ ID NO: 622); R targets the sequence: TCTCCTGGCCTTCCTGCCTC

(SEQ ID NO: 612); a target sequence is near the end of exon 73 of COL7A1).

FIG. 49 depicts the results of an experiment in which 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) per well of a 6-well plate were transfected with 2 ug RNA encoding hGDF15. The culture medium was analyzed for GDF15 at the indicated time after transfection by ELISA (R&D DGD150).

FIG. 50 depicts the results of an experiment in which 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) per well of a 6-well plate were transfected with 2 ug RNA encoding the indicated protein. The culture medium was analyzed for IFKB at the indicated time after transfection by ELISA (Abcam ab176644). For each time point, the histograms indicate (left to right): IFKB WT, IFKB S32A, S36A, and Neg.

FIG. 51 depicts the results of an experiment in which 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) per well of a 6-well plate were transfected with 2 µg RNA encoding the indicated protein. Images were taken 24h after transfection.

FIG. 52 depicts the results of an experiment in which 20,000 primary human neonatal epidermal keratinocytes (animal-protein free) per well of a 24-well plate were transfected with 0.2 µg RNA encoding SOD3. Cells were fixed and stained 24h after transfection with a 1:100 dilution of NBP2-38493 (Novus) rabbit anti human SOD3 primary antibody and a 1:1000 dilution of 488 donkey anti-rabbit secondary antibody. “BF” indicates brightfield and “FL” indicates fluorescence.

FIG. 53 depicts the results of an experiment in which ZDF rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (Group 4, grey curve (bottom)) or with vehicle only (Group 3, black curve (top)). ALT serum levels were measured at the indicated times.

FIG. 54 depicts the results of an experiment in which ZDF rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (Group 4, grey curve (bottom)) or with vehicle only (Group 3, black curve (top)). AST serum levels were measured at the indicated times.

FIG. 55 depicts the results of an experiment in which ZDF rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (Group 4, grey curve (top)) or with vehicle only (Group 3, black curve (bottom)). Total cholesterol serum levels were measured at the indicated times.

FIG. 56 depicts the results of an experiment in which ZDF rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (Group 4, grey (bottom at day 7)) or with vehicle only (Group 3, black (top at day 7)). Glucose serum levels were measured at the indicated times.

FIG. 57 depicts the results of an experiment in which ZDF rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (Group 4, grey (top)) or with vehicle only (Group 3, black (bottom)). Triglycerides serum levels were measured at the indicated times.

FIG. 58 depicts the results of an experiment in which ZDF rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (treatment group) or with vehicle only (control group). % change of ALT, AST, Total cholesterol, Glucose, and Triglycerides serum levels in treatment group vs control group are

shown.

FIG. 59 depicts the results of an experiment in which lean Sprague-Dawley rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (Group 2) or with vehicle only (Group 1) and ZDF rats were administered RNA encoding hGDF15 by intradermal injection on Days 1, 8, and 15 (Group 4) or with vehicle only (Group 3). GDF15 serum levels were measured at the indicated times. For each timepoint, the histograms indicate (left to right) Group 1, Group 2, Group 3, and Group 4.

FIG. 60 depicts the results of an experiment in which 200,000 primary human neonatal epidermal keratinocytes (animal-protein free) per well of a 6-well plate were transfected with 2 µg RNA encoding hESM1. The culture medium was analyzed for ESM1 52 hours after transfection by ELISA (Abcam ab213776).

FIG. 61 depicts the results of an experiment in which 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) were transfected with 2 µg RNA encoding the HBB exon 1 TALEN L and HBB exon 1 TALEN R gene-editing proteins (1 µg each). DNA was harvested after 48h and analyzed for gene editing (T7E1 assay; forward primer: gccaaggacaggtacggctgtcatc (SEQ ID NO: 627); reverse primer: cttgccatgagccttcaccttagggttg (SEQ ID NO: 628); product size: 518nt; predicted band sizes: 300nt, 218nt).

FIG. 62 depicts the results of an experiment in which 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) were transfected with 2 µg RNA encoding the PD1 exon 1 TALEN L and PD1 exon 1 TALEN R gene-editing proteins (1 µg each). DNA was harvested after 48h and analyzed for gene editing (T7E1 assay; forward primer: tcctctgtctccctgtctctgtctctctctc (SEQ ID NO: 594); reverse primer: ggacttgggccaggggaggag (SEQ ID NO: 595); product size: 612nt; predicted band sizes: 349nt, 263nt).

DETAILED DESCRIPTION OF THE INVENTION

The present invention is based, in part, on the discovery of a safe and effective dosing strategy for nucleic acid drugs, including RNA, such as RNA comprising non-canonical (or "modified") nucleotides, in humans. The inventors believe this to be the first report of safe and effective dosing of RNA molecules, including those comprising non-canonical nucleotides, in humans. Despite reports in the art that very large doses of RNA molecules are needed for mammalian dosing, and minimal therapeutic effect is achieved despite high dosing (*see, e.g.* US Patent Publication No. 2013/0245103), the present inventors have surprisingly managed to dose synthetic RNA in a human and achieve significant target protein expression with minimal immunological or other side effects.

In various embodiments, the present invention provides improved doses, formulations, administration and methods of use of nucleic acid drugs, which include RNA, which may contain non-canonical nucleotides (*e.g.* a residue other than adenine, guanine, thymine, uracil, and cytosine or the standard nucleoside, nucleotide, deoxynucleoside or deoxynucleotide derivatives thereof). In various embodiments, the RNA comprising non-canonical nucleotides leads to the expression of a protein encoded by the RNA, the protein often being one of

therapeutic benefit (sometimes called the “target” or “protein of interest”). Further, this expression of therapeutic protein is achieved with minimal or negligible toxicity.

In various aspects, the present invention is based on the surprising discovery of safe and effective doses and administration parameters of nucleic acid drugs for human subjects. Nucleic acid drugs include a dsDNA molecule, a ssDNA molecule, a RNA molecule, a dsRNA molecule, a ssRNA molecule, a plasmid, an oligonucleotide, a synthetic RNA molecule, a miRNA molecule, an mRNA molecule, and an siRNA molecule. In various embodiments, the RNA comprises non-canonical nucleotides.

In some aspects, there is provided a method for delivering a nucleic acid drug, comprising administering an effective dose of a nucleic acid drug to a human subject in need thereof, wherein the nucleic acid drug comprises a synthetic RNA. In various embodiments, the effective dose is an amount sufficient to substantially increase an amount of a protein encoded by the nucleic acid drug in the human subject. For example, when the nucleic acid drug is a synthetic RNA comprising one or more modified nucleotides, the nucleic acid drug may result in higher protein expression than levels obtainable with a nucleic acid drug that does not comprise one or more modified nucleotides (*e.g.*, RNA comprising the canonical nucleotides A, G, U, and C). In some embodiments, the nucleic acid drug results in about a 2-fold, or about a 3-fold, or about a 4-fold, or about a 5-fold, or about a 10-fold, or about a 15-fold, or about a 20-fold, or about a 25-fold, or about a 30-fold, or about a 35-fold, or about a 40-fold, or about a 45-fold, or about a 50-fold, or about a 100-fold increase in protein expression as compared to levels obtainable with a nucleic acid drug that does not comprise one or more modified nucleotides.

In some embodiments, the nucleic acid drug provides a sustained therapeutic effect that is optionally mediated by a sustained expression of target protein. For instance, in some embodiments, the therapeutic effect is present for over about 1 day, or over about 2 days, or over about 3 days, or over about 4 days, or over about 5 days, or over about 6 days, or over about 7 days, or over about 8 days, or over about 9 days, or over about 10 days, or over about 14 days after administration. In some embodiments, this sustained effect obviates the need for, or reduces the amount of, maintenance doses.

In some embodiments, the nucleic acid drug provides a sustained target protein level. For instance, in some embodiments, the target protein is present (*e.g.* in measurable amounts, *e.g.* in the serum of a patient to whom the nucleic acid drug has been administered) for over about 1 day, or over about 2 days, or over about 3 days, or over about 4 days, or over about 5 days, or over about 6 days, or over about 7 days, or over about 8 days, or over about 9 days, or over about 10 days, or over about 14 days after administration. In some embodiments, this sustained effect obviates the need for, or reduces the amount of, maintenance doses.

In various embodiments, the nucleic acid drug provides therapeutic action without sustained presence of the nucleic acid drug itself. In some embodiments, the nucleic acid drug is rapidly metabolized, for instance, within about 6 hours, or about 12 hours, or about 18 hours, or about 24 hours, or about 2 days, or about 3 days, or about 4 days, or about 5 days, or about 1 week from administration.

In various embodiments, the effective dose is an amount that substantially avoids cell toxicity *in vivo*. In various embodiments, the effective dose is an amount that substantially avoids an immune reaction in a human subject. For example, the immune reaction may be an immune response mediated by the innate immune system. Immune response can be monitored using markers known in the art (*e.g.* cytokines, interferons, TLRs). In some embodiments, the effective dose obviates the need for treatment of the human subject with immune suppressants agents (*e.g.* B18R) used to moderate the residual toxicity. Accordingly, in some embodiments, the present methods allow for dosing that provides increased protein expression and reduces toxicity.

In some embodiments, the immune response is reduced by about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 99%, about 99.9%, or greater than about 99.9% as compared to the immune response induced by a corresponding unmodified nucleic acid. In some embodiments, upregulation of one or more immune response markers is reduced by about 10%, about 20%, about 30%, about 40%, about 50%, about 60%, about 70%, about 80%, about 90%, about 95%, about 99%, about 99.9%, or greater than about 99.9% as compared to the upregulation of the one or more immune response markers induced by a corresponding unmodified nucleic acid. In some embodiments, the immune response marker comprises an mRNA or protein product of an interferon gene, including an interferon alpha gene, IFNB1, TLR3, RARRES3, EIF2AK2, STAT1, STAT2, IFIT1, IFIT2, IFIT3, IFIT5, OAS1, OAS2, OAS3, OASL, ISG20 or a fragment, variant, analogue, or family-member thereof. In some embodiments, the immune response marker comprises an mRNA or protein product of an TNF gene, including an TNF alpha gene, TNFRSF1A; TNFRSF1B; LTBR; TNFRSF4; CD40; FAS; TNFRSF6B; CD27; TNFRSF8; TNFRSF9; TNFRSF10A; TNFRSF10B; TNFRSF10C; TNFRSF10D; TNFRSF11A; TNFRSF11B; TNFRSF12A; TNFRSF13B; TNFRSF13C; TNFRSF14; NGFR; TNFRSF17; TNFRSF18; TNFRSF19; TNFRSF21; TNFRSF25; and EDA2R or a fragment, variant, analogue, or family-member thereof. In some embodiments, the immune response marker comprises an mRNA or protein product of an interleukin gene, including an IL-6 gene, IL-1; IL-2; IL-3; IL-4; IL-5; IL-6; IL-7; IL-8 or CXCL8; IL-9; IL-10; IL-11; IL-12; IL-13; IL-14; IL-15; IL-16; IL-17; IL-18; IL-19; IL-20; IL-21; IL-22; IL-23; IL-24; IL-25; IL-26; IL-27; IL-28; IL-29; IL-30; IL-31; IL-32; IL-33; IL-35; IL-36 or a fragment, variant, analogue, or family-member thereof.

In some embodiments, cell death is about 10%, about 25%, about 50%, about 75%, about 85%, about 90%, about 95%, or over about 95% less than the cell death observed with a corresponding unmodified nucleic acid. Moreover, cell death may affect fewer than about 50%, about 40%, about 30%, about 20%, about 10%, about 5%, about 1%, about 0.1%, about 0.01% or fewer than about 0.01% of cells contacted with the modified nucleic acids.

In some embodiments, there is provided a method for expressing a protein of interest in a population of cells in a mammalian subject, comprising administering a non-viral transfection composition comprising an effective dose of a RNA encoding the protein of interest to said cells, the RNA containing one or more non-canonical nucleotides that avoid substantial cellular toxicity, where the transfection composition is administered in an amount that allows for expression of said protein in said cells for at least about five days (*e.g.* about 5, or about

6, or about 7, about 8, or about 9, or about 10, or about 14 days) without substantial cellular toxicity. In some embodiments, there is provided a method for expressing a protein of interest in a population of cells in a mammalian subject, comprising administering a non-viral transfection composition comprising an effective dose of a RNA encoding the protein of interest to said cells, the RNA containing one or more non-canonical nucleotides that avoid substantial cellular toxicity, where the transfection composition is administered in an amount that allows for expression of said protein in said cells for at least about six hours (*e.g.* about six hours, or about 12 hours, or about 1 day, or about 2 days, or about 3 days, or about 4 days, or about 5 days) without substantial cellular toxicity.

In some embodiments, the effective dose of the nucleic acid drug, including synthetic RNA, is about 100 ng to about 2000 ng, or about 200 ng to about 1900 ng, or about 300 ng to about 1800 ng, or about 400 ng to about 1700 ng, or about 500 ng to about 1600 ng, or about 600 ng to about 1500 ng, or about 700 ng to about 1400 ng, or about 800 ng to about 1300 ng, or about 900 ng to about 1200 ng, or about 1000 ng to about 1100 ng, or about 500 ng to about 2000 ng, or about 500 ng to about 1500 ng, or about 500 ng to about 1000 ng, or about 1000 ng to about 1500 ng, or about 1000 ng to about 2000 ng, or about 1500 ng to about 2000 ng, or about 100 ng to about 500 ng, or about 200 ng to about 400 ng, or about 10 ng to about 100 ng, or about 20 ng to about 90 ng, or about 30 ng to about 80 ng, or about 40 ng to about 70 ng, or about 50 ng to about 60 ng.

In some embodiments, the effective dose of the nucleic acid drug, including synthetic RNA, is no more than about 50 ng, or about 100 ng, or about 200 ng, or about 300 ng, or about 400 ng, or about 500 ng, or about 600 ng, or about 700 ng, or about 800 ng, or about 900 ng, or about 1000 ng, or about 1100 ng, or about 1200 ng, or about 1300 ng, or about 1400 ng, or about 1500 ng, or about 1600 ng, or about 1700 ng, or about 1800 ng, or about 1900 ng, or about 2000 ng, or about 3000 ng, or about 4000 ng, or about 5000 ng.

In some embodiments, the effective dose of the nucleic acid drug, including synthetic RNA, is about 50 ng, or about 100 ng, or about 200 ng, or about 300 ng, or about 400 ng, or about 500 ng, or about 600 ng, or about 700 ng, or about 800 ng, or about 900 ng, or about 1000 ng, or about 1100 ng, or about 1200 ng, or about 1300 ng, or about 1400 ng, or about 1500 ng, or about 1600 ng, or about 1700 ng, or about 1800 ng, or about 1900 ng, or about 2000 ng, or about 3000 ng, or about 4000 ng, or about 5000 ng.

In some embodiments, the effective dose of the nucleic acid drug, including synthetic RNA, is about 0.028 pmol, or about 0.05 pmol, or about 0.1 pmol, or about 0.2 pmol, or about 0.3 pmol, or about 0.4 pmol, or about 0.5 pmol, or about 0.6 pmol, or about 0.7 pmol, or about 0.8 pmol, or about 0.9 pmol, or about 1.0 pmol, or about 1.2 pmol, or about 1.4 pmol, or about 1.6 pmol, or about 1.8 pmol, or about 2.0 pmol, or about 2.2 pmol, or about 2.4 pmol, or about 2.6 pmol, or about 2.8 pmol, or about 3.0 pmol, or about 3.2 pmol, or about 3.4 pmol, or about 3.6 pmol, or about 3.8 pmol, or about 4.0 pmol, or about 4.2 pmol, or about 4.4 pmol, or about 4.6 pmol, or about 4.8 pmol, or about 5.0 pmol, or about 5.5 pmol, or about 5.7 pmol.

In some embodiments, the nucleic acid drug, including synthetic RNA, is administered at a concentration of about 0.1 nM, or about 0.25 nM, or about 0.5 nM, or about 0.75 nM, or about 1 nM, or about 2.5 nM, or about 5

nM, or about 7.5 nM, or about 10 nM, or about 20 nM, or about 30 nM, or about 40 nM, or about 50 nM, or about 60 nM, or about 70 nM, or about 80 nM, or about 90 nM, or about 100 nM, or about 110 nM, or about 120 nM, or about 150 nM, or about 175 nM, or about 200 nM.

In some embodiments, the effective dose of the nucleic acid drug is about 350 ng/cm^2, or about 500 ng/cm^2, or about 750 ng/cm^2, or about 1000 ng/cm^2, or about 2000 ng/cm^2, or about 3000 ng/cm^2, or about 4000 ng/cm^2, or about 5000 ng/cm^2, or about 6000 ng/cm^2, or about 7000 ng/cm^2. In other embodiments, the effective dose is less than about 350 ng/cm^2. In certain embodiments, the effective dose is about 35 ng/cm^2, or about 50 ng/cm^2, or about 75 ng/cm^2, or about 100 ng/cm^2, or about 150 ng/cm^2, or about 200 ng/cm^2, or about 250 ng/cm^2, or about 300 ng/cm^2, or about 350 ng/cm^2.

In some embodiments, the effective dose of the nucleic acid drug is about 35 ng/cm^2 to about 7000 ng/cm^2, or about 50 ng/cm^2 to about 5000 ng/cm^2, or about 100 ng/cm^2 to about 3000 ng/cm^2, or about 500 ng/cm^2 to about 2000 ng/cm^2, or about 750 ng/cm^2 to about 1500 ng/cm^2, or about 800 ng/cm^2 to about 1200 ng/cm^2, or about 900 ng/cm^2 to about 1100 ng/cm^2.

In some embodiments, the effective dose of the nucleic acid drug is about 1 picomole/cm^2, or about 2 picomoles/cm^2, or about 3 picomoles/cm^2, or about 4 picomoles/cm^2, or about 5 picomoles/cm^2, or about 6 picomoles/cm^2, or about 7 picomoles/cm^2, or about 8 picomoles/cm^2, or about 9 picomoles/cm^2, or about 10 picomoles/cm^2, or about 12 picomoles/cm^2, or about 14 picomoles/cm^2, or about 16 picomoles/cm^2, or about 18 picomoles/cm^2, or about 20 picomoles/cm^2. In other embodiments, the effective dose is less than about 1 picomole/cm^2. In certain embodiments, the effective dose is about 0.1 picomoles/cm^2, or about 0.2 picomoles/cm^2, or about 0.3 picomoles/cm^2, or about 0.4 picomoles/cm^2, or about 0.5 picomoles/cm^2, or about 0.6 picomoles/cm^2, or about 0.7 picomoles/cm^2, or about 0.8 picomoles/cm^2, or about 0.9 picomoles/cm^2, or about 1 picomole/cm^2.

In some embodiments, the effective dose of the nucleic acid drug is about 0.1 picomoles/cm^2 to about 20 picomoles/cm^2, or about 0.2 picomoles/cm^2 to about 15 picomoles/cm^2, or about 0.5 picomoles/cm^2 to about 10 picomoles/cm^2, or about 0.8 picomoles/cm^2 to about 8 picomoles/cm^2, or about 1 picomole/cm^2 to about 5 picomoles/cm^2, or about 2 picomoles/cm^2 to about 4 picomoles/cm^2.

In various embodiments, the nucleic acid drug, including synthetic RNA, is administered in a pharmaceutically acceptable formulation. In various embodiments, the nucleic acid drug, including synthetic RNA, is formulated for one or more of injection and topical administration. By way of example, the nucleic acid drug, including synthetic RNA, may be formulated for injection to a tissue of interest, *e.g.* a disease site (by way of non-limiting example, a tumor). In various embodiments, injection includes delivery via a patch. In some embodiments, the delivery is mediated by electrical stimulation. In various embodiments, the nucleic acid drug, including synthetic RNA, is formulated for administration to one or more of the epidermis (optionally selected from the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum germinativum), basement membrane, dermis (optionally selected from the papillary region and the reticular region), subcutis, conjunctiva cornea,

sclera, iris, lens, corneal limbus, optic nerve, choroid, ciliary body, anterior segment, anterior chamber, and retina. In various embodiments, the nucleic acid drug, including synthetic RNA, is formulated for one or more of subcutaneous injection, intradermal injection, subdermal injection, intramuscular injection, intraocular injection, intravitreal injection, intra-articular injection, intracardiac injection, intravenous injection, epidural injection, intrathecal injection, intraportal injection, intratumoral injection, and topical administration. In various embodiments, the nucleic acid drug, including synthetic RNA, is formulated for intradermal (ID) injection to one or more of the dermis or epidermis. In various embodiments, the nucleic acid drug, including synthetic RNA, is administered in a manner such that it effects one or more of keratinocytes and fibroblasts (*e.g.* causes these cells to express one or more therapeutic proteins).

Accordingly, the present invention provides various formulations as described herein. Further, in some embodiments, the formulations described herein find use in the various delivery and/or treatment methods of the present invention. For instance, formulations can comprise a vesicle, for instance, a liposome (*see* Langer, 1990, *Science* 249:1527-1533; Treat *et al.*, in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989). In various embodiments, the formulation comprises an aqueous suspension of liposomes. Illustrative liposome components are set forth in **Table 1**, and are given by way of example, and not by way of limitation. In various embodiments, one or more, or two or more, or three or more, or four or more, or five or more of the lipids of **Table 1** are combined in a formulation.

Table 1. *Illustrative Biocompatible Lipids*

1	3β -[N-(N',N'-dimethylaminoethane)-carbamoyl]cholesterol (DC-Cholesterol)
2	1,2-dioleoyl-3-trimethylammonium-propane (DOTAP / 18:1 TAP)
3	N-(4-carboxybenzyl)-N,N-dimethyl-2,3-bis(oleoyloxy)propan-1-aminium (DOBAQ)
4	1,2-dimyristoyl-3-trimethylammonium-propane (14:0 TAP)
5	1,2-dipalmitoyl-3-trimethylammonium-propane (16:0 TAP)
6	1,2-stearoyl-3-trimethylammonium-propane (18:0 TAP)
7	1,2-dioleoyl-3-dimethylammonium-propane (DODAP / 18:1 DAP)
8	1,2-dimyristoyl-3-dimethylammonium-propane (14:0 DAP)
9	1,2-dipalmitoyl-3-dimethylammonium-propane (16:0 DAP)
10	1,2-distearoyl-3-dimethylammonium-propane (18:0 DAP)
11	dimethyldioctadecylammonium (18:0 DDAB)
12	1,2-dilauroyl-sn-glycero-3-ethylphosphocholine (12:0 EthylPC)
13	1,2-dimyristoyl-sn-glycero-3-ethylphosphocholine (14:0 EthylPC)
14	1,2-dimyristoleoyl-sn-glycero-3-ethylphosphocholine (14:1 EthylPC)
15	1,2-dipalmitoyl-sn-glycero-3-ethylphosphocholine (16:0 EthylPC)
16	1,2-distearoyl-sn-glycero-3-ethylphosphocholine (18:0 EthylPC)
17	1,2-dioleoyl-sn-glycero-3-ethylphosphocholine (18:1 EthylPC)
18	1-palmitoyl-2-oleoyl-sn-glycero-3-ethylphosphocholine (16:1-18:1 EthylPC)
19	1,2-di-O-octadecenyl-3-trimethylammonium propane (DOTMA)
20	N1-[2-((1S)-1-[(3-aminopropyl)amino]-4-[di(3-amino-propyl)amino]butylcarboxamido)ethyl]-3,4-di[oleyloxy]-benzamide (MVL5)

21	2,3-dioleyloxy-N-[2-spermine carboxamide]ethyl-N,N-dimethyl-1-propanammonium trifluoroacetate (DOSPA)
22	1,3-di-oleoyloxy-2-(6-carboxy-spermyl)-propylamid (DOSPER)
23	N-[1-(2,3-dimyristyloxy)propyl]-N,N-dimethyl-N-(2-hydroxyethyl)ammonium bromide (DMRIE)
24	LIPOFECTAMINE, LIPOFECTAMINE 2000, LIPOFECTAMINE RNAiMAX, LIPOFECTAMINE 3000, LIPOFECTAMINE MessengerMAX, TransIT mRNA
25	dioctadecyl amidoglyceryl spermine (DOGS)
26	dioleoyl phosphatidyl ethanolamine (DOPE)

In some embodiments, the liposomes include LIPOFECTAMINE 3000. In some embodiments, the liposomes include one or more lipids described in US Patent Nos. 4,897,355 or 7,479,573 or in International Patent Publication No. WO/2015/089487, or in Felgner, P. L. *et al.* (1987) Proc. Natl. Acad. Sci. USA 84:7413–7417, the entire contents of each is incorporated by reference in their entireties).

In some embodiments, the liposome comprises N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTMA). In some embodiments, the liposome comprises dioleoylphosphatidylethanolamine (DOPE).

In one embodiment, the liposomes include one or more polyethylene glycol (PEG) chains, optionally selected from PEG200, PEG300, PEG400, PEG600, PEG800, PEG1000, PEG1500, PEG2000, PEG3000, and PEG4000. In some embodiments, the PEG is PEG2000. In some embodiments, the liposomes include 1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE) or a derivative thereof.

In some embodiments, the formulation comprises one or more of N-(carbonyl-ethoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine (MPEG2000-DSPE), fully hydrogenated phosphatidylcholine, cholesterol, LIPOFECTAMINE 3000, a cationic lipid, a polycationic lipid, and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[folate(polyethylene glycol)-5000] (FA-MPEG5000-DSPE).

In one embodiment, the formulation comprises about 3.2 mg/mL N-(carbonyl-ethoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine (MPEG2000-DSPE), about 9.6 mg/mL fully hydrogenated phosphatidylcholine, about 3.2 mg/mL cholesterol, about 2 mg/mL ammonium sulfate, and histidine as a buffer, with about 0.27 mg/mL 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[folate(polyethylene glycol)-5000] (FA-MPEG5000-DSPE) added to the lipid mixture. In another embodiment, the nucleic acids are complexed by combining 1 μL of LIPOFECTAMINE 3000 per about 1 μg of nucleic acid and incubating at room temperature for at least about 5 minutes. In one embodiment, the LIPOFECTAMINE 3000 is a solution comprising a lipid at a concentration of about 1 mg/mL. In some embodiments, nucleic acids are encapsulated by combining about 10μg of the liposome formulation per about 1μg of nucleic acid and incubating at room temperature for about 5 minutes.

In some embodiments, the formulation comprises one or more nanoparticles. In one embodiment, the nanoparticle is a polymeric nanoparticle. In various embodiments, the formulation comprises one or more of a diblock copolymer, a triblock copolymer, a tetrablock copolymer, and a multiblock copolymer. In various

embodiments, the formulation comprises one or more of polymeric nanoparticles comprising a polyethylene glycol (PEG)-modified polylactic acid (PLA) diblock copolymer (PLA-PEG) and PEG-polypropylene glycol-PEG-modified PLA-tetrablock copolymer (PLA-PEG-PPG-PEG).

In some embodiments, the formulation comprises one or more lipids that are described in WO/2000/027795, the entire contents of which are hereby incorporated by reference.

In one embodiment, the therapeutic comprises one or more ligands. In another embodiment, the therapeutic comprises at least one of: androgen, CD30 (TNFRSF8), a cell-penetrating peptide, CXCR, estrogen, epidermal growth factor, EGFR, HER2, folate, insulin, insulin-like growth factor-I, interleukin-13, integrin, progesterone, stromal-derived-factor-1, thrombin, vitamin D, and transferrin or a biologically active fragment or variant thereof.

The active compositions of the present invention may include classic pharmaceutical preparations. Administration of these compositions according to the present invention may be via any common route so long as the target tissue is available via that route. This includes oral, nasal, or buccal. Alternatively, administration may be by intradermal, subcutaneous, intramuscular, intraperitoneal, intraportall or intravenous injection, or by direct injection into diseased, *e.g.* cancer, tissue. The agents disclosed herein may also be administered by catheter systems. Such compositions would normally be administered as pharmaceutically acceptable compositions as described herein.

Administration of the compositions described herein may be, for example, by injection, topical administration, ophthalmic administration and intranasal administration. The injection, in some embodiments, may be linked to an electrical force (*e.g.* electroporation, including with devices that find use in electrochemotherapy (*e.g.* CLINIPORATOR, IGEA Srl, Carpi [MO], Italy)). The topical administration may be, but is not limited to, a cream, lotion, ointment, gel, spray, solution and the like. The topical administration may further include a penetration enhancer such as, but not limited to, surfactants, fatty acids, bile salts, chelating agents, non-chelating non-surfactants, polyoxyethylene-9-lauryl ether, polyoxyethylene-20-cetyl ether, fatty acids and/or salts in combination with bile acids and/or salts, sodium salt in combination with lauric acid, capric acid and UDCA, and the like. The topical administration may also include a fragrance, a colorant, a sunscreen, an antibacterial and/or a moisturizer. The compositions described herein may be administered to at least one site such as, but not limited to, forehead, scalp, hair follicles, hair, upper eyelids, lower eyelids, eyebrows, eyelashes, infraorbital area, periorbital areas, temple, nose, nose bridge, cheeks, tongue, nasolabial folds, lips, periobicular areas, jaw line, ears, neck, breast, forearm, upper arm, palm, hand, finger, nails, back, abdomen, sides, buttocks, thigh, calf, feet, toes and the like.

Routes of administration include, for example: intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, sublingual, intracerebral, intravaginal, transdermal, intraportal, rectally, by inhalation, or topically, particularly to the ears, nose, eyes, or skin. In some embodiments, the administering is effected orally or by parenteral injection.

Upon formulation, solutions may be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective, as described herein. The formulations may easily be administered in a variety of dosage forms such as injectable solutions, drug release capsules and the like. For parenteral administration in an aqueous solution, for example, the solution generally is suitably buffered and the liquid diluent first rendered isotonic with, for example, sufficient saline or glucose. Such aqueous solutions may be used, for example, for intravenous, intramuscular, subcutaneous and intraperitoneal administration. Preferably, sterile aqueous media are employed as is known to those of skill in the art, particularly in light of the present disclosure.

In various embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, and/or formulations comprising the same, is administered locally, optionally by one or more of subcutaneous injection, intradermal injection, subdermal injection and intramuscular injection, and the effective dose is administered to a surface area of about 4 mm^2 to about 150 mm^2 (*e.g.* about, or no more than about, 4 mm^2, or about 5 mm^2, or about 6mm^2, or about 7 mm^2, or about 8 mm^2, or about 10 mm^2, or about 20 mm^2, or about 50 mm^2, or about 100 mm^2, or about 150 mm^2). In various embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, and/or formulations comprising the same, is administered locally, optionally by one or more of subcutaneous injection, intradermal injection, subdermal injection and intramuscular injection, and the effective dose administered to a surface area of no more than about 4 mm^2, or about 5 mm^2, or about 6mm^2, or about 7 mm^2, or about 8 mm^2, or about 10 mm^2, or about 20 mm^2, or about 50 mm^2, or about 100 mm^2, or about 150 mm^2. In various embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, and/or formulations comprising the same, is administered locally, optionally by one or more of subcutaneous injection, intradermal injection, subdermal injection and intramuscular injection, and the effective dose administered to a surface area of about 4 mm^2, or about 5 mm^2, or about 6 mm^2, or about 7 mm^2, or about 8 mm^2, or about 10 mm^2, or about 20 mm^2, or about 50 mm^2, or about 100 mm^2, or about 150 mm^2.

In various embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, and/or formulations comprising the same, is administered locally, optionally by one or more of subcutaneous injection, intradermal injection, subdermal injection and intramuscular injection, and the effective dose (weight RNA / surface area of injection) is about 35 ng/cm^2 to about 7000 ng/cm^2. In various embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, and/or formulations comprising the same, is administered locally, optionally by one or more of subcutaneous injection, intradermal injection, subdermal injection and intramuscular injection, and the effective dose (weight RNA / surface area of injection) is no more than about 35 ng/cm^2, or about 50 ng/cm^2, or about 75 ng/cm^2, or about 100 ng/cm^2, or about 125 ng/cm^2, or about 150 ng/cm^2, or about 175 ng/cm^2, or about 200 ng/cm^2, or about 225 ng/cm^2, or about 250 ng/cm^2, or about 500 ng/cm^2, or about 1000 ng/cm^2, or about 2000 ng/cm^2, or about 5000 ng/cm^2, or about 7000 ng/cm^2. In various embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, and/or formulations comprising the same, is administered locally, optionally by one or

more of subcutaneous injection, intradermal injection, subdermal injection and intramuscular injection, and the effective dose (weight RNA / surface area of injection) is about 35 ng/cm^2, or about 50 ng/cm^2, or about 75 ng/cm^2, or about 100 ng/cm^2, or about 125 ng/cm^2, or about 150 ng/cm^2, or about 175 ng/cm^2, or about 200 ng/cm^2, or about 225 ng/cm^2, or about 250 ng/cm^2, or about 500 ng/cm^2, or about 1000 ng/cm^2, or about 2000 ng/cm^2, or about 5000 ng/cm^2, or about 7000 ng/cm^2.

Pharmaceutical preparations may additionally comprise delivery reagents (a.k.a. “transfection reagents”, a.k.a. “vehicles”, a.k.a. “delivery vehicles”) and/or excipients. Pharmaceutically acceptable delivery reagents, excipients, and methods of preparation and use thereof, including methods for preparing and administering pharmaceutical preparations to patients (a.k.a. “subjects”) are well known in the art, and are set forth in numerous publications, including, for example, in US Patent Appl. Pub. No. US 2008/0213377, the entirety of which is incorporated herein by reference.

For example, the present compositions can be in the form of pharmaceutically acceptable salts. Such salts include those listed in, for example, *J. Pharma. Sci.* 66, 2-19 (1977) and *The Handbook of Pharmaceutical Salts; Properties, Selection, and Use.* P. H. Stahl and C. G. Wermuth (eds.), Verlag, Zurich (Switzerland) 2002, which are hereby incorporated by reference in their entirety. Non-limiting examples of pharmaceutically acceptable salts include: sulfate, citrate, acetate, oxalate, chloride, bromide, iodide, nitrate, bisulfate, phosphate, acid phosphate, isonicotinate, lactate, salicylate, acid citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucaronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate, camphorsulfonate, pamoate, phenylacetate, trifluoroacetate, acrylate, chlorobenzoate, dinitrobenzoate, hydroxybenzoate, methoxybenzoate, methylbenzoate, o-acetoxybenzoate, naphthalene-2-benzoate, isobutyrate, phenylbutyrate, α- hydroxybutyrate, butyne-1,4-dicarboxylate, hexyne-1,4-dicarboxylate, caprate, caprylate, cinnamate, glycollate, heptanoate, hippurate, malate, hydroxymaleate, malonate, mandelate, mesylate, nicotinate, phthalate, teraphthalate, propiolate, propionate, phenylpropionate, sebacate, suberate, p-bromobenzenesulfonate, chlorobenzenesulfonate, ethylsulfonate, 2-hydroxyethylsulfonate, methylsulfonate, naphthalene-1-sulfonate, naphthalene-2-sulfonate, naphthalene-1,5-sulfonate, xylenesulfonate, tartarate salts, hydroxides of alkali metals such as sodium, potassium, and lithium; hydroxides of alkaline earth metal such as calcium and magnesium; hydroxides of other metals, such as aluminum and zinc; ammonia, and organic amines, such as unsubstituted or hydroxy-substituted mono-, di-, or tri-alkylamines, dicyclohexylamine; tributyl amine; pyridine; N-methyl, N-ethylamine; diethylamine; triethylamine; mono-, bis-, or tris-(2-OH-lower alkylamines), such as mono-; bis-, or tris-(2-hydroxyethyl)amine, 2-hydroxy-tert-butylamine, or tris-(hydroxymethyl)methylamine, N,N-di-lower alkyl-N-(hydroxyl-lower alkyl)-amines, such as N,N-dimethyl-N-(2-hydroxyethyl)amine or tri- (2-hydroxyethyl)amine; N-methyl-D-glucamine; and amino acids such as arginine, lysine, and the like.

The present pharmaceutical compositions can comprises excipients, including liquids such as water and oils, including those of petroleum, animal, vegetable, or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. The pharmaceutical excipients can be, for example, saline, gum acacia, gelatin, starch

paste, talc, keratin, colloidal silica, urea and the like. In addition, auxiliary, stabilizing, thickening, lubricating, and coloring agents can be used. In one embodiment, the pharmaceutically acceptable excipients are sterile when administered to a subject. Suitable pharmaceutical excipients also include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. Any agent described herein, if desired, can also comprise minor amounts of wetting or emulsifying agents, or pH buffering agents.

Dosage forms suitable for parenteral administration (*e.g.* subcutaneous, intradermal, subdermal, intramuscular, intravenous, intraperitoneal, intra-articular, and infusion) include, for example, solutions, suspensions, dispersions, emulsions, and the like. They may also be manufactured in the form of sterile solid compositions (*e.g.* lyophilized composition), which can be dissolved or suspended in sterile injectable medium immediately before use. They may contain, for example, suspending or dispersing agents known in the art.

In some embodiments, the formulations described herein may comprise albumin and a nucleic acid molecule.

In some embodiments, the invention relates to a cosmetic composition. In one embodiment, the cosmetic composition comprises albumin. In another embodiment, the albumin is treated with an ion-exchange resin or charcoal. In yet another embodiment, the cosmetic composition comprises a nucleic acid molecule. In a further embodiment, the cosmetic composition comprises both albumin and a nucleic acid molecule. Still other embodiments are directed to a cosmetic treatment article comprising a cosmetic composition contained in a device configured to deliver the composition to a patient. Still other embodiments are directed to a device configured to deliver a cosmetic composition to a patient. In one embodiment, the nucleic acid molecule encodes a member of the group: elastin, collagen, tyrosinase, melanocortin 1 receptor, keratin, filaggren, an antibody, and hyaluronan synthase or a biologically active fragment, variant, analogue or family member thereof.

In some embodiments, the present invention provides treatment regimens. The inventors have discovered that the doses and administration described herein can produce a substantial protein expression effect quickly (*e.g.* in about 6, or about 12, or about 24, or about 36, or about 48 hours). Further, these effects can be sustained for about 7 days, or longer. In some embodiments, the present methods provide for administration of a nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, about weekly to about once every 20 weeks.

In some embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, is administered about weekly, for at least 2 weeks (*e.g.* 3, or 4, or 5, or 6, or 7, or 8, or 9, or 10 weeks). In some embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, is administered about every other week for at least one month (*e.g.* 1, or 2, or 3, or 4, or 5, or 6, or 12 months). In some embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, is administered monthly or about every other month. In some embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, is administered is administered for at least two months, or at least 4 months, or at least 6 months, or at least 9 months, or at least one year.

In some embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, is administered about weekly, or about once every 2 weeks, or about once every 3 weeks, or about once every 4 weeks, or about once every 5 weeks, or about once every 6 weeks, or about once every 7 weeks, or about once every 8 weeks, or about once every 9 weeks, or about once every 10 weeks, or about once every 11 weeks, or about once every 12 weeks, or about once every 13 weeks, or about once every 14 weeks, or about once every 15 weeks, or about once every 20 weeks, or about once every 24 weeks.

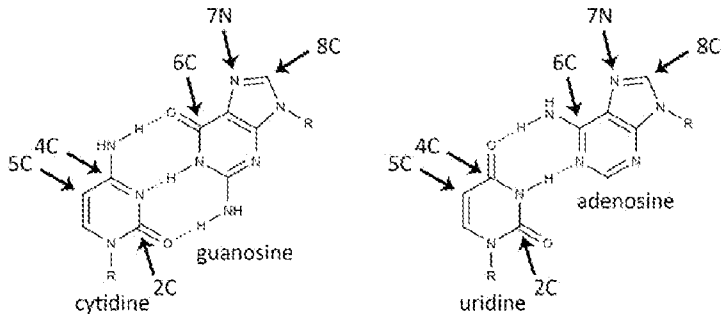
In some embodiments, the nucleic acid drug, including RNA comprising one or more non-canonical nucleotides, is administered no more than about weekly, or about once every 2 weeks, or about once every 3 weeks, or about once every 4 weeks, or about once every 5 weeks, or about once every 6 weeks, or about once every 7 weeks, or about once every 8 weeks, or about once every 9 weeks, or about once every 10 weeks, or about once every 11 weeks, or about once every 12 weeks, or about once every 13 weeks, or about once every 14 weeks, or about once every 15 weeks, or about once every 20 weeks, or about 24 weeks.

Certain proteins have long half-lives, and can persist in tissues for several hours, days, weeks, months or years. It has now been discovered that certain methods of treating a patient can result in accumulation of one or more proteins, including, for example, one or more beneficial proteins. Certain embodiments are therefore directed to a method for treating a patient comprising delivering to a patient in a series of doses a nucleic acid encoding one or more proteins. In one embodiment the nucleic acid comprises RNA comprising one or more non-canonical nucleotides. In another embodiment, a first dose is given at a first time-point. In yet another embodiment, a second dose is given at a second time-point. In a further embodiment, the amount of at least one of the one or more proteins in the patient at the second time-point is greater than the amount of said protein at the first time-point. In a still further embodiment, the method results in the accumulation of said protein in the patient.

In various embodiments, the present invention relates to nucleic acid drugs, which, in various embodiments are RNA comprising one or more non-canonical nucleotides. Certain non-canonical nucleotides, when incorporated into RNA molecules, can reduce the toxicity of the RNA molecules, in part, without wishing to be bound by theory, by interfering with binding of proteins that detect exogenous nucleic acids, for example, protein kinase R, Rig-1 and the oligoadenylate synthetase family of proteins. Non-canonical nucleotides that have been reported to reduce the toxicity of RNA molecules when incorporated therein include: pseudouridine, 5-methyluridine, 2-thiouridine, 5-methylcytidine, N6-methyladenosine, and certain combinations thereof. However, the chemical characteristics of non-canonical nucleotides that can enable them to lower the *in vivo* toxicity of RNA molecules have, until this point, remained unknown. Furthermore, incorporation of large amounts of most non-canonical nucleotides, for example, 5-methyluridine, 2-thiouridine, 5-methylcytidine, and N6-methyladenosine, can reduce the efficiency with which RNA molecules can be translated into protein, limiting the utility of RNA molecules containing these nucleotides in applications that require protein expression. In addition, while pseudouridine can be completely substituted for uridine in RNA molecules without reducing the efficiency with which the synthetic RNA molecules can be translated into protein, in certain situations, for example, when performing frequent,

repeated transfections, synthetic RNA molecules containing only adenosine, guanosine, cytidine, and pseudouridine can exhibit excessive toxicity.

It has now been discovered that, and in some embodiments the invention pertains to, RNA molecules containing one or more non-canonical nucleotides that include one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine can be less toxic than synthetic RNA molecules containing only canonical nucleotides, due in part to the ability of substitutions at these positions to interfere with recognition of synthetic RNA molecules by proteins that detect exogenous nucleic acids, and furthermore, that substitutions at these positions can have minimal impact on the efficiency with which the synthetic RNA molecules can be translated into protein, due in part to the lack of interference of substitutions at these positions with base-pairing and base-stacking interactions.



Examples of non-canonical nucleotides that include one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine include, but are not limited to: 2-thiouridine, 5-azauridine, pseudouridine, 4-thiouridine, 5-methyluridine, 5-methylpseudouridine, 5-aminouridine, 5-aminopseudouridine, 5-hydroxyuridine, 5-hydroxypseudouridine, 5-methoxyuridine, 5-methoxypseudouridine, 5-hydroxymethyluridine, 5-hydroxymethylpseudouridine, 5-carboxyuridine, 5-carboxypseudouridine, 5-formyluridine, 5-formylpseudouridine, 5-methyl-5-azauridine, 5-amino-5-azauridine, 5-hydroxy-5-azauridine, 5-methylpseudouridine, 5-aminopseudouridine, 5-hydroxypseudouridine, 4-thio-5-azauridine, 4-thiopseudouridine, 4-thio-5-methyluridine, 4-thio-5-aminouridine, 4-thio-5-hydroxyuridine, 4-thio-5-methyl-5-azauridine, 4-thio-5-amino-5-azauridine, 4-thio-5-hydroxy-5-azauridine, 4-thio-5-methylpseudouridine, 4-thio-5-aminopseudouridine, 4-thio-5-hydroxypseudouridine, 2-thiocytidine, 5-azacytidine, pseudoisocytidine, N4-methylcytidine, N4-aminocytidine, N4-hydroxycytidine, 5-methylcytidine, 5-aminocytidine, 5-hydroxycytidine, 5-methoxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytydine, 5-methyl-5-azacytidine, 5-amino-5-azacytidine, 5-hydroxy-5-azacytidine, 5-methylpseudoisocytidine, 5-aminopseudoisocytidine, 5-hydroxypseudoisocytidine, N4-methyl-5-azacytidine, N4-methylpseudoisocytidine, 2-thio-5-azacytidine, 2-thiopseudoisocytidine, 2-thio-N4-methylcytidine, 2-thio-N4-aminocytidine, 2-thio-N4-hydroxycytidine, 2-thio-5-methylcytidine, 2-thio-5-aminocytidine, 2-thio-5-hydroxycytidine, 2-thio-5-methyl-5-azacytidine, 2-thio-5-amino-5-azacytidine, 2-thio-5-hydroxy-5-azacytidine, 2-thio-5-methylpseudoisocytidine, 2-thio-5-aminopseudoisocytidine, 2-thio-5-hydroxypseudoisocytidine, 2-thio-N4-methyl-5-azacytidine, 2-thio-N4-methylpseudoisocytidine, N4-methyl-5-methylcytidine, N4-methyl-5-

aminocytidine, N4-methyl-5-hydroxycytidine, N4-methyl-5-methyl-5-azacytidine, N4-methyl-5-amino-5-azacytidine, N4-methyl-5-hydroxy-5-azacytidine, N4-methyl-5-methylpseudoisocytidine, N4-methyl-5-aminopseudoisocytidine, N4-methyl-5-hydroxypseudoisocytidine, N4-amino-5-azacytidine, N4-aminopseudoisocytidine, N4-amino-5-methylcytidine, N4-amino-5-aminocytidine, N4-amino-5-hydroxycytidine, N4-amino-5-methyl-5-azacytidine, N4-amino-5-amino-5-azacytidine, N4-amino-5-hydroxy-5-azacytidine, N4-amino-5-methylpseudoisocytidine, N4-amino-5-aminopseudoisocytidine, N4-amino-5-hydroxypseudoisocytidine, N4-hydroxy-5-azacytidine, N4-hydroxypseudoisocytidine, N4-hydroxy-5-methylcytidine, N4-hydroxy-5-aminocytidine, N4-hydroxy-5-hydroxycytidine, N4-hydroxy-5-methyl-5-azacytidine, N4-hydroxy-5-amino-5-azacytidine, N4-hydroxy-5-hydroxy-5-azacytidine, N4-hydroxy-5-methylpseudoisocytidine, N4-hydroxy-5-aminopseudoisocytidine, N4-hydroxy-5-hydroxypseudoisocytidine, 2-thio-N4-methyl-5-methylcytidine, 2-thio-N4-methyl-5-aminocytidine, 2-thio-N4-methyl-5-hydroxycytidine, 2-thio-N4-methyl-5-methyl-5-azacytidine, 2-thio-N4-methyl-5-amino-5-azacytidine, 2-thio-N4-methyl-5-hydroxy-5-azacytidine, 2-thio-N4-methyl-5-methylpseudoisocytidine, 2-thio-N4-methyl-5-aminopseudoisocytidine, 2-thio-N4-methyl-5-hydroxypseudoisocytidine, 2-thio-N4-amino-5-azacytidine, 2-thio-N4-aminopseudoisocytidine, 2-thio-N4-amino-5-methylcytidine, 2-thio-N4-amino-5-aminocytidine, 2-thio-N4-amino-5-hydroxycytidine, 2-thio-N4-amino-5-methyl-5-azacytidine, 2-thio-N4-amino-5-amino-5-azacytidine, 2-thio-N4-amino-5-hydroxy-5-azacytidine, 2-thio-N4-amino-5-methylpseudoisocytidine, 2-thio-N4-amino-5-aminopseudoisocytidine, 2-thio-N4-amino-5-hydroxypseudoisocytidine, 2-thio-N4-hydroxy-5-azacytidine, 2-thio-N4-hydroxypseudoisocytidine, 2-thio-N4-hydroxy-5-methylcytidine, N4-hydroxy-5-aminocytidine, 2-thio-N4-hydroxy-5-hydroxycytidine, 2-thio-N4-hydroxy-5-methyl-5-azacytidine, 2-thio-N4-hydroxy-5-amino-5-azacytidine, 2-thio-N4-hydroxy-5-hydroxy-5-azacytidine, 2-thio-N4-hydroxy-5-methylpseudoisocytidine, 2-thio-N4-hydroxy-5-aminopseudoisocytidine, 2-thio-N4-hydroxy-5-hydroxypseudoisocytidine, N6-methyladenosine, N6-aminoadenosine, N6-hydroxyadenosine, 7-deazaadenosine, 8-azaadenosine, N6-methyl-7-deazaadenosine, N6-methyl-8-azaadenosine, 7-deaza-8-azaadenosine, N6-methyl-7-deaza-8-azaadenosine, N6-amino-7-deazaadenosine, N6-amino-8-azaadenosine, N6-amino-7-deaza-8-azaadenosine, N6-hydroxyadenosine, N6-hydroxy-7-deazaadenosine, N6-hydroxy-8-azaadenosine, N6-hydroxy-7-deaza-8-azaadenosine, 6-thioguanosine, 7-deazaguanosine, 8-azaguanosine, 6-thio-7-deazaguanosine, 6-thio-8-azaguanosine, 7-deaza-8-azaguanosine, 6-thio-7-deaza-8-azaguanosine, and 5-methoxyuridine.

In some embodiments, the invention relates to one or more non-canonical nucleotides selected from 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine, 5-hydroxyuridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, pseudouridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine. In some embodiments, at least 50%, or at least 55%, or at least 60%, or at least 65%, or at least 70%, or at least 75%, or at least 80%, or at least 85%, or at least 90%, or at least 95%, or 100% of the non-canonical nucleotides are one or more of 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-

methoxycytidine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, pseudouridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine.

In some embodiments, at least about 50%, or at least about 55%%, or at least 60%, or at least 65%, or at least 70%, or at least 75%, or at least 80%, or at least 85%, or at least 90%, or at least 95%, or 100% of cytidine residues are non-canonical nucleotides selected from 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine.

In some embodiments, at least about 20%, or about 30%, or about 40%, or about 50%, or at least about 55%, or at least 60%, or at least 65%, or at least 70%, or at least 75%, or at least 80%, or at least 85%, or at least 90%, or at least 95%, or 100% of uridine residues are non-canonical nucleotides selected from 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, pseudouridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine.

In some embodiments, at least about 10% (*e.g.* 10%, or about 20%, or about 30%, or about 40%, or about 50%) of guanosine residues are non-canonical nucleotides, and the non-canonical nucleotide is optionally 7-deazaguanosine. In some embodiments, the RNA contains no more than about 50% 7-deazaguanosine in place of guanosine residues.

In some embodiments, the RNA does not contain non-canonical nucleotides in place of adenosine residues.

Note that alternative naming schemes exist for certain non-canonical nucleotides. For example, in certain situations, 5-methylpseudouridine can be referred to as “3-methylpseudouridine” or “N3-methylpseudouridine” or “1-methylpseudouridine” or “N1-methylpseudouridine”.

Nucleotides that contain the prefix “amino” can refer to any nucleotide that contains a nitrogen atom bound to the atom at the stated position of the nucleotide, for example, 5-aminocytidine can refer to 5-aminocytidine, 5-methylaminocytidine, and 5-nitrocytidine. Similarly, nucleotides that contain the prefix “methyl” can refer to any nucleotide that contains a carbon atom bound to the atom at the stated position of the nucleotide, for example, 5-methylcytidine can refer to 5-methylcytidine, 5-ethylcytidine, and 5-hydroxymethylcytidine, nucleotides that contain the prefix “thio” can refer to any nucleotide that contains a sulfur atom bound to the atom at the given position of the nucleotide, and nucleotides that contain the prefix “hydroxy” can refer to any nucleotide that contains an oxygen atom bound to the atom at the given position of the nucleotide, for example, 5-hydroxyuridine can refer to 5-hydroxyuridine and uridine with a methyl group bound to an oxygen atom, wherein the oxygen atom is bound to the atom at the 5C position of the uridine.

Certain embodiments are therefore directed to RNA comprising one or more non-canonical nucleotides, wherein the RNA molecule contains one or more nucleotides that includes one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine.

Other embodiments are directed to a therapeutic, wherein the therapeutic contains one or more RNA molecules comprising one or more non-canonical nucleotides, and wherein the one or more RNA molecules comprising one or more non-canonical nucleotides contains one or more nucleotides that includes one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine. In one embodiment, the therapeutic comprises a transfection reagent. In another embodiment, the transfection reagent comprises a cationic lipid, liposome or micelle. In still another embodiment, the liposome or micelle comprises folate and the therapeutic composition has anti-cancer activity. In another embodiment, the one or more nucleotides includes at least one of pseudouridine, 2-thiouridine, 4-thiouridine, 5-azauridine, 5-hydroxyuridine, 5-methyluridine, 5-aminouridine, 2-thiopseudouridine, 4-thiopseudouridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-aminopseudouridine, pseudoisocytidine, N4-methylcytidine, 2-thiocytidine, 5-azacytidine, 5-hydroxycytidine, 5-aminocytidine, 5-methylcytidine, N4-methylpseudoisocytidine, 2-thiopseudoisocytidine, 5-hydroxypseudoisocytidine, 5-aminopseudoisocytidine, 5-methylpseudoisocytidine, 7-deazaadenosine, 7-deazaguanosine, 6-thioguanosine, and 6-thio-7-deazaguanosine. In another embodiment, the one or more nucleotides includes at least one of pseudouridine, 2-thiouridine, 4-thiouridine, 5-azauridine, 5-hydroxyuridine, 5-methyluridine, 5-aminouridine, 2-thiopseudouridine, 4-thiopseudouridine, 5-hydroxypseudouridine, 5-methylpseudouridine, and 5-aminopseudouridine and at least one of pseudoisocytidine, N4-methylcytidine, 2-thiocytidine, 5-azacytidine, 5-hydroxycytidine, 5-aminocytidine, 5-methylcytidine, N4-methylpseudoisocytidine, 2-thiopseudoisocytidine, 5-hydroxypseudoisocytidine, 5-aminopseudoisocytidine, and 5-methylpseudoisocytidine. In still another embodiment, the one or more nucleotides include at least one of pseudouridine, 2-thiouridine, 4-thiouridine, 5-azauridine, 5-hydroxyuridine, 5-methyluridine, 5-aminouridine, 2-thiopseudouridine, 4-thiopseudouridine, 5-hydroxypseudouridine, and 5-methylpseudouridine, 5-aminopseudouridine and at least one of pseudoisocytidine, N4-methylcytidine, 2-thiocytidine, 5-azacytidine, 5-hydroxycytidine, 5-aminocytidine, 5-methylcytidine, N4-methylpseudoisocytidine, 2-thiopseudoisocytidine, 5-hydroxypseudoisocytidine, 5-aminopseudoisocytidine, and 5-methylpseudoisocytidine and at least one of 7-deazaguanosine, 6-thioguanosine, 6-thio-7-deazaguanosine, and 5-methoxyuridine. In yet another embodiment, the one or more nucleotides includes: 5-methylcytidine and 7-deazaguanosine. In another embodiment, the one or more nucleotides also includes pseudouridine or 4-thiouridine or 5-methyluridine or 5-aminouridine or 4-thiopseudouridine or 5-methylpseudouridine or 5-aminopseudouridine. In a still another embodiment, the one or more nucleotides also includes 7-deazaadenosine. In another embodiment, the one or more nucleotides includes: pseudoisocytidine and 7-deazaguanosine and 4-thiouridine. In yet another embodiment, the one or more nucleotides includes: pseudoisocytidine or 7-deazaguanosine and pseudouridine. In still another embodiment, the one or more nucleotides includes: 5-methyluridine and 5-methylcytidine and 7-deazaguanosine. In a further embodiment, the one or more nucleotides includes: pseudouridine or 5-methylpseudouridine and 5-methylcytidine and 7-deazaguanosine. In another embodiment, the one or more nucleotides includes: pseudoisocytidine and 7-deazaguanosine and pseudouridine. In one embodiment, the RNA comprising one or more non-canonical nucleotides is present *in vivo*.

Certain non-canonical nucleotides can be incorporated more efficiently than other non-canonical nucleotides into RNA molecules by RNA polymerases that are commonly used for *in vitro* transcription, due in part to the tendency of these certain non-canonical nucleotides to participate in standard base-pairing interactions and base-stacking interactions, and to interact with the RNA polymerase in a manner similar to that in which the corresponding canonical nucleotide interacts with the RNA polymerase. As a result, certain nucleotide mixtures containing one or more non-canonical nucleotides can be beneficial in part because *in vitro*-transcription reactions containing these nucleotide mixtures can yield a large quantity of RNA. Certain embodiments are therefore directed to a nucleotide mixture containing one or more nucleotides that includes one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine. Nucleotide mixtures include, but are not limited to (numbers preceding each nucleotide indicate an exemplary fraction of the non-canonical nucleotide triphosphate in an *in vitro*-transcription reaction, for example, 0.2 pseudoisocytidine refers to a reaction containing adenosine-5'-triphosphate, guanosine-5'-triphosphate, uridine-5'-triphosphate, cytidine-5'-triphosphate, and pseudoisocytidine-5'-triphosphate, wherein pseudoisocytidine-5'-triphosphate is present in the reaction at an amount approximately equal to 0.2 times the total amount of pseudoisocytidine-5'-triphosphate + cytidine-5'-triphosphate that is present in the reaction, with amounts measured either on a molar or mass basis, and wherein more than one number preceding a nucleoside indicates a range of exemplary fractions): 1.0 pseudouridine, 0.1 – 0.8 2-thiouridine, 0.1 – 0.8 5-methyluridine, 0.2 – 1.0 5-hydroxyuridine, 0.2 – 1.0 5-methoxyuridine, 0.1 – 1.0 5-aminouridine, 0.1 – 1.0 4-thiouridine, 0.1 – 1.0 2-thiopseudouridine, 0.1 – 1.0 4-thiopseudouridine, 0.1 – 1.0 5-hydroxypseudouridine, 0.2 – 1 5-methylpseudouridine, 0.2 – 1.0 5-methoxypseudouridine, 0.1 – 1.0 5-aminopseudouridine, 0.2 – 1.0 2-thiocytidine, 0.1 – 0.8 pseudoisocytidine, 0.2 – 1.0 5-methylcytidine, 0.2 – 1.0 5-hydroxycytidine, 0.2 – 1.0 5-hydroxymethylcytidine, 0.2 – 1.0 5-methoxycytidine, 0.1 – 1.0 5-aminocytidine, 0.2 – 1.0 N4-methylcytidine, 0.2 – 1.0 5-methylpseudoisocytidine, 0.2 – 1.0 5-hydroxypseudoisocytidine, 0.2 – 1.0 5-aminopseudoisocytidine, 0.2 – 1.0 N4-methylpseudoisocytidine, 0.2 – 1.0 2-thiopseudoisocytidine, 0.2 – 1.0 7-deazaguanosine, 0.2 – 1.0 6-thioguanosine, 0.2 – 1.0 6-thio-7-deazaguanosine, 0.2 – 1.0 8-azaguanosine, 0.2 – 1.0 7-deaza-8-azaguanosine, 0.2 – 1.0 6-thio-8-azaguanosine, 0.1 – 0.5 7-deazaadenosine, and 0.1 – 0.5 N6-methyladenosine.

In various embodiments, the RNA comprising one or more non-canonical nucleotides composition or synthetic polynucleotide composition (*e.g.*, which may be prepared by in vitro transcription) contains substantially or entirely the canonical nucleotide at positions having adenine or "A" in the genetic code. The term "substantially" in this context refers to at least 90%. In these embodiments, the RNA composition or synthetic polynucleotide composition may further contain (*e.g.*, consist of) 7-deazaguanosine at positions with "G" in the genetic code as well as the corresponding canonical nucleotide "G", and the canonical and non-canonical nucleotide at positions with G may be in the range of 5:1 to 1:5, or in some embodiments in the range of 2:1 to 1:2. In these embodiments, the RNA composition or synthetic polynucleotide composition may further contain (*e.g.*, consist of) one or more (*e.g.*, two, three or four) of 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine at positions with "C" in the genetic code as well as the

canonical nucleotide "C", and the canonical and non-canonical nucleotide at positions with C may be in the range of 5:1 to 1:5, or in some embodiments in the range of 2:1 to 1:2. In some embodiments, the level of non-canonical nucleotide at positions of "C" are as described in the preceding paragraph. In these embodiments, the RNA composition or synthetic polynucleotide composition may further contain (*e.g.*, consist of) one or more (*e.g.*, two, three, or four) of 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, pseudouridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridineat positions with "U" in the genetic code as well as the canonical nucleotide "U", and the canonical and non-canonical nucleotide at positions with "U" may be in the range of 5:1 to 1:5, or in some embodiments in the range of 2:1 to 1:2. In some embodiments, the level of non-canonical nucleotide at positions of "U" are as described in the preceding paragraph.

It has now been discovered that combining certain non-canonical nucleotides can be beneficial in part because the contribution of non-canonical nucleotides to lowering the toxicity of RNA molecules can be additive. Certain embodiments are therefore directed to a nucleotide mixture, wherein the nucleotide mixture contains more than one of the non-canonical nucleotides listed above, for example, the nucleotide mixture contains both pseudoisocytidine and 7-deazaguanosine or the nucleotide mixture contains both N4-methylcytidine and 7-deazaguanosine, *etc.* In one embodiment, the nucleotide mixture contains more than one of the non-canonical nucleotides listed above, and each of the non-canonical nucleotides is present in the mixture at the fraction listed above, for example, the nucleotide mixture contains 0.1 – 0.8 pseudoisocytidine and 0.2 – 1.0 7-deazaguanosine or the nucleotide mixture contains 0.2 – 1.0 N4-methylcytidine and 0.2 – 1.0 7-deazaguanosine, *etc.*

In certain situations, for example, when it may not be necessary or desirable to maximize the yield of an *in vitro*-transcription reaction, nucleotide fractions other than those given above may be used. The exemplary fractions and ranges of fractions listed above relate to nucleotide-triphosphate solutions of typical purity (greater than 90% purity). Larger fractions of these and other nucleotides can be used by using nucleotide-triphosphate solutions of greater purity, for example, greater than about 95% purity or greater than about 98% purity or greater than about 99% purity or greater than about 99.5% purity, which can be achieved, for example, by purifying the nucleotide triphosphate solution using existing chemical-purification technologies such as high-pressure liquid chromatography (HPLC) or by other means. In one embodiment, nucleotides with multiple isomers are purified to enrich the desired isomer.

Other embodiments are directed to a method for inducing a cell *in vivo* to express a protein of interest by contacting the cell with a RNA molecule that contains one or more non-canonical nucleotides that includes one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine. Still other embodiments are directed to a method for transfecting, reprogramming, and/or gene-editing a cell *in vivo* by contacting the cell with a RNA molecule that contains one or more non-canonical nucleotides that includes one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine. In one embodiment,

the RNA molecule is produced by *in vitro* transcription. In one embodiment, the RNA molecule encodes one or more reprogramming factors. In another embodiment, the one or more reprogramming factors includes Oct4 protein. In another embodiment, the cell is also contacted with a RNA molecule that encodes Sox2 protein. In yet another embodiment, the cell is also contacted with a RNA molecule that encodes Klf4 protein. In yet another embodiment, the cell is also contacted with a RNA molecule that encodes c-Myc protein. In yet another embodiment, the cell is also contacted with a RNA molecule that encodes Lin28 protein.

Enzymes such as T7 RNA polymerase may preferentially incorporate canonical nucleotides in an *in vitro*-transcription reaction containing both canonical and non-canonical nucleotides. As a result, an *in vitro*-transcription reaction containing a certain fraction of a non-canonical nucleotide may yield RNA containing a different, often lower, fraction of the non-canonical nucleotide than the fraction at which the non-canonical nucleotide was present in the reaction. In certain embodiments, references to nucleotide incorporation fractions (for example, "a synthetic RNA molecule containing 50% pseudoisocytidine" or "0.1 – 0.8 pseudoisocytidine") therefore can refer both to RNA molecules containing the stated fraction of the nucleotide, and to RNA molecules synthesized in a reaction containing the stated fraction of the nucleotide (or nucleotide derivative, for example, nucleotide-triphosphate), even though such a reaction may yield RNA containing a different fraction of the nucleotide than the fraction at which the non-canonical nucleotide was present in the reaction.

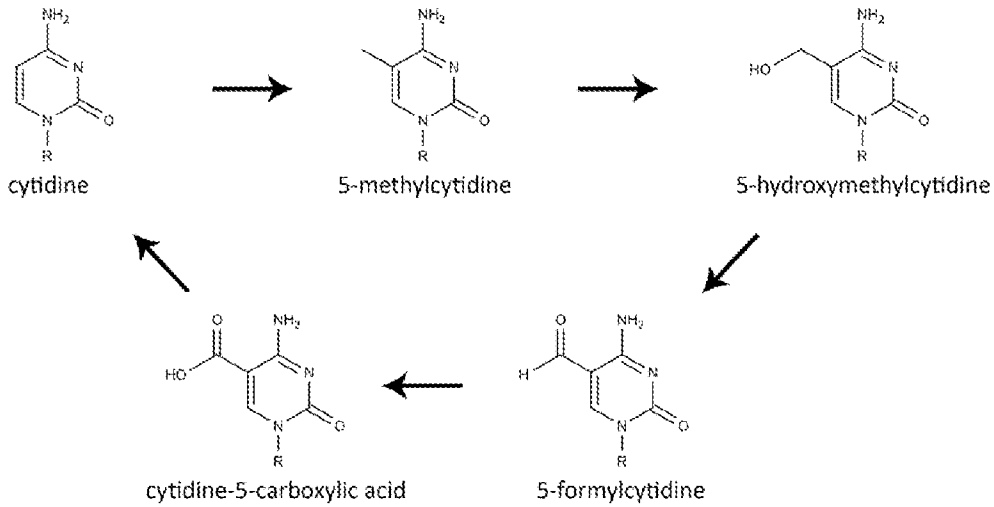
Different nucleotide sequences can encode the same protein by utilizing alternative codons. In certain embodiments, references to nucleotide incorporation fractions therefore can refer both to RNA molecules containing the stated fraction of the nucleotide, and to RNA molecules encoding the same protein as a different RNA molecule, wherein the different RNA molecule contains the stated fraction of the nucleotide.

Certain embodiments are directed to a kit containing one or more materials needed to practice the present invention. In one embodiment, the kit contains one or more synthetic RNA molecules. In one embodiment, the kit contains one or more synthetic RNA molecules that encode one or more reprogramming factors and/or gene-editing proteins. In another embodiment, the one or more synthetic RNA molecules contain one or more non-canonical nucleotides that include one or more substitutions at the 2C and/or 4C and/or 5C positions in the case of a pyrimidine or the 6C and/or 7N and/or 8C positions in the case of a purine. In another embodiment, the kit contains one or more of: a transfection medium, a transfection reagent, a complexation medium, and a matrix solution. In one embodiment, the matrix solution contains fibronectin and/or vitronectin or recombinant fibronectin and/or recombinant vitronectin. In one embodiment, one or more of the components of the kit are present as a plurality of aliquots. In one embodiment, the kit contains aliquots of nucleic acid transfection-reagent complexes. In another embodiment, the kit contains aliquots of nucleic acid transfection-reagent complexes that are provided in a solid form, for example, as frozen or freeze-dried pellets. In yet another embodiment, the kit contains aliquots of medium, wherein each aliquot contains transfection reagent-nucleic acid complexes that are stabilized either by chemical treatment or by freezing.

Transfection, in general, and reprogramming, in particular, can be difficult and time-consuming techniques that can be repetitive and prone to error. However, these techniques are often performed manually due to the lack of automated transfection equipment. Certain embodiments are therefore directed to a system that can transfect, reprogram, and/or gene-edit cells *in vivo* in an automated or semi-automated manner.

It has now been discovered that the non-canonical nucleotide members of the 5-methylcytidine de-methylation pathway, when incorporated into synthetic RNA, can increase the efficiency with which the synthetic RNA can be translated into protein *in vivo*, and can decrease the toxicity of the synthetic RNA *in vivo*. These non-canonical nucleotides include, for example: 5-methylcytidine, 5-hydroxymethylcytidine, 5-formylcytidine, and 5-carboxycytidine (a.k.a. "cytidine-5-carboxylic acid"). Certain embodiments are therefore directed to a nucleic acid. In some embodiments, the nucleic acid is present *in vivo*. In one embodiment, the nucleic acid is a synthetic RNA molecule. In another embodiment, the nucleic acid comprises one or more non-canonical nucleotides. In one embodiment, the nucleic acid comprises one or more non-canonical nucleotide members of the 5-methylcytidine de-methylation pathway. In another embodiment, the nucleic acid comprises at least one of: 5-methylcytidine, 5-hydroxymethylcytidine, 5-formylcytidine, and 5-carboxycytidine or a derivative thereof. In a further embodiment, the nucleic acid comprises at least one of: pseudouridine, 5-methylpseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-methylcytidine, 5-hydroxymethylcytidine, N4-methylcytidine, N4-acetylcytidine, and 7-deazaguanosine or a derivative thereof.

5-methylcytidine De-Methylation Pathway



Certain embodiments are directed to a protein. Other embodiments are directed to a nucleic acid that encodes a protein. In one embodiment, the protein is a protein of interest. In another embodiment, the protein is selected from: a reprogramming protein and a gene-editing protein. In one embodiment, the nucleic acid is a plasmid. In another embodiment, the nucleic acid is present in a virus or viral vector. In a further embodiment, the virus or viral vector is replication incompetent. In a still further embodiment, the virus or viral vector is replication competent. In one embodiment, the virus or viral vector includes at least one of: an adenovirus, a retrovirus, a

lentivirus, a herpes virus, an adeno-associated virus or a natural or engineered variant thereof, and an engineered virus.

It has also been discovered that certain combinations of non-canonical nucleotides can be particularly effective at increasing the efficiency with which synthetic RNA can be translated into protein *in vivo*, and decreasing the toxicity of synthetic RNA *in vivo*, for example, the combinations: 5-methyluridine and 5-methylcytidine, 5-hydroxyuridine and 5-methylcytidine, 5-hydroxyuridine and 5-hydroxymethylcytidine, 5-methyluridine and 7-deazaguanosine, 5-methylcytidine and 7-deazaguanosine, 5-methyluridine, 5-methylcytidine, and 7-deazaguanosine, and 5-methyluridine, 5-hydroxymethylcytidine, and 7-deazaguanosine. Certain embodiments are therefore directed to a nucleic acid comprising at least two of: 5-methyluridine, 5-methylcytidine, 5-hydroxymethylcytidine, and 7-deazaguanosine or one or more derivatives thereof. Other embodiments are directed to a nucleic acid comprising at least three of: 5-methyluridine, 5-methylcytidine, 5-hydroxymethylcytidine, and 7-deazaguanosine or one or more derivatives thereof. Other embodiments are directed to a nucleic acid comprising all of: 5-methyluridine, 5-methylcytidine, 5-hydroxymethylcytidine, and 7-deazaguanosine or one or more derivatives thereof. In one embodiment, the nucleic acid comprises one or more 5-methyluridine residues, one or more 5-methylcytidine residues, and one or more 7-deazaguanosine residues or one or more 5-methyluridine residues, one or more 5-hydroxymethylcytidine residues, and one or more 7-deazaguanosine residues.

It has been further discovered that synthetic RNA molecules containing certain fractions of certain non-canonical nucleotides and combinations thereof can exhibit particularly high translation efficiency and low toxicity *in vivo*. Certain embodiments are therefore directed to a nucleic acid comprising at least one of: one or more uridine residues, one or more cytidine residues, and one or more guanosine residues, and comprising one or more non-canonical nucleotides. In one embodiment, between about 20% and about 80% of the uridine residues are 5-methyluridine residues. In another embodiment, between about 30% and about 50% of the uridine residues are 5-methyluridine residues. In a further embodiment, about 40% of the uridine residues are 5-methyluridine residues. In one embodiment, between about 60% and about 80% of the cytidine residues are 5-methylcytidine residues. In another embodiment, between about 80% and about 100% of the cytidine residues are 5-methylcytidine residues. In a further embodiment, about 100% of the cytidine residues are 5-methylcytidine residues. In a still further embodiment, between about 20% and about 100% of the cytidine residues are 5-hydroxymethylcytidine residues. In one embodiment, between about 20% and about 80% of the guanosine residues are 7-deazaguanosine residues. In another embodiment, between about 40% and about 60% of the guanosine residues are 7-deazaguanosine residues. In a further embodiment, about 50% of the guanosine residues are 7-deazaguanosine residues. In one embodiment, between about 20% and about 80% or between about 30% and about 60% or about 40% of the cytidine residues are N4-methylcytidine and/or N4-acetylcytidine residues. In another embodiment, each cytidine residue is a 5-methylcytidine residue. In a further embodiment, about 100% of the cytidine residues are 5-methylcytidine residues and/or 5-hydroxymethylcytidine residues and/or N4-methylcytidine residues and/or N4-acetylcytidine residues and/or one or more derivatives thereof. In a

still further embodiment, about 40% of the uridine residues are 5-methyluridine residues, between about 20% and about 100% of the cytidine residues are N4-methylcytidine and/or N4-acetylcytidine residues, and about 50% of the guanosine residues are 7-deazaguanosine residues. In one embodiment, about 40% of the uridine residues are 5-methyluridine residues and about 100% of the cytidine residues are 5-methylcytidine residues. In another embodiment, about 40% of the uridine residues are 5-methyluridine residues and about 50% of the guanosine residues are 7-deazaguanosine residues. In a further embodiment, about 100% of the cytidine residues are 5-methylcytidine residues and about 50% of the guanosine residues are 7-deazaguanosine residues. In a further embodiment, about 100% of the uridine residues are 5-hydroxyuridine residues. In one embodiment, about 40% of the uridine residues are 5-methyluridine residues, about 100% of the cytidine residues are 5-methylcytidine residues, and about 50% of the guanosine residues are 7-deazaguanosine residues. In another embodiment, about 40% of the uridine residues are 5-methyluridine residues, between about 20% and about 100% of the cytidine residues are 5-hydroxymethylcytidine residues, and about 50% of the guanosine residues are 7-deazaguanosine residues. In some embodiments, less than 100% of the cytidine residues are 5-methylcytidine residues. In other embodiments, less than 100% of the cytidine residues are 5-hydroxymethylcytidine residues. In one embodiment, each uridine residue in the synthetic RNA molecule is a pseudouridine residue or a 5-methylpseudouridine residue. In another embodiment, about 100% of the uridine residues are pseudouridine residues and/or 5-methylpseudouridine residues. In a further embodiment, about 100% of the uridine residues are pseudouridine residues and/or 5-methylpseudouridine residues, about 100% of the cytidine residues are 5-methylcytidine residues, and about 50% of the guanosine residues are 7-deazaguanosine residues.

Other non-canonical nucleotides that can be used in place of or in combination with 5-methyluridine include, but are not limited to: pseudouridine, 5-hydroxyuridine, 5-hydroxypseudouridine, 5-methoxyuridine, 5-methoxypseudouridine, 5-carboxyuridine, 5-carboxypseudouridine, 5-formyluridine, 5-formylpseudouridine, 5-hydroxymethyluridine, 5-hydroxymethylpseudouridine, and 5-methylpseudouridine (a.k.a. "1-methylpseudouridine", a.k.a. "N1-methylpseudouridine") or one or more derivatives thereof. Other non-canonical nucleotides that can be used in place of or in combination with 5-methylcytidine and/or 5-hydroxymethylcytidine include, but are not limited to: pseudoisocytidine, 5-methylpseudoisocytidine, 5-hydroxymethylcytidine, 5-formylcytidine, 5-carboxycytidine, 5-methoxycytidine, N4-methylcytidine, N4-acetylcytidine or one or more derivatives thereof. In certain embodiments, for example, when performing only a single transfection, injection or delivery or when the cells, tissue, organ or patient being transfected, injected or delivered to are not particularly sensitive to transfection-associated toxicity or innate-immune signaling, the fractions of non-canonical nucleotides can be reduced. Reducing the fraction of non-canonical nucleotides can be beneficial, in part, because reducing the fraction of non-canonical nucleotides can reduce the cost of the nucleic acid. In certain situations, for example, when minimal immunogenicity of the nucleic acid is desired, the fractions of non-canonical nucleotides can be increased.

Enzymes such as T7 RNA polymerase may preferentially incorporate canonical nucleotides in an *in vitro*-transcription reaction containing both canonical and non-canonical nucleotides. As a result, an *in vitro*-transcription reaction containing a certain fraction of a non-canonical nucleotide may yield RNA containing a different, often lower, fraction of the non-canonical nucleotide than the fraction at which the non-canonical nucleotide was present in the reaction. In certain embodiments, references to nucleotide incorporation fractions (for example, "50% 5-methyluridine") therefore can refer both to nucleic acids containing the stated fraction of the nucleotide, and to nucleic acids synthesized in a reaction containing the stated fraction of the nucleotide (or nucleotide derivative, for example, nucleotide-triphosphate), even though such a reaction may yield a nucleic acid containing a different fraction of the nucleotide than the fraction at which the non-canonical nucleotide was present in the reaction. In addition, different nucleotide sequences can encode the same protein by utilizing alternative codons. In certain embodiments, references to nucleotide incorporation fractions therefore can refer both to nucleic acids containing the stated fraction of the nucleotide, and to nucleic acids encoding the same protein as a different nucleic acid, wherein the different nucleic acid contains the stated fraction of the nucleotide.

Certain embodiments are directed to a nucleic acid comprising a 5'-cap structure selected from Cap 0, Cap 1, Cap 2, and Cap 3 or a derivative thereof. In one embodiment, the nucleic acid comprises one or more UTRs. In another embodiment, the one or more UTRs increase the stability of the nucleic acid. In a further embodiment, the one or more UTRs comprise an alpha-globin or beta-globin 5'-UTR. In a still further embodiment, the one or more UTRs comprise an alpha-globin or beta-globin 3'-UTR. In a still further embodiment, the synthetic RNA molecule comprises an alpha-globin or beta-globin 5'-UTR and an alpha-globin or beta-globin 3'-UTR. In one embodiment, the 5'-UTR comprises a Kozak sequence that is substantially similar to the Kozak consensus sequence. In another embodiment, the nucleic acid comprises a 3'-poly(A) tail. In a further embodiment, the 3'-poly(A) tail is between about 20 nt and about 250 nt or between about 120 nt and about 150 nt long. In a further embodiment, the 3'-poly(A) tail is about 20 nt, or about 30 nt, or about 40 nt, or about 50 nt, or about 60 nt, or about 70 nt, or about 80 nt, or about 90 nt, or about 100 nt, or about 110 nt, or about 120 nt, or about 130 nt, or about 140 nt, or about 150 nt, or about 160 nt, or about 170 nt, or about 180 nt, or about 190 nt, or about 200 nt, or about 210 nt, or about 220 nt, or about 230 nt, or about 240 nt, or about 250 nt long.

Certain embodiments are directed to methods of making nucleic acid drugs, including RNA comprising one or more non-canonical nucleotides. Such methods yield substantially stable RNA.

In various embodiments, the present methods and compositions find use in methods of treating, preventing or ameliorating a disease, disorder and/or condition. For instance, in some embodiments, the described methods of in vivo delivery, including various effective doses, administration strategies and formulations are used in a method of treatment.

In various embodiments, the present methods and compositions find use in methods of altering, modifying and/or changing a tissue (*e.g.* cosmetically).

In various embodiments, the present methods and compositions include using a nucleic acid drug, including a synthetic RNA, in the diagnosing, treating, preventing or ameliorating of a disease, disorder and/or condition described herein. In various embodiments, the present methods and compositions include using a nucleic acid drug, including a synthetic RNA, in the altering, modifying and/or changing of a tissue (*e.g.* cosmetically).

Generally speaking, in various embodiments, a synthetic RNA as described herein is administered to a human at specific doses described herein and the synthetic RNA comprises a sequence, sometimes referred to as a target sequence that encodes a protein of interest, which may be a therapeutic protein.

Synthetic RNA comprising only canonical nucleotides can bind to pattern recognition receptors, can be recognized as a pathogen-associated molecular pattern, and can trigger a potent immune response in cells, which can result in translation block, the secretion of inflammatory cytokines, and cell death. It has now been discovered that synthetic RNA comprising certain non-canonical nucleotides can evade detection by the innate immune system, and can be translated at high efficiency into protein, including in humans. It has been further discovered that synthetic RNA comprising at least one of the non-canonical nucleotides described herein, including, for example, a member of the group: 5-methylcytidine, 5-hydroxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine, pseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-methoxyuridine, 5-formyluridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-methoxypseudouridine, and 5-formylpseudouridine can evade detection by the innate immune system, and can be translated at high efficiency into protein, including in humans. Certain embodiments are therefore directed to a method for inducing a cell to express a protein of interest comprising contacting a cell with synthetic RNA. Other embodiments are directed to a method for transfecting a cell with synthetic RNA comprising contacting a cell with a solution comprising one or more synthetic RNA molecules. Still other embodiments are directed to a method for treating a patient comprising administering to the patient synthetic RNA. In one embodiment, the synthetic RNA comprises at least one of the non-canonical nucleotides described herein, including, for example, a member of the group: 5-methylcytidine, 5-hydroxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine, pseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-methoxyuridine, 5-formyluridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-methoxypseudouridine, and 5-formylpseudouridine. In another embodiment, the synthetic RNA encodes a protein of interest. Exemplary RNAs may contain combinations and levels of non-canonical and non-canonical nucleotides as described elsewhere herein, including with respect to the expression of any protein of interest described herein. In yet another embodiment, the method results in the expression of the protein of interest. In a further embodiment, the method results in the expression of the protein of interest in the patient's skin.

Other embodiments are directed to a method for delivering a nucleic acid to a cell *in vivo*. Still other embodiments are directed to a method for inducing a cell *in vivo* to express a protein of interest. Still other embodiments are directed to a method for treating a patient. In one embodiment, the method comprises

disrupting the stratum corneum. In another embodiment, the method comprises contacting a cell with a nucleic acid. In yet another embodiment, the method results in the cell internalizing the nucleic acid. In a further embodiment, the method results in the cell expressing the protein of interest. In a still further embodiment, the method results in the expression of the protein of interest in the patient. In a still further embodiment, the method results in the amelioration of one or more of the patient's symptoms. In a still further embodiment, the patient is in need of the protein of interest. In a still further embodiment, the patient is deficient in the protein of interest.

Still other embodiments are directed to a method for treating a patient comprising delivering to a patient a composition. In one embodiment, the composition comprises albumin that is treated with an ion-exchange resin or charcoal. In another embodiment, the composition comprises one or more nucleic acid molecules. In yet another embodiment, at least one of the one or more nucleic acid molecules encodes a protein of interest. In one embodiment, the method results in the expression of the protein in the patient's skin. In another embodiment, the method results in the expression of a therapeutically or cosmetically effective amount of the protein of interest in the patient. In yet another embodiment, the method comprises administering a steroid. In a further embodiment, the steroid is a member of the group: hydrocortisone and dexamethasone.

Some embodiments are directed to a therapeutic composition and/or methods of treatment comprising a nucleic acid molecule encoding one or more proteins, wherein at least one of the one or more proteins is an extracellular matrix protein. Still other embodiments are directed to a cosmetic composition comprising a nucleic acid molecule encoding one or more proteins, wherein at least one of the one or more proteins is an extracellular matrix protein.

Pigmentation disorders can cause severe symptoms in patients. It has now been discovered that pigmentation disorders can be treated by delivering to a patient a nucleic acid encoding tyrosinase. Certain embodiments are therefore directed to a method for treating a pigmentation disorder. Other embodiments are directed to a method for altering the pigmentation of a patient. In one embodiment, the method comprises delivering to a patient a nucleic acid encoding tyrosinase. Other embodiments are directed to a cosmetic composition comprising a nucleic acid encoding tyrosinase. Still other embodiments are directed to a therapeutic composition comprising a nucleic acid encoding tyrosinase. Still other embodiments are directed to a method for increasing the ultraviolet absorption of a patient's skin. In one embodiment the method comprises delivering to a patient a nucleic acid encoding tyrosinase. In another embodiment, the method results in an increase in the ultraviolet absorption of the patient's skin. Still other embodiments are directed to a method for reducing photodamage to a person's skin upon exposure to ultraviolet light. In one embodiment, the method results in the reduction of photodamage to the person's skin upon exposure to ultraviolet light. Still other embodiments are directed to a method for treating xeroderma pigmentosum. In one embodiment, the method comprises delivering to a patient a nucleic acid encoding tyrosinase. Still other embodiments are directed to a method for treating epidermolysis bullosa. In one embodiment, the method comprises delivering to a patient a nucleic acid encoding one or more of keratin 5, keratin 14, plectin, an integrin family member, laminin, a laminin subunit, collagen XVII, collagen VII or a biologically active fragment, variant, analogue or family-member thereof. In one embodiment, the method

comprises delivering to a patient a nucleic acid encoding collagen type VII. In another embodiment, the method comprises delivering to a patient a nucleic acid encoding melanocortin 1 receptor. Still other embodiments are directed to a method for treating xerosis. In one embodiment, the method comprises delivering to a patient a nucleic acid encoding a hyaluronan synthase. In another embodiment, the patient is diagnosed with atopic dermatitis. In yet another embodiment, the patient is diagnosed with ichthyosis. Certain embodiments are directed to a method for treating a cosmetic condition. Other embodiments are directed to a method for inducing tissue healing. In one embodiment, the method comprises delivering to a patient a nucleic acid encoding a hyaluronan synthase. In another embodiment, the cosmetic condition is a member of the group: wrinkles, sagging skin, thin skin, discoloration, and dry skin. In yet another embodiment, the patient has had cataract surgery. In some embodiments, the nucleic acid is synthetic RNA. In other embodiments, the method results in the amelioration of one or more of the patient's symptoms. Other embodiments are directed to a method for treating an indication by delivering to a cell or a patient a nucleic acid encoding a protein or a peptide. Still other embodiments are directed to a composition comprising a nucleic acid encoding a protein or a peptide. Indications that can be treated using the methods and compositions of the present invention and proteins and peptides that can be encoded by compositions of the present invention are set forth in **Table 2A** and/or **Table 2B**, and are given by way of example, and not by way of limitation. In one embodiment, the indication is selected from **Table 2A** and/or **Table 2B**. In another embodiment the protein or peptide is selected from **Table 2A** and/or **Table 2B**. In yet another embodiment, the indication and the protein or peptide are selected from the same row of **Table 2A** and/or **Table 2B**. In a further embodiment, the protein of interest is a member of the group: UCP1, UCP2, and UCP3. Other embodiments are directed to methods for inducing a cell to express a plurality of proteins of interest. In one embodiment, the proteins of interest include at least two members of the group: a lipase, UCP1, UCP2, and UCP3. In another embodiment, the proteins of interest include a lipase and a member of the group: UCP1, UCP2, and UCP3. In another embodiment, the protein is a gene-editing protein. In yet another embodiment, the gene-editing protein targets a gene that is at least partly responsible for a disease phenotype. In yet another embodiment, the gene-editing protein targets a gene that encodes a protein selected from **Table 2A** and/or **Table 2B**. In still another embodiment, the gene-editing protein corrects or eliminates, either alone or in combination with one or more other molecules or gene-editing proteins, a mutation that is at least partly responsible for a disease phenotype.

In various embodiments, the present invention contemplates the targeting of the precursor forms and/or mature forms and/or isoforms and/or mutants of any of the proteins disclosed in **Table 2A** and/or **Table 2B** and such proteins. In some embodiments, any of the precursor forms and/or mature forms and/or isoforms and/or mutants have enhanced secretion relative to the corresponding wild type proteins. In some embodiments, any of the precursor forms and/or mature forms and/or isoforms and/or mutants have altered half-lives (*e.g.* serum, plasma, intracellular) - for instance, longer or shorter half-lives. In some embodiments, this is relative to wild type.

Table 2A. *Illustrative Indications*

Illustrative Indication	**Illustrative Protein / Peptide**

Acne	Retinol Dehydrogenase 10
Aging	Elastin sp|P15502|ELN_HUMAN Elastin (isoform 3) (SEQ ID NO:486)
Aging	Collagen Type I P02452|CO1A1_HUMAN Collagen alpha-1(I) chain (SEQ ID NO:487) P08123|CO1A2_HUMAN Collagen alpha-2(I) chain (SEQ ID NO:488)
Aging	Collagen Type III P02461|CO3A1_HUMAN Collagen alpha-1(III) chain (isoform 1) (SEQ ID NO:489)
Aging	Collagen Type VII Q02388|CO7A1_HUMAN Collagen alpha-1(VII) chain (SEQ ID NO:490)
Aging	Hyaluronan Synthase
Aging	Telomerase Reverse Transcriptase
Albinism	Tyrosinase P14679|TYRO_HUMAN Tyrosinase (isoform 1) (SEQ ID NO:491)
Alport Syndrome	Collagen Type IV P02462|CO4A1_HUMAN Collagen alpha-1(IV) chain (isoform 1) (SEQ ID NO:492) P08572|CO4A2_HUMAN Collagen alpha-2(IV) chain (SEQ ID NO:493) Q01955|CO4A3_HUMAN Collagen alpha-3(IV) chain (isoform 1) (SEQ ID NO:494) P53420|CO4A4_HUMAN Collagen alpha-4(IV) chain (SEQ ID NO:495) P29400|CO4A5_HUMAN Collagen alpha-5(IV) chain (isoform 1) (SEQ ID NO:496) Q14031|CO4A6_HUMAN Collagen alpha-6(IV) (isoform A) (SEQ ID NO:497)
Anemia	Erythropoietin
Atopic Dermatitis	Filaggrin
Cutis Laxa	Elastin sp|P15502|ELN_HUMAN Elastin

	(isoform 3) (SEQ ID NO:486)
Dry Skin	Filaggrin
Dystrophic Epidermolysis Bullosa	Collagen Type VII Q02388|CO7A1_HUMAN Collagen alpha-1(VII) chain (SEQ ID NO:498)
Ehlers-Danlos Syndrome	Collagen Type V P20908|CO5A1_HUMAN Collagen alpha-1(V) chain (SEQ ID NO:499) P05997|CO5A2_HUMAN Collagen alpha-2(V) chain (SEQ ID NO:500) P25940|CO5A3_HUMAN Collagen alpha-3(V) chain (SEQ ID NO:501)
Ehlers-Danlos Syndrome	Collagen Type I P02452|CO1A1_HUMAN Collagen alpha-1(I) chain (SEQ ID NO:487) P08123|CO1A2_HUMAN Collagen alpha-2(I) chain (SEQ ID NO:488)
Epidermolysis bullosa, lethal acantholytic	ADAM17 P78536|ADA17_HUMAN Disintegrin and metalloproteinase domain-containing protein 17 (isoform A) (SEQ ID NO:502)
Epidermolysis bullosa, type IV	Collagen Type III P02461|CO3A1_HUMAN Collagen alpha-1(III) chain (isoform 1) (SEQ ID NO:489)
Erythropoietic Protoporphyria	Ferrochelatase P22830|HEMH_HUMAN Ferrochelatase, mitochondrial (isoform 1) (SEQ ID NO:503)
Eczema	Filaggrin
Excess Fat	Thermogenin P25874|UCP1_HUMAN Mitochondrial brown fat uncoupling protein 1 (SEQ ID NO:504)
Excess Fat	Lipase Lipoprotein lipase P06858|LIPL_HUMAN Lipoprotein lipase (SEQ ID NO:516) Hepatic lipase P11150|LIPC_HUMAN Hepatic triacylglycerol lipase (SEQ ID NO:517)

	Pancreatic lipase P16233|LIPP_HUMAN Pancreatic triacylglycerol lipase (SEQ ID NO:518) Endothelial lipase (isoform 1) Q9Y5X9|LIPE_HUMAN Endothelial lipase (SEQ ID NO:519) Lysosomal lipase P38571|LICH_HUMAN Lysosomal acid lipase/cholesteryl ester hydrolase (isoform 1) (SEQ ID NO:520) Hormone sensitive lipase Q05469|LIPS_HUMAN Hormone-sensitive lipas (isoform 1) (SEQ ID NO:521) Gastric lipase P07098|LIPG_HUMAN Gastric triacylglycerol lipase (isoform 1) (SEQ ID NO:522) Pancreatic Lipase-Related Protein 1) P54315|LIPR1_HUMAN Inactive pancreatic lipase-related protein 1 (isoform 1) (SEQ ID NO:523) Pancreatic Lipase-Related Protein 2 P54317|LIPR2_HUMAN Pancreatic lipase-related protein 2 (SEQ ID NO:524) Carboxyl Ester Lipase P19835|CEL_HUMAN Bile salt-activated lipase (isoform long) (SEQ ID NO:525)
Hypotrichosis	ADAM17 P78536|ADA17_HUMAN Disintegrin and metalloproteinase domain-containing protein 17 (isoform A) (SEQ ID NO:502)
Ichthyosis Vulgaris	Filaggrin
Infections	Genetic Antibiotics (*e.g.* Anti-Sigma Factors)
Inflammatory and Bullous Skin Bowel Syndrome	Desmoglein 2 Q14126|DSG2_HUMAN Desmoglein-2 (SEQ ID NO:505)
Keratosis Pilaris	Retinol Dehydrogenase 10
Oily Skin	Retinol Dehydrogenase 10

Osteoarthritis	Hyaluronan Synthase
Pemphigus Vulgaris	Plakophilin-1 Q13835|PKP1_HUMAN Plakophilin-1 (isoform 2) (SEQ ID NO:506)
Pseudoxanthoma elasticum	Elastin sp|P15502|ELN_HUMAN Elastin (isoform 3) (SEQ ID NO:486)
Psoriasis	Retinol Dehydrogenase 10
Scar Treatment	Tyrosinase P14679|TYRO_HUMAN Tyrosinase (isoform 1) (SEQ ID NO:491)
Scarring	Elastin sp|P15502|ELN_HUMAN Elastin (isoform 3) (SEQ ID NO:486)
Scarring	Collagen Type I P02452|CO1A1_HUMAN Collagen alpha-1(I) chain (SEQ ID NO:487) P08123|CO1A2_HUMAN Collagen alpha-2(I) chain (SEQ ID NO:488)
Scarring	Collagen Type III P02461|CO3A1_HUMAN Collagen alpha-1(III) chain (isoform 1) (SEQ ID NO:489)
Skin Cancer	Interferon Interferon, Alpha 1 P01562|IFNA1_HUMAN Interferon alpha-1/13 (SEQ ID NO:530) Interferon, Alpha 2 P01563|IFNA2_HUMAN Interferon alpha-2 (SEQ ID NO:531) Interferon, Alpha 4 P05014|IFNA4_HUMAN Interferon alpha-4 (SEQ ID NO:532) Interferon, Alpha 5 P01569|IFNA5_HUMAN Interferon alpha-5 (SEQ ID NO:533) Interferon, Alpha 6 P05013|IFNA6_HUMAN Interferon alpha-6 (SEQ ID NO:534) Interferon, Alpha 7 P01567|IFNA7_HUMAN Interferon alpha-7 (SEQ ID NO:535) Interferon, Alpha 8

	P32881|IFNA8_HUMAN Interferon alpha-8 (SEQ ID NO:536) Interferon, Alpha 10 P01566|IFN10_HUMAN Interferon alpha-10 (SEQ ID NO:537) Interferon, Alpha 14 P01570|IFN14_HUMAN Interferon alpha-14 OS (SEQ ID NO:538) Interferon, Alpha 16 P05015|IFN16_HUMAN Interferon alpha-16 (SEQ ID NO:539) Interferon, Alpha 17 P01571|IFN17_HUMAN Interferon alpha-17 (SEQ ID NO:540) Interferon, Alpha 21 P01568|IFN21_HUMAN Interferon alpha-21 (SEQ ID NO:541) Interferon, Gamma P01579|IFNG_HUMAN Interferon gamma (SEQ ID NO:542) Interferon, Beta P01574|IFNB_HUMAN Interferon beta (SEQ ID NO:543) Interferon, Kappa Q9P0W0|IFNK_HUMAN Interferon kappa (SEQ ID NO:544) Interferon, Epsilon Q86WN2|IFNE_HUMAN Interferon epsilon (SEQ ID NO:545)
Striate Palmoplantar Keratoderma	ADAM17 P78536|ADA17_HUMAN Disintegrin and metalloproteinase domain-containing protein 17 (isoform A) (SEQ ID NO:502)
Tanning	Tyrosinase P14679|TYRO_HUMAN Tyrosinase (isoform 1) (SEQ ID NO:491)
Vitiligo	Melanocyte-Stimulating Hormone Alpha-MSH P01189|138-150 (SEQ ID NO:526)

	Beta-MSH P01189|217-234 (SEQ ID NO:527) Gamma-MSH P01189|77-87 (SEQ ID NO:528) Proopiomelanocortin P01189|COLI_HUMAN Pro-opiomelanocortin (SEQ ID NO:529)
Vitiligo	Tyrosinase P14679|TYRO_HUMAN Tyrosinase (isoform 1) (SEQ ID NO:491)
Warts	Interferon Interferon, Alpha 1 P01562|IFNA1_HUMAN Interferon alpha-1/13 (SEQ ID NO:530) Interferon, Alpha 2 P01563|IFNA2_HUMAN Interferon alpha-2 (SEQ ID NO:531) Interferon, Alpha 4 P05014|IFNA4_HUMAN Interferon alpha-4 (SEQ ID NO:532) Interferon, Alpha 5 P01569|IFNA5_HUMAN Interferon alpha-5 (SEQ ID NO:533) Interferon, Alpha 6 P05013|IFNA6_HUMAN Interferon alpha-6 (SEQ ID NO:534) Interferon, Alpha 7 P01567|IFNA7_HUMAN Interferon alpha-7 (SEQ ID NO:535) Interferon, Alpha 8 P32881|IFNA8_HUMAN Interferon alpha-8 (SEQ ID NO:536) Interferon, Alpha 10 P01566|IFN10_HUMAN Interferon alpha-10 (SEQ ID NO:537) Interferon, Alpha 14 P01570|IFN14_HUMAN Interferon alpha-14 OS (SEQ ID NO:538) Interferon, Alpha 16 P05015|IFN16_HUMAN Interferon alpha-16 (SEQ ID NO:539)

	Interferon, Alpha 17 P01571|IFN17_HUMAN Interferon alpha-17 (SEQ ID NO:540) Interferon, Alpha 21 P01568|IFN21_HUMAN Interferon alpha-21 (SEQ ID NO:541) Interferon, Gamma P01579|IFNG_HUMAN Interferon gamma (SEQ ID NO:542) Interferon, Beta P01574|IFNB_HUMAN Interferon beta (SEQ ID NO:543) Interferon, Kappa Q9P0W0|IFNK_HUMAN Interferon kappa (SEQ ID NO:544) Interferon, Epsilon Q86WN2|IFNE_HUMAN Interferon epsilon (SEQ ID NO:545)
Wound Healing	Elastin sp|P15502|ELN_HUMAN Elastin (isoform 3) (SEQ ID NO:486)
Wound Healing	Collagen Type I P02452|CO1A1_HUMAN Collagen alpha-1(I) chain (SEQ ID NO:487) P08123|CO1A2_HUMAN Collagen alpha-2(I) chain (SEQ ID NO:488)
Wound Healing	Collagen Type III P02461|CO3A1_HUMAN Collagen alpha-1(III) chain (isoform 1) (SEQ ID NO:489)
Xeroderma Pigmentosum	DNA Polymerase Eta Q9Y253|POLH_HUMAN DNA polymerase eta (isoform 1) (SEQ ID NO:507)

Additional illustrative targets of the present invention include the cosmetic targets listed in Table 6 of International Patent Publication No. WO 2013/151671, the contents of which are hereby incorporated by reference in their entirety.

In various embodiments, the agents of the present invention are used in methods the effect the integumentary system of a human. The present compositions and methods may be used to alter a biological and/or physiological process to, for example, reduce skin sagging, increase skin thickness, increase skin volume, reduce the number of wrinkles, the length of wrinkles and/or the depth of wrinkles, increase skin tightness, firmness, tone and/or elasticity, increase skin hydration and ability to retain moisture, water flow and osmotic

balance, increase the levels of skin lipids; increase the extracellular matrix and/or adhesion and communication polypeptides; increase skin energy production; utilization and conservation; improve oxygen utilization; improve skin cell life; improve skin cell immunity defense, heat shock stress response, antioxidant defense capacity to neutralize free radicals, and/or toxic defense; improve the protection and recovery from ultraviolet rays; improve skin cell communication and skin cell innervations; improve cell cohesion/adhesion; improve calcium mineral and other mineral metabolism; improve cell turnover; and improve cell circadian rhythms.

Further still, in some embodiments, the present compositions may be used in the treatment, control, or prevention of a disease, disorder and/or condition and/or may alter, modify or change the appearance of a member of the integumentary system of a subject suffering from a disease, disorder and/or condition such as, but not limited to, acne vulgaris, acne aestivalis, acne conglobata, acne cosmetic, acne fulminans, acne keloidalis nuchae, acne mechanica, acne medicamentosa, acne miliaris necrotica, acne necrotica, acne rosacea, actinic keratosis, acne vulgaris, acne aestivalis, acne conglobata, acne cosmetic, acne fulminans, acne keloidalis nuchae, acne mechanica, acne medicamentosa, acne miliaris necrotica, acne necrotica, acne rosacea, acute urticaria, allergic contact dermatitis, alopecia areata, angioedema, athlete's foot, atopic dermatitis, autoeczematization, baby acne, balding, bastomycosis, blackheads, birthmarks and other skin pigmentation problems, boils, bruises, bug bites and stings, burns, cellulitis, chiggers, chloracne, cholinergic or stress uricara, chronic urticara, cold type urticara, confluent and reticulated papillomatosis, corns, cysts, dandruff, dermatitis herpetiformis, dermatographism, dyshidrotic eczema, diaper rash, dry skin, dyshidrosis, ectodermal dysplasia such as, hyprohidrotic ectodermal dysplasia and X-linked hyprohidrotic ectodermal dysplasia, eczema, epidermaodysplasia verruciformis, erythema nodosum, excoriated acne, exercise-induced anaphylasis folliculitis, excess skin oil, folliculitis, freckles, frostbite, fungal nails, hair density, hair growth rate, halogen acne, hair loss, heat rash, hematoma, herpes simplex infections (*e.g.* non-genital), hidradenitis suppurativa, hives, hyperhidrosis, hyperpigmentation, hypohidrotic ectodermal dysplasia, hypopigmentation, impetigo, ingrown hair, heat type urticara, ingrown toenail, infantile acne or neonatal acne, itch, irritant contact dermatitis, jock itch, keloid, keratosis pilaris, lichen planus, lichen sclerosus, lupus miliaris disseminatus faciei, melasma, moles, molluscum contagiosum, nail growth rate, nail health, neurodermatitis, nummular eczema, occupational acne, oil acne, onychomycosis, physical urticara, pilonidal cyst, pityriasis rosea, pityriasis versicolor, poison ivy, pomade acne, pseudofolliculitis barbae or acne keloidalis nuchae, psoriasis, psoriatic arthritis, pressure or delayed pressue urticara, puncture wounds such as cuts and scrapes, rash, rare or water type urticara, rhinoplasty, ringworm, rosacea, rothmund-thomson syndrome, sagging of the skin, scabis, scars, seborrhea, seborrheic dermatitis, shingles, skin cancer, skin tag, solar type urticara, spider bite, stretch marks, sunburn, tar acne, tropical acne, thinning of skin, thrush, tinea versicolor, transient acantholytic dermatosis, tycoon's cap or acne necrotica miliaris, uneven skin tone, varicose veins, venous eczema, vibratory angioedema, vitiligo, warts, Weber-Christian disease, wrinkles, x-linked hypohidrotic ectodermal dysplasia, xerotic eczema, yeast infection and general signs of aging.

In some embodiments, there is provided methods of treating, controlling or preventing dry skin with the present compositions. In some embodiments profilaggrin (a protein which is converted to filaggrin) is a protein of interest (*e.g.* when treating ichthyosis vulgaris).

In some embodiments, there is provided methods of treating, controlling or preventing any one of the various types of psoriasis (*e.g.* plague psoriasis, guttate psoriasis, pustular psoriasis, inverse psoriasis, and erythrodermic psoriasis). In various embodiments, the protein of interest is any of the products of the genes psoriasis susceptibility 1 through 9 (PSORSI - PSORS9).

Various embodiments relate to the treatment, control, or prevention of eczema (*e.g.* atopic dermatitis, nummular eczema, dyshidrotic eczema, seborrheic dermatitis, irritant contact dermatitis, allergic contact dermatitis, dyshidrosis, venous eczema, dermatitis herpetiformis, neurodermatitis, autoeczematization and xerotic eczema) and, optionally, one or more of the following may be targeted: filaggrin; three genetic variants, ovo-like 1 (OVOL1), actin-like 9 (ACTL9) and kinesin family member 3 A (KIF3A) have been associated with eczema; and the genes brain-derived neurotrophic factor (BDNF) and tachykinin, precursor 1 (TAC1).

Hives, or urticaria, including, but not limited to, acute urticaria, chronic urticara and angioedema, physical urticara, pressure or delayed pressue urticara, cholinergic or stress uricara, cold type urticara, heat type urticara, solar type urticara, rare or water type urticara, vibratory angioedema, exercise-induced anaphylasis and dermatographism may be treated with the present compositions by, for example, targeting PLCG-2.

Various embodiments relate to the treatment, control, or prevention of rosacea, which includes, but is not limited to, erthematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea, and ocular rosacea. Optionally, cathelicidin antimicrobial peptide (CAMP) and/or kallikrein-related peptidase 5 (also known as stratum corneum tryptic enzyme (SCTE)) are proteins of interest.

In some embodiments, there is provided methods of treating, controlling or preventing acne with the present compositions. For example, acne may include, but is not limited to, acneiform eruptions, acne aestivalis, acne conglobata, acne cosmetic, acne fulminans, acne keloidalis nuchae, acne mechanica, acne medicamentosa, acne miliaris necrotica, acne necrotica, acne rosacea, baby acne, blackheads, chloracne, excoriated acne, halogen acne, infantile acne or neonatal acne, lupus miliaris disseminatus faciei, occupational acne, oil acne, pomade acne, tar acne, tropical acne, tycoon's cap or acne necrotica miliaris, pseudofolliculitis barbae or acne keloidalis nuchae, and hidradenitis suppurativa. In these embodiments, the protein of interest may be one or more matrix metalloproteinases (MMP), *e.g.*, matrix metalloproteinase-1 (MMP-1 or interstitial collagenase), matrix metalloproteinase-9 (MMP-9), and matrix metalloproteinase-13 (MMP-13).

In further embodiments, vitiligo is treated with the present compositions, *e.g.* wherein the NLR family, pyrin domain containing 1 gene (NALP1) gene is targeted.

In some embodiments, the present compositions find use in the treatment, control, or prevention of hyprohidrotic ectodermal dysplasia (HED), *e.g.* via the ectodysplasin A gene (EDA), receptor (EDAR), and receptor associated death domain (EDARADD).

In some embodiments, the present compositions find use in the treatment, control, or prevention of balding, or hair thinning (*e.g.* male pattern baldness, or androgenetic alopecia (AGA)) and, optionally, one or more of the following may be the protein of interest: androgen receptor (AR), ectodysplasin A2 receptor (EDA2R) and lysophosphatidic acid receptor 6 (P2RY5).

The present compositions also find use in methods of treatment, control, or prevention of scars and stretch marks (striae), *e.g.* via collagen, ribosomal s6 kinase, sectrected phosphoprotein 1 (also known as osteopontin), or transforming growth factor beta 3.

Epidermodysplasia verruciformis (also known as Lutz-Lewandowsky epidermodysplasia), a rare autosomal recessive genetic hereditary skin disorder, may also be treated with compositions of the present invention, *e.g.* by targeted transmembrane channel-like 6 (EVER1) or transmembrane channellike 8 (EVER2) genes.

In some embodiments, skin sagging, thinning or wrinkling may be treated, controlled or prevented with present composition, *e.g.* by targeting one or more of the proteins of interest such as collagen, elastin, fibroblast growth factor 7, TIMP metallopeptidase inhibitors, matrix metallopeptidases, superoxide dismutase and other extracellular matrix proteins and proteoglycans.

Further embodiments are used in tanning of the skin, such as via melanocyte-stimulating hormone and/or pro-opiomelanocortin.

In some embodiments, the present compositions may be used for wound treatment. In some embodiments, methods of treating, controlling or preventing wounds with the present compositions comprises additional steps of, for example, cleaning the wound bed to facilitate wound healing and closure, including, but not limited to: debridement, sharp debridement (surgical removal of dead or infected tissue from a wound), optionally including chemical debriding agents, such as enzymes, to remove necrotic tissue; wound dressings to provide the wound with a moist, warm environment and to promote tissue repair and healing (*e.g.*, wound dressings comprising hydrogels (*e.g.*, AQUASORB; DUODERM), hydrocolloids (*e.g.*, AQUACEL; COMFEEL), foams (*e.g.*, LYOFOAM; SPYROSORB), and alginates (*e.g.*, ALGISITE; CURASORB); administration of growth factors to stimulate cell division and proliferation and to promote wound healing *e.g.* becaplermin; and (iv) soft-tissue wound coverage, a skin graft may be necessary to obtain coverage of clean, non-healing wounds (*e.g.*, autologous skin grafts, cadaveric skin graft, bioengineered skin substitutes (*e.g.*, APLIGRAF; DERMAGRAFT)).

In various embodiments, the nucleic acid drug described herein can be used in a variety of cosmetic/plastic surgery procedures, including, without limitation, a surgical procedure involving skin grafting and an aesthetic or cosmetic surgery (*e.g.* a facial plastic surgery procedure including, but not limited to blepharoplasty, rhinoplasty, rhytidectomy, genioplasty, facial implants, otoplasty, hair implantation, cleft lip and cleft palate repair, and/or a

body plastic surgery procedure including but not limited to abdominoplasty, brachioplasty, thigh lift, breast reduction, breast augmentation, body contouring, liposuction, hand surgery).

In various embodiments, a variety of cancers are treated, controlled or prevented with the present compositions (*e.g.*, colorectal cancer, gallbladder cancer, lung cancer, pancreatic cancer, and stomach cancer). In some embodiments, skin cancer is treated with the present compositions. For instance, the skin cancer is one or more of actinic keratosis, basal cell carcinoma, melanoma, Kaposi's sarcoma, and squamous cell carcinoma. In some embodiments, the present compositions are used adjuvant to complete circumferential peripheral and deep margin assessment, Mohs surgery, radiation (*e.g.* external beam radiotherapy or brachytherapy), chemotherapy (including but not limited to topical chemotherapy, *e.g.* with imiquimod or 5-fluorouracil), and cryotherapy. The present compositions also find use in the treatment of various stages of cancers, including skin cancers (*e.g.* basal cell cancer (BCC), squamous cell cancer (SCC), and melanoma), such as a stage of the American Joint Committee on Cancer (AJCC) TNM system (*e.g.* one or more of TX, T0, Tis, T1, T1a, T1b, T2, T2A, T2B, T3, T3a, T3b, T4, T4a, T4b, NX, N0, N1, N2, N3, M0, M1a, M1b, M1c) and/or a staging system (*e.g.* Stage 0, Stage IA, Stage IB, Stage IIA, Stage IIB, Stage IIC, Stage IIIA, Stage IIIB, Stage IIIC, Stage IV).

Illustrative cancers and/or tumors of the present invention include, but are not limited to, a basal cell carcinoma, biliary tract cancer; bladder cancer; bone cancer; brain and central nervous system cancer; breast cancer; cancer of the peritoneum; cervical cancer; choriocarcinoma; colon and rectum cancer; connective tissue cancer; cancer of the digestive system; endometrial cancer; esophageal cancer; eye cancer; cancer of the head and neck; gastric cancer (including gastrointestinal cancer); glioblastoma; hepatic carcinoma; hepatoma; intra-epithelial neoplasm; kidney or renal cancer; larynx cancer; leukemia; liver cancer; lung cancer (*e.g.*, small-cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of the lung); melanoma; myeloma; neuroblastoma; oral cavity cancer (lip, tongue, mouth, and pharynx); ovarian cancer; pancreatic cancer; prostate cancer; retinoblastoma; rhabdomyosarcoma; rectal cancer; cancer of the respiratory system; salivary gland carcinoma; sarcoma; skin cancer; squamous cell cancer; stomach cancer; testicular cancer; thyroid cancer; uterine or endometrial cancer; cancer of the urinary system; vulval cancer; lymphoma including Hodgkin's and non-Hodgkin's lymphoma, as well as B-cell lymphoma (including low grade/follicular non-Hodgkin's lymphoma (NHL); small lymphocytic (SL) NHL; intermediate grade/follicular NHL; intermediate grade diffuse NHL; high grade immunoblastic NHL; high grade lymphoblastic NHL; high grade small non-cleaved cell NHL; bulky disease NHL; mantle cell lymphoma; AIDS-related lymphoma; and Waldenstrom's Macroglobulinemia; chronic lymphocytic leukemia (CLL); acute lymphoblastic leukemia (ALL); Hairy cell leukemia; chronic myeloblastic leukemia; as well as other carcinomas and sarcomas; and post-transplant lymphoproliferative disorder (PTLD), as well as abnormal vascular proliferation associated with phakomatoses, edema (such as that associated with brain tumors), and Meigs' syndrome.

In various embodiments, one or more rare diseases are treated, controlled or prevented with the present compositions, including, by way of illustration, Erythropoietic Protoporphyria, Hailey-Hailey Disease, Epidermolysis Bullosa (EB), Xeroderma Pigmentosum, Ehlers-Danlos Syndrome, Cutis Laxa, Protein C & Protein

S Deficiency, Alport Syndrome, Striate Palmoplantar Keratoderma, Lethal Acantholytic EB, Pseudoxanthoma Elasticum (PXE), Ichthyosis Vulgaris, Pemphigus Vulgaris, and Basal Cell Nevus Syndrome.

In various embodiments, the present compositions are used to treat, control or prevent one or more inflammatory diseases or conditions, such as inflammation, acute inflammation, chronic inflammation, respiratory disease, atherosclerosis, restenosis, asthma, allergic rhinitis, atopic dermatitis, septic shock, rheumatoid arthritis, inflammatory bowel disease, inflammatory pelvic disease, pain, ocular inflammatory disease, celiac disease, Leigh Syndrome, Glycerol Kinase Deficiency, Familial eosinophilia (FE), autosomal recessive spastic ataxia, laryngeal inflammatory disease; Tuberculosis, Chronic cholecystitis, Bronchiectasis, Silicosis and other pneumoconioses.

In various embodiments, the present compositions are used to treat, control or prevent one or more autoimmune diseases or conditions, such as multiple sclerosis, diabetes mellitus, lupus, celiac disease, Crohn's disease, ulcerative colitis, Guillain-Barre syndrome, scleroderms, Goodpasture's syndrome, Wegener's granulomatosis, autoimmune epilepsy, Rasmussen's encephalitis, Primary biliary sclerosis, Sclerosing cholangitis, Autoimmune hepatitis, Addison's disease, Hashimoto's thyroiditis, Fibromyalgia, Menier's syndrome; transplantation rejection (*e.g.*, prevention of allograft rejection) pernicious anemia, rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, Sjogren's syndrome, lupus erythematosus, multiple sclerosis, myasthenia gravis, Reiter's syndrome, Grave's disease, and other autoimmune diseases.

In various embodiments, the present compositions are used to treat, control or prevent one or more neurologic diseases, including ADHD, AIDS—Neurological Complications, Absence of the Septum Pellucidum, Acquired Epileptiform Aphasia, Acute Disseminated Encephalomyelitis, Adrenoleukodystrophy, Agenesis of the Corpus Callosum, Agnosia, Aicardi Syndrome, Alexander Disease, Alpers' Disease, Alternating Hemiplegia, Alzheimer's Disease, Amyotrophic Lateral Sclerosis, Anencephaly, Aneurysm, Angelman Syndrome, Angiomatosis, Anoxia, Aphasia, Apraxia, Arachnoid Cysts, Arachnoiditis, Arnold-Chiari Malformation, Arteriovenous Malformation, Aspartame, Asperger Syndrome, Ataxia Telangiectasia, Ataxia, Attention Deficit-Hyperactivity Disorder, Autism, Autonomic Dysfunction, Back Pain, Barth Syndrome, Batten Disease, Behcet's Disease, Bell's Palsy, Benign Essential Blepharospasm, Benign Focal Amyotrophy, Benign Intracranial Hypertension, Bernhardt-Roth Syndrome, Binswanger's Disease, Blepharospasm, Bloch-Sulzberger Syndrome, Brachial Plexus Birth Injuries, Brachial Plexus Injuries, Bradbury-Eggleston Syndrome, Brain Aneurysm, Brain Injury, Brain and Spinal Tumors, Brown-Sequard Syndrome, Bulbospinal Muscular Atrophy, Canavan Disease, Carpal Tunnel Syndrome, Causalgia, Cavernomas, Cavernous Angioma, Cavernous Malformation, Central Cervical Cord Syndrome, Central Cord Syndrome, Central Pain Syndrome, Cephalic Disorders, Cerebellar Degeneration, Cerebellar Hypoplasia, Cerebral Aneurysm, Cerebral Arteriosclerosis, Cerebral Atrophy, Cerebral Beriberi, Cerebral Gigantism, Cerebral Hypoxia, Cerebral Palsy, Cerebro-Oculo-Facio-Skeletal Syndrome, Charcot-Marie-Tooth Disorder, Chiari Malformation, Chorea, Choreoacanthocytosis, Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Chronic Orthostatic Intolerance, Chronic Pain, Cockayne Syndrome Type II, Coffin Lowry Syndrome, Coma, including Persistent Vegetative State, Complex Regional Pain Syndrome, Congenital

Facial Diplegia, Congenital Myasthenia, Congenital Myopathy, Congenital Vascular Cavernous Malformations, Corticobasal Degeneration, Cranial Arteritis, Craniosynostosis, Creutzfeldt-Jakob Disease, Cumulative Trauma Disorders, Cushing's Syndrome, Cytomegalic Inclusion Body Disease (CIBD), Cytomegalovirus Infection, Dancing Eyes-Dancing Feet Syndrome, Dandy-Walker Syndrome, Dawson Disease, De Morsier's Syndrome, Dejerine-Klumpke Palsy, Dementia—Multi-Infarct, Dementia—Subcortical, Dementia With Lewy Bodies, Dermatomyositis, Developmental Dyspraxia, Devic's Syndrome, Diabetic Neuropathy, Diffuse Sclerosis, Dravet's Syndrome, Dysautonomia, Dysgraphia, Dyslexia, Dysphagia, Dyspraxia, Dystonias, Early Infantile Epileptic Encephalopathy, Empty Sella Syndrome, Encephalitis Lethargica, Encephalitis and Meningitis, Encephaloceles, Encephalopathy, Encephalotrigeminal Angiomatosis, Epilepsy, Erb's Palsy, Erb-Duchenne and Dejerine-Klumpke Palsies, Fabry's Disease, Fahr's Syndrome, Fainting, Familial Dysautonomia, Familial Hemangioma, Familial Idiopathic Basal Ganglia Calcification, Familial Spastic Paralysis, Febrile Seizures (*e.g.*, GEFS and GEFS plus), Fisher Syndrome, Floppy Infant Syndrome, Friedreich's Ataxia, Gaucher's Disease, Gerstmann's Syndrome, Gerstmann-Straussler-Scheinker Disease, Giant Cell Arteritis, Giant Cell Inclusion Disease, Globoid Cell Leukodystrophy, Glossopharyngeal Neuralgia, Guillain-Barre Syndrome, HTLV-1 Associated Myelopathy, Hallervorden-Spatz Disease, Head Injury, Headache, Hemicrania Continua, Hemifacial Spasm, Hemiplegia Alterans, Hereditary Neuropathies, Hereditary Spastic Paraplegia, Heredopathia Atactica Polyneuritiformis, Herpes Zoster Oticus, Herpes Zoster, Hirayama Syndrome, Holoprosencephaly, Huntington's Disease, Hydranencephaly, Hydrocephalus—Normal Pressure, Hydrocephalus, Hydromyelia, Hypercortisolism, Hypersomnia, Hypertonia, Hypotonia, Hypoxia, Immune-Mediated Encephalomyelitis, Inclusion Body Myositis, Incontinentia Pigmenti, Infantile Hypotonia, Infantile Phytanic Acid Storage Disease, Infantile Refsum Disease, Infantile Spasms, Inflammatory Myopathy, Intestinal Lipodystrophy, Intracranial Cysts, Intracranial Hypertension, Isaac's Syndrome, Joubert Syndrome, Kearns-Sayre Syndrome, Kennedy's Disease, Kinsbourne syndrome, Kleine-Levin syndrome, Klippel Feil Syndrome, Klippel-Trenaunay Syndrome (KTS), Klüver-Bucy Syndrome, Korsakoffs Amnesic Syndrome, Krabbe Disease, Kugelberg-Welander Disease, Kuru, Lambert-Eaton Myasthenic Syndrome, Landau-Kleffner Syndrome, Lateral Femoral Cutaneous Nerve Entrapment, Lateral Medullary Syndrome, Learning Disabilities, Leigh's Disease, Lennox-Gastaut Syndrome, Lesch-Nyhan Syndrome, Leukodystrophy, Levine-Critchley Syndrome, Lewy Body Dementia, Lissencephaly, Locked-In Syndrome, Lou Gehrig's Disease, Lupus—Neurological Sequelae, Lyme Disease—Neurological Complications, Machado-Joseph Disease, Macrencephaly, Megalencephaly, Melkersson-Rosenthal Syndrome, Meningitis, Menkes Disease, Meralgia Paresthetica, Metachromatic Leukodystrophy, Microcephaly, Migraine, Miller Fisher Syndrome, Mini-Strokes, Mitochondrial Myopathies, Mobius Syndrome, Monomelic Amyotrophy, Motor Neuron Diseases, Moyamoya Disease, Mucolipidoses, Mucopolysaccharidoses, Multi-Infarct Dementia, Multifocal Motor Neuropathy, Multiple Sclerosis, Multiple System Atrophy with Orthostatic Hypotension, Multiple System Atrophy, Muscular Dystrophy, Myasthenia—Congenital, Myasthenia Gravis, Myelinoclastic Diffuse Sclerosis, Myoclonic Encephalopathy of Infants, Myoclonus, Myopathy—Congenital, Myopathy—Thyrotoxic, Myopathy, Myotonia Congenita, Myotonia, Narcolepsy, Neuroacanthocytosis, Neurodegeneration with Brain Iron Accumulation, Neurofibromatosis, Neuroleptic Malignant Syndrome, Neurological Complications of AIDS, Neurological

Manifestations of Pompe Disease, Neuromyelitis Optica, Neuromyotonia, Neuronal Ceroid Lipofuscinosis, Neuronal Migration Disorders, Neuropathy—Hereditary, Neurosarcoidosis, Neurotoxicity, Nevus Cavernosus, Niemann-Pick Disease, O'Sullivan-McLeod Syndrome, Occipital Neuralgia, Occult Spinal Dysraphism Sequence, Ohtahara Syndrome, Olivopontocerebellar Atrophy, Opsoclonus Myoclonus, Orthostatic Hypotension, Overuse Syndrome, Pain—Chronic, Paraneoplastic Syndromes, Paresthesia, Parkinson's Disease, Parnyotonia Congenita, Paroxysmal Choreoathetosis, Paroxysmal Hemicrania, Parry-Romberg, Pelizaeus-Merzbacher Disease, Pena Shokeir II Syndrome, Perineural Cysts, Periodic Paralyses, Peripheral Neuropathy, Periventricular Leukomalacia, Persistent Vegetative State, Pervasive Developmental Disorders, Phytanic Acid Storage Disease, Pick's Disease, Piriformis Syndrome, Pituitary Tumors, Polymyositis, Pompe Disease, Porencephaly, Post-Polio Syndrome, Postherpetic Neuralgia, Postinfectious Encephalomyelitis, Postural Hypotension, Postural Orthostatic Tachycardia Syndrome, Postural Tachycardia Syndrome, Primary Lateral Sclerosis, Prion Diseases, Progressive Hemifacial Atrophy, Progressive Locomotor Ataxia, Progressive Multifocal Leukoencephalopathy, Progressive Sclerosing Poliodystrophy, Progressive Supranuclear Palsy, Pseudotumor Cerebri, Pyridoxine Dependent and Pyridoxine Responsive Siezure Disorders, Ramsay Hunt Syndrome Type I, Ramsay Hunt Syndrome Type II, Rasmussen's Encephalitis and other autoimmune epilepsies, Reflex Sympathetic Dystrophy Syndrome, Refsum Disease—Infantile, Refsum Disease, Repetitive Motion Disorders, Repetitive Stress Injuries, Restless Legs Syndrome, Retrovirus-Associated Myelopathy, Rett Syndrome, Reye's Syndrome, Riley-Day Syndrome, SUNCT Headache, Sacral Nerve Root Cysts, Saint Vitus Dance, Salivary Gland Disease, Sandhoff Disease, Schilder's Disease, Schizencephaly, Seizure Disorders, Septo-Optic Dysplasia, Severe Myoclonic Epilepsy of Infancy (SMEI), Shaken Baby Syndrome, Shingles, Shy-Drager Syndrome, Sjogren's Syndrome, Sleep Apnea, Sleeping Sickness, Soto's Syndrome, Spasticity, Spina Bifida, Spinal Cord Infarction, Spinal Cord Injury, Spinal Cord Tumors, Spinal Muscular Atrophy, Spinocerebellar Atrophy, Steele-Richardson-Olszewski Syndrome, Stiff-Person Syndrome, Striatonigral Degeneration, Stroke, Sturge-Weber Syndrome, Subacute Sclerosing Panencephalitis, Subcortical Arteriosclerotic Encephalopathy, Swallowing Disorders, Sydenham Chorea, Syncope, Syphilitic Spinal Sclerosis, Syringohydromyelia, Syringomyelia, Systemic Lupus Erythematosus, Tabes Dorsalis, Tardive Dyskinesia, Tarlov Cysts, Tay-Sachs Disease, Temporal Arteritis, Tethered Spinal Cord Syndrome, Thomsen Disease, Thoracic Outlet Syndrome, Thyrotoxic Myopathy, Tic Douloureux, Todd's Paralysis, Tourette Syndrome, Transient Ischemic Attack, Transmissible Spongiform Encephalopathies, Transverse Myelitis, Traumatic Brain Injury, Tremor, Trigeminal Neuralgia, Tropical Spastic Paraparesis, Tuberous Sclerosis, Vascular Erectile Tumor, Vasculitis including Temporal Arteritis, Von Economo's Disease, Von Hippel-Lindau disease (VHL), Von Recklinghausen's Disease, Wallenberg's Syndrome, Werdnig-Hoffman Disease, Wernicke-Korsakoff Syndrome, West Syndrome, Whipple's Disease, Williams Syndrome, Wilson's Disease, X-Linked Spinal and Bulbar Muscular Atrophy, and Zellweger Syndrome.

In various embodiments, the present compositions are used to treat one or more respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), bronchiectasis, allergic rhinitis, sinusitis, pulmonary

vasoconstriction, inflammation, allergies, impeded respiration, respiratory distress syndrome, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, Hantavirus pulmonary syndrome (HPS), Loeffler's syndrome, Goodpasture's syndrome, Pleurisy, pneumonitis, pulmonary edema, pulmonary fibrosis, Sarcoidosis, complications associated with respiratory syncitial virus infection, and other respiratory diseases.

In various embodiments, the present compositions are used to treat, control or prevent cardiovascular disease, such as a disease or condition affecting the heart and vasculature, including but not limited to, coronary heart disease (CHD), cerebrovascular disease (CVD), aortic stenosis, peripheral vascular disease, atherosclerosis, arteriosclerosis, myocardial infarction (heart attack), cerebrovascular diseases (stroke), transient ischaemic attacks (TIA), angina (stable and unstable), atrial fibrillation, arrhythmia, vavular disease, and/or congestive heart failure.

In various embodiments, the present compositions are used to treat, control or prevent one or more metabolic-related disorders. In various embodiments, the present invention is useful for the treatment, controlling or prevention of diabetes, including Type 1 and Type 2 diabetes and diabetes associated with obesity. The compositions and methods of the present invention are useful for the treatment or prevention of diabetes-related disorders, including without limitation diabetic nephropathy, hyperglycemia, impaired glucose tolerance, insulin resistance, obesity, lipid disorders, dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL levels, high LDL levels, atherosclerosis and its sequelae, vascular restenosis, irritable bowel syndrome, inflammatory bowel disease, including Crohn's disease and ulcerative colitis, other inflammatory conditions, pancreatitis, abdominal obesity, neurodegenerative disease, retinopathy, neoplastic conditions, adipose cell tumors, adipose cell carcinomas, such as liposarcoma, prostate cancer and other cancers, including gastric, breast, bladder and colon cancers, angiogenesis, Alzheimer's disease, psoriasis, high blood pressure, Metabolic Syndrome (*e.g.* a person has three or more of the following disorders: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, high blood pressure, and high fasting plasma glucose), ovarian hyperandrogenism (polycystic ovary syndrome), and other disorders where insulin resistance is a component, such as sleep apnea. The compositions and methods of the present invention are useful for the treatment, control, or prevention of obesity, including genetic or environmental, and obesity-related disorders. The obesity-related disorders herein are associated with, caused by, or result from obesity. Examples of obesity-related disorders include obesity, diabetes, overeating, binge eating, and bulimia, hypertension, elevated plasma insulin concentrations and insulin resistance, dyslipidemia, hyperlipidemia, endometrial, breast, prostate, kidney and colon cancer, osteoarthritis, obstructive sleep apnea, gallstones, heart disease, abnormal heart rhythms and arrythmias, myocardial infarction, congestive heart failure, coronary heart disease, sudden death, stroke, polycystic ovary disease, craniopharyngioma, Prader-Willi Syndrome, Frohlich's syndrome, GH-deficient subjects, normal variant short stature, Turner's syndrome, and other pathological conditions showing reduced metabolic activity or a decrease in resting energy expenditure as a percentage of total fat-free mass, e.g, children with acute lymphoblastic leukemia. Further examples of obesity-related disorders are Metabolic Syndrome, insulin resistance syndrome, reproductive hormone abnormalities, sexual and reproductive dysfunction, such as impaired fertility, infertility,

hypogonadism in males and hirsutism in females, fetal defects associated with maternal obesity, gastrointestinal motility disorders, such as obesity-related gastro-esophageal reflux, respiratory disorders, such as obesity-hypoventilation syndrome (Pickwickian syndrome), breathlessness, cardiovascular disorders, inflammation, such as systemic inflammation of the vasculature, arteriosclerosis, hypercholesterolemia, lower back pain, gallbladder disease, hyperuricemia, gout, and kidney cancer, and increased anesthetic risk. The compositions and methods of the present invention are also useful to treat Alzheimer's disease.

Nucleic acids, including liposomal formulations containing nucleic acids, when delivered in vivo, can accumulate in the liver and/or spleen. It has now been discovered that nucleic acids encoding proteins can modulate protein expression in the liver and spleen, and that nucleic acids used in this manner can constitute potent therapeutics for the treatment of liver and spleen diseases. Certain embodiments are therefore directed to a method for treating liver and/or spleen disease by delivering to a patient a nucleic acid encoding a protein of interest. Other embodiments are directed to a therapeutic composition comprising a nucleic acid encoding a protein of interest, for the treatment of liver and/or spleen disease. Diseases and conditions of the liver and/or spleen that can be treated include, but are not limited to: hepatitis, alcohol-induced liver disease, drug-induced liver disease, Epstein Barr virus infection, adenovirus infection, cytomegalovirus infection, toxoplasmosis, Rocky Mountain spotted fever, non-alcoholic fatty liver disease, hemochromatosis, Wilson's Disease, Gilbert's Disease, and cancer of the liver and/or spleen.

In some embodiments, the present compositions and methods relate to the treatment of type 1 diabetes, heart disease, including ischemic and dilated cardiomyopathy, macular degeneration, Parkinson's disease, cystic fibrosis, sickle-cell anemia, thalassemia, Fanconi anemia, severe combined immunodeficiency, hereditary sensory neuropathy, xeroderma pigmentosum, Huntington's disease, muscular dystrophy, amyotrophic lateral sclerosis, Alzheimer's disease, cancer, and infectious diseases including hepatitis and HIV/AIDS.

In various embodiments, the present methods and compositions find use in treating or preventing one or more metabolic diseases or disorders. In various embodiments, the present methods and compositions find use in treating or preventing one or more of diseases or disorders of carbohydrate metabolism. diseases or disorders of amino acid metabolism, diseases or disorders of the urea cycle, diseases or disorders of fatty acid metabolism, diseases or disorders of porphyrin metabolism, lysosomal storage disorders, peroxisome biogenesis disorders, and diseases or disorders of purine or pyrimidine metabolism.

In various embodiments, the present methods and compositions find use in treating or preventing one or more of diseases or disorders in the table below. In various embodiments, the present methods and compositions find use in treating or preventing one or more of diseases or disorders in the table below for instance by modulating the genes associated with the diseases in the table below. In some embodiments, the present methods and compositions find use in gene-editing the genes described in the table below using the present compositions.

Category	Disease	Genes	Entrez ID

Disorders of carbohydrate metabolism	Galactosemia	GALT, GALK1, GALE	2592, 2584, 2582
	Essential fructosuria	KHK	3795
	Hereditary fructose intolerance	ALDOB	229
	Glycogen storage disease type I	G6PC, SLC37A4, SLC17A3	2538, 2542, 10786
	Glycogen storage disease type II	GAA	2548
	Glycogen storage disease type III	AGL	178
	Glycogen storage disease type IV	GBE1	2632
	Glycogen storage disease type V	PYGM	5837
	Glycogen storage disease type VI	PYGL	5836
	Glycogen storage disease type VII	PYGM	5837
	Glycogen storage disease type IX	PHKA1, PHKA2, PHKB, PHKG1, PHKG2	5255, 5256, 5257, 5260, 5261
	Glycogen storage disease type XI	SLC2A2	6514
	Glycogen storage disease type XII	ALDOA	226
	Glycogen storage disease type XIII	ENO1, ENO2, ENO3	2023, 2026, 2027
	Glycogen storage disease type 0	GYS1, GYS2	2997, 2998
	Pyruvate carboxylase deficiency	PC	5091
	Pyruvate kinase deficiency	PKLR	5313
	Transaldolase deficiency	TALDO1	6888
	Triosephosphate isomerase	TPI1	7167

	deficiency		
	Fructose bisphosphatase deficiency	FBP1	2203
	Hyperoxaluria	AGXT, GRHPR	189, 9380
	Hexokinase deficiency	HK1	3098
	Glucose-galactose malabsorption	SLC5A1	6523
	Glucose-6-phosphate dehydrogenase deficiency	G6PD	2539
Disorders of amino acid metabolism	Alkaptonuria	HGD	3081
	Aspartylglucosaminuria	AGA	175
	Methylmalonic acidemia	MUT, MCEE, MMAA, MMAB, MMACHC, MMADHC, LMBRD1	4594, 84693, 166785, 326625, 25974, 27249, 55788
	Maple syrup urine disease	BCKDHA, BCKDHB, DBT, DLD	593, 594, 1629, 1738
	Homocystinuria	CBS	875
	Tyrosinemia	FAH, TAT, HPD	2184, 6898, 3242
	Trimethylaminuria	FMO3	2328
	Hartnup disease	SLC6A19	340024
	Biotinidase deficiency	BTD	686
	Ornithine carbamoyltransferase deficiency	OTC	5009
	Carbamoyl-phosphate synthase I deficiency disease	CPS1	1373
	Citrullinemia	ASS, SLC25A13	445, 10165
	Hyperargininemia	ARG1	383
	Hyperhomocysteinemia	MTHFR	4524
	Hypermethioninemia	MAT1A, GNMT, AHCY	4143, 27232, 191
	Hyperlysinemias	AASS	10157

	Nonketotic hyperglycinemia	GLDC, AMT, GCSH	2731, 275, 2653
	Propionic acidemia	PCCA, PCCB	5095, 5096
	Hyperprolinemia	ALDH4A1, PRODH	8659, 5625
	Cystinuria	SLC3A1, SLC7A9	6519, 11136
	Dicarboxylic aminoaciduria	SLC1A1	6505
	Glutaric acidemia type 2	ETFA, ETFB, ETFDH	2108, 2109, 2110
	Isovaleric acidemia	IVD	3712
	2-Hydroxyglutaric aciduria	L2HGDH, D2HGDH	79944, 728294
Disorders of the urea cycle	N-Acetylglutamate synthase deficiency	NAGS	162417
	Argininosuccinic aciduria	ASL	435
	Argininemia	ARG1	383
Disorders of fatty acid metabolism	Very long-chain acyl-coenzyme A dehydrogenase deficiency	ACADVL	37
	Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency	HADHA	3030
	Medium-chain acyl-coenzyme A dehydrogenase deficiency	ACADM	34
	Short-chain acyl-coenzyme A dehydrogenase deficiency	ACADS	35
	3-hydroxyacyl-coenzyme A dehydrogenase deficiency	HADH	3033
	2,4 Dienoyl-CoA reductase deficiency	NADK2	133686
	3-Hydroxy-3-methylglutaryl-CoA lyase deficiency	HMGCL	3155
	Malonyl-CoA decarboxylase deficiency	MLYCD	23417
	Systemic primary carnitine deficiency	SLC22A5	6584

	Carnitine-acylcarnitine translocase deficiency	SLC25A20	788
	Carnitine palmitoyltransferase I deficiency	CPT1A	1374
	Carnitine palmitoyltransferase II deficiency	CPT2	1376
	Lysosomal acid lipase deficiency	LIPA	3988
	Gaucher's disease	GBA	2629
Disorders of porphyrin metabolism	Acute intermittent porphyria	HMBS	3145
	Gunther disease	UROS	7390
	Porphyria cutanea tarda	UROD	7389
	Hepatoerythropoietic porphyria	UROD	7389
	Hereditary coproporphyria	CPOX	1371
	Variegate porphyria	PPOX	5498
	Erythropoietic protoporphyria	FECH	2235
	Aminolevulinic acid dehydratase deficiency porphyria	ALAD	210
Lysosomal storage disorders	Farber disease	ASAH1	427
	Krabbe disease	GALC	2581
	Galactosialidosis	CTSA	5476
	Fabry disease	GLA	2717
	Schindler disease	NAGA	4668
	GM1 gangliosidosis	GLB1	2720
	Tay–Sachs disease	HEXA	3073
	Sandhoff disease	HEXB	3074
	GM2-gangliosidosis, AB	GM2A	2760

	variant		
	Niemann–Pick disease	SMPD1, NPC1, NPC2	6609, 4864, 10577
	Metachromatic leukodystrophy	ARSA, PSAP	410, 5660
	Multiple sulfatase deficiency	SUMF1	285362
	Hurler syndrome	IDUA	3425
	Hunter syndrome	IDS	3423
	Sanfilippo syndrome	SGSH, NAGLU, HGSNAT, GNS	6448, 4669, 138050, 2799
	Morquio syndrome	GALNS, GLB1	2588, 2720
	Maroteaux–Lamy syndrome	ARSB	411
	Sly syndrome	GUSB	2990
	Sialidosis	NEU1, NEU2, NEU3, NEU4	4758, 4759, 10825, 129807
	I-cell disease	GNPTAB, GNPTG	79158, 84572
	Mucolipidosis type IV	MCOLN1	57192
	Infantile neuronal ceroid lipofuscinosis	PPT1, PPT2	5538, 9374
	Jansky–Bielschowsky disease	TPP1	1200
	Batten disease	CLN1, CLN2, CLN3, CLN5, CLN6, MFSD8, CLN8, CTSD	5538, 1200, 1201, 1203, 54982, 256471, 2055, 1509
	Kufs disease, Type A	CLN6, PPT1	54982, 5538
	Kufs disease, Type B	DNAJC5, CTSF	80331, 8722
	Alpha-mannosidosis	MAN2B1, MAN2B2, MAN2C1	4125, 23324, 4123
	Beta-mannosidosis	MANBA	4226
	Fucosidosis	FUCA1	2517
	Cystinosis	CTNS	1497
	Pycnodysostosis	CTSK	1513
	Salla disease	SLC17A5	26503

	Infantile free sialic acid storage disease	SLC17A5	26503
	Danon disease	LAMP2	3920
Peroxisome biogenesis disorders	Zellweger syndrome	PEX1, PEX2, PEX3, PEX5, PEX6, PEX12, PEX14, PEX26	5189, 5828, 8504, 5830, 5190, 5193, 5195, 55670
	Infantile Refsum disease	PEX1, PEX2, PEX26	5189, 5828, 55670
	Neonatal adrenoleukodystrophy	PEX5, PEX1, PEX10, PEX13, PEX26	5830, 5189, 5192, 5194, 55670
	RCDP Type 1	PEX7	5191
	Pipecolic acidemia	PAHX	5264
	Acatalasia	CAT	847
	Hyperoxaluria type 1	AGXT	189
	Acyl-CoA oxidase deficiency	ACOX1	51
	D-bifunctional protein deficiency	HSD17B4	3295
	Dihydroxyacetonephosphate acyltransferase deficiency	GNPAT	8443
	X-linked adrenoleukodystrophy	ABCD1	215
	α-Methylacyl-CoA racemase deficiency	AMACR	23600
	RCDP Type 2	DHAPAT	8443
	RCDP Type 3	AGPS	8540
	Adult Refsum disease-1	PHYH	5264
	Mulibrey nanism	TRIM37	4591
Disorders of purine or pyrimidine metabolism	Lesch–Nyhan syndrome	HPRT	3251
	Adenine phosphoribosyltransferase deficiency	APRT	353
	Adenosine deaminase deficiency	ADA	100

	Adenosine monophosphate deaminase deficiency type 1	AMPD1	270
	Adenylosuccinate lyase deficiency	ADSL	158
	Dihydropyrimidine dehydrogenase deficiency	DPYD	1806
	Miller syndrome	DHODH	1723
	Orotic aciduria	UMPS	7372
	Purine nucleoside phosphorylase deficiency	PNP	4860
	Xanthinuria	XDH, MOCS1, MOCS2, GEPH	7498, 4337, 4338, 10243

The Entrez entries listed in the table above are hereby incorporated by reference in their entireties.

Further, in some embodiments, the present methods and compositions find use in targeting any of the proteins or in treatment of any of the diseases or disorders of **Table 2B**. In various embodiments, the present invention contemplates the targeting of the full-length and/or truncated forms of any of the proteins disclosed in Table 2B. In various embodiments, the present invention contemplates the targeting of the precursor forms and/or mature forms and/or isoforms of any of the proteins disclosed in **Table 2B**.

In various embodiments, the present invention contemplates the targeting of a protein having about 60% (*e.g.* about 60%, or about 61%, or about 62%, or about 63%, or about 64%, or about 65%, or about 66%, or about 67%, or about 68%, or about 69%, or about 70%, or about 71%, or about 72%, or about 73%, or about 74%, or about 75%, or about 76%, or about 77%, or about 78%, or about 79%, or about 80%, or about 81%, or about 82%, or about 83%, or about 84%, or about 85%, or about 86%, or about 87%, or about 88%, or about 89%, or about 90%, or about 91%, or about 92%, or about 93%, or about 94%, or about 95%, or about 96%, or about 97%, or about 98%, or about 99%) sequence identity with any of the protein sequences disclosed herein (*e.g.* in **Table 2B**).

In various embodiments, the present invention contemplates the targeting of a protein comprising an amino acid sequence having one or more amino acid mutations relative to any of the protein sequences described herein (*e.g.* in **Table 2B**). For example, the present invention contemplates the targeting of a protein comprising an amino acid sequence having 1, or 2, or 3, or 4, or 5, or 6, or 7, or 8, or 9, or 10, or 11, or 12 amino acid mutations relative to any of the protein sequences described herein (*e.g.* in **Table 2B**). In some embodiments, the one or more amino acid mutations may be independently selected from substitutions, insertions, deletions, and truncations.

In some embodiments, the amino acid mutations are amino acid substitutions, and may include conservative and/or non-conservative substitutions.

"Conservative substitutions" may be made, for instance, on the basis of similarity in polarity, charge, size, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the amino acid residues involved. The 20 naturally occurring amino acids can be grouped into the following six standard amino acid groups: (1) hydrophobic: Met, Ala, Val, Leu, Ile; (2) neutral hydrophilic: Cys, Ser, Thr; Asn, Gln; (3) acidic: Asp, Glu; (4) basic: His, Lys, Arg; (5) residues that influence chain orientation: Gly, Pro; and (6) aromatic: Trp, Tyr, Phe.

As used herein, "conservative substitutions" are defined as exchanges of an amino acid by another amino acid listed within the same group of the six standard amino acid groups shown above. For example, the exchange of Asp by Glu retains one negative charge in the so modified polypeptide. In addition, glycine and proline may be substituted for one another based on their ability to disrupt α-helices.

As used herein, "non-conservative substitutions" are defined as exchanges of an amino acid by another amino acid listed in a different group of the six standard amino acid groups (1) to (6) shown above.

In various embodiments, the substitutions may also include non-classical amino acids (*e.g.* selenocysteine, pyrrolysine, *N*-formylmethionine β-alanine, GABA and δ-Aminolevulinic acid, 4-aminobenzoic acid (PABA), D-isomers of the common amino acids, 2,4-diaminobutyric acid, α-amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, γ-Abu, ε-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosme, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, β-alanine, fluoro-amino acids, designer amino acids such as β methyl amino acids, C α-methyl amino acids, N α-methyl amino acids, and amino acid analogs in general).

In **Table 2B**, all Illustrative Identifiers (*e.g.* Gene Seq nos. and references are hereby incorporated by reference in their entireties).

Table 2B. *Illustrative Proteins, Illustrative Peptides, and Illustrative Indications*

Protein / Peptide Illustrative Identifier Reference	**Description / Illustrative Indication(s)**
Transthyretin (TTR) (SEQ ID NOs: 637 and 638) Gene ID: 7276	his gene encodes transthyretin, one of the three prealbumins including alpha-1-antitrypsin, transthyretin and orosomucoid. Transthyretin is a carrier protein; it transports thyroid hormones in the plasma and cerebrospinal fluid, and also transports retinol (vitamin A) in the plasma. The protein consists of a tetramer of identical subunits. More than 80 different mutations in this gene have been reported; most mutations are related to amyloid deposition, affecting predominantly peripheral nerve and/or the heart, and a small portion of the gene mutations is non-amyloidogenic. The diseases caused by mutations include amyloidotic polyneuropathy, euthyroid hyperthyroxinaemia, amyloidotic vitreous opacities, cardiomyopathy, oculoleptomeningeal amyloidosis, meningocerebrovascular amyloidosis, carpal tunnel syndrome, etc.
Endothelial Cell Specific Molecule 1	This gene encodes a secreted protein which is mainly expressed in the endothelial cells in human lung and kidney tissues. The expression of this gene is regulated by cytokines, suggesting that it may play a role in endothelium-dependent pathological

(SEQ ID NO: 629 to 632) Gene ID: 11082	disorders. The transcript contains multiple polyadenylation and mRNA instability signals. Two transcript variants encoding different isoforms have been found for this gene
Parathyroid hormone P01270|PTHY_HUMAN Parathyroid hormone (SEQ ID NO:508)	PTH is secreted by the chief cells of the parathyroid glands. PTH plays an important role in the regulation of serum calcium, serum phosphate, and vitamin D synthesis.
BMP-1 GeneSeq Accession P80618 WO8800205 P13497/BMP1_HUMAN Bone morphogenetic protein 1 (isoform BMP1-3) (SEQ ID NO:169) P13497-2|BMP1_HUMAN Isoform BMP1-1 of Bone morphogenetic protein 1 (isoform BMP1-1) (SEQ ID NO:509) P13497-3|BMP1_HUMAN Isoform BMP1-4 of Bone morphogenetic protein 1 (isoform BMP1-4) (SEQ ID NO:510) P13497-4|BMP1_HUMAN Isoform BMP1-5 of Bone morphogenetic protein 1 (isoform BMP1-5) (SEQ ID NO:511) P13497-5|BMP1_HUMAN Isoform BMP1-6 of Bone morphogenetic protein 1 (isoform BMP1-6) (SEQ ID NO:512) P13497-6|BMP1_HUMAN Isoform BMP1-7 of Bone morphogenetic protein 1 (isoform BMP1-7)	BMP1 belongs to the transforming growth factor-beta (TGFB) super- family. Bone morphogenic proteins induce cartilage and bone formation, play important role in nephrogesis, and play an important role in the development of many organs, including lung, heart, teeth, gut, skin, and particularly the kidney. BMP-1 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes

(SEQ ID NO:513)	
BMP-2 GeneSeq Accession P80619 WO8800205 P12643/BMP2_HUMAN Bone morphogenetic protein 2 (SEQ ID NO:170)	BMP-2 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-2 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes. Infarction recovery. Bone repair. Osteoporosis.
BMP-3 P12645|BMP3_HUMAN Bone morphogenetic protein 3 (SEQ ID NO:514)	BMP-3 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-3 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-2B GeneSeq Accession W24850 US Pat. No. 5,631,142 P12644/BMP4_HUMAN Bone morphogenetic protein 4 (SEQ ID NO:171)	BMP-2b belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-2b activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; I Biol Cbcre, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-4 GeneSeq Accession B02796 WO0020591 P12644/BMP4_HUMAN Bone morphogenetic protein 4 (SEQ ID NO:172)	BMP-4 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-4 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-5 GeneSeq Accession B02797 WO0020591 P22003/BMP5_HUMAN Bone morphogenetic protein 5 (isoform 1) (SEQ ID NO:173) P22003-2|BMP5_HUMAN Isoform 2 of Bone morphogenetic protein 5 (isoform 2) (SEQ ID NO:515)	BMP-5 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-5 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-6 GeneSeq Accession R32904 US	BMP-6 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-6 activity can be determined

Pat. No. 5,187,076 P22004/BMP6_HUMAN Bone morphogenetic protein 6 (SEQ ID NO:174)	using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes. Hemochromatosis.
Osteogenic Protein-1; OP-1; BMP-7 GeneSeq Accession W34783 WO973462 P18075/BMP7_HUMAN Bone morphogenetic protein 7 (SEQ ID NO:175)	OP-1 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. OP-1 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84-8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP7 Variant A (SEQ ID NO:579)	OP-1 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. OP-1 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84-8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP7 Variant B (SEQ ID NO:580)	OP-1 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. OP-1 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84-8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP7 Variant C (SEQ ID NO:581)	OP-1 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. OP-1 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84-8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
Osteogenic Protein-2 GeneSeq Accession R57973 WO9406399 P34820/BMP8B_HUMAN Bone morphogenetic protein 8B (SEQ ID NO:176)	OP-2 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. OP-2 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84-8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 0, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
GDF-1 GeneSeq Accession R60961 WO9406449 P27539/GDF1_HUMAN Embryonic growth/differentiation factor 1 (SEQ ID NO:177)	Members of the TGF-beta family of proteins initiate cell signaling by binding to heteromeric receptor complexes of type I (TbetaRI) and type II (TbetaRII) serine/threonine kinase receptors (reviewed by Massague, J. *et al.* (1994) Trends Cell Biol. 4: 172 178; Miyazono, K. *et al.* (1994) Adv. Immunol. 55: 181-220). Activation of this heteromeric receptor complex occurs when TGF-beta binds to TbetaRII, which then recruits and phosphorylates TbetaRI. Activated TbetaRI then propagates the signal to downstream targets (Chen, F. and Weinberg, R. A. (1995) PNA892: 1565-1569; Wrana, J. L. *et al.* (1994) Nature 370: 341 347). The effect of GDF-1 on signaling can be assayed by treating Primary BAECs transferred with a construct called p3TP-Lux, containing a TGF-beta responsive promoter fused to a

	reporter gene, and measuring luciferase gene expression (Wrana *et al.*, 1994, Nature 370: 341-347). Developmental disorders, Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-9 GeneSeq Accession R86903 WO9533830 Q9UK05/GDF2_HUMAN Growth/differentiation factor 2 (SEQ ID NO:178)	BMP-9 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-9 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-10 GeneSeq Accession R66202 WO9426893 O95393/BMP10_HUMAN Bone morphogenetic protein 10 (SEQ ID NO:179)	BMP-10 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-10 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-12 GeneSeq Accession R78734 WO9516035 Q7Z4P5/GDF7_HUMAN Growth/differentiation factor 7 (SEQ ID NO:180)	BMP-12 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-12 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-15 GeneSeq Accession W11261 W09636710 O95972/BMP15_HUMAN Bone morphogenetic protein 15 (SEQ ID NO:181)	BMP-15 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-15 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-17 GeneSeq Accession Y17870 WO9929718 SEQ ID NO:2 from US Patent No. 7151086 (SEQ ID NO:182)	BMP-17 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-17 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes
BMP-18 GeneSeq Accession Y17871 WO9929718 SEQ ID NO:4 from US Patent No. 7151086	BMP-18 belongs to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP-18 activity can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Induction of Cartilage, Tissue and Bone Growth, and Diabetes

(SEQ ID NO:183)	
Inhibin alpha GeneSeq Accession B02806 WO0020591 P05111/INHA_HUMAN Inhibin alpha chain (SEQ ID NO:184)	The inhibin beta A subunit joins the alpha subunit to form a pituitary FSH secretion inhibitor. Inhibin has been shown to regulate gonadal stromal cell proliferation negatively and to have tumor-suppressor activity. In addition, serum levels of inhibin have been shown to reflect the size of granulosa-cell tumors and can therefore be used as a marker for primary as well as recurrent disease. Tumor suppressor activity of inhibin can be determined using assays known in the art: Matzuk *et al.*, Nature 1992 Nov. 26: 360 (6402); 313-9. Tumor suppression.
Inhibin beta GeneSeq Accession H02808 WO0020591 P08476/INHBA_HUMAN Inhibin beta A chain (SEQ ID NO:185) P09529/INHBB_HUMAN Inhibin beta B chain (SEQ ID NO:186)	The inhibin beta A subunit joins the alpha subunit to form a pituitary FSH secretion inhibitor. Inhibin has been shown to regulate gonadal stromal cell proliferation negatively and to have tumour-suppressor activity. In addition, serum levels of inhibin have been shown to reflect the size of granulosa-cell tumors and can therefore be used as a marker for primary as well as recurrent disease. Tumor suppressor activity of inhibin can be determined using assays known in the art: Matzuk *et al.*, Nature 1992 Nov. 26: 360 (6402); 313-9. Tumor suppression.
Cerberus Protein GeneSeq Accession W86032 WO9849296 O95813/CER1_HUMAN Cerberus (SEQ ID NO:187)	Cerebus is believed to be involved in the inhibition of BMP activity BMP activity, in the presence of the antagonist Cerebus, can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. BMP Antagonist useful for Osteosarcoma, abnormal bone growth.
Soluble BMP Receptor Kinase Protein- 3 GeneSeq Accession R95227 WO9614579 Q13873/BMPR2_HUMAN Bone morphogenetic protein receptor type-2 (SEQ ID NO:188)	Soluble BMP receptor kinase protein-3 is involved in the binding of BMPs. Soluble BMP receptor kinase protein-3 is useful as an antagonist for the inhibition of BMP activity. BMP activity, in the presence of the soluble antagonist BMP receptor kinase protein-3, can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84- 8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. BMP Antagonist useful for Osteosarcoma, abnormal bone growth.
BMP Processing Enzyme Furin GeneSeq Accession W36099 WO9741250 P09958/FURIN_HUMAN Furin (SEQ ID NO:189)	BMPs belong to the transforming growth factor-beta (TGFB) superfamily. Bone morphogenic protein induces bone formation. BMP activity, in the presence of the Furin, can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84-8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 10897-10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Dev. 10, 1580-1594. Bone formation or Regeneration Abnormalities
TGF-beta 1 GeneSeq Accession R29657 WO9216228 P01137/TGFB1_HUMAN Transforming growth	Members of the TGF-beta family of proteins initiate cell signaling by binding to heteromeric receptor complexes of type I (TbetaRI) and type II (TbetaRII) serine/threonine kinase receptors (reviewed by Massague, J. *et al.* (1994) Trends Cell Biol. 4: 172 178; Miyazono, K. *et al.* (1994) Adv. Immunol. 55: 181-220). Activation of this heteromeric receptor complex occurs when TGF-beta. binds to TbetaRII, which then recruits and phosphorylates TbetaRI. Activated TbetaRI then

factor beta-1 (SEQ ID NO:190)	propagates the signal to downstream targets (Chen, F. and Weinberg. R. A. (1995) PNA892: 1565-1569; Wrana, J. L. *et al.* (1994) Nature 370: 341. The effect of TGF betas on signaling can be assayed by treating Primary BAECs transfected with a construct called p3TP-Lux, containing a TGF- beta responsive promoter fused to a reporter gene, and measuring luciferase gene expression (Wrana *et al.*, 1994, Nature 370: 341-347). Useful for treating cancer and to promote wound healing.
TGF-beta 2 GeneSeq Accession R39659 EP542679 P61812/TGFB2_HUMAN Transforming growth factor beta-2 (SEQ ID NO:191)	Members of the TGF-beta family of proteins initiate cell signaling by binding to heteromeric receptor complexes of type I (TbetaRI) and type II (TbetaRII) serine/threonine kinase receptors (reviewed by Massague, J. *et al.* (1994) Trends Cell Biol. 4: 172 178; Miyazono, K. *et al.* (1994) Adv. Immunol. 55: 181-220). Activation of this heteromeric receptor complex occurs when TGF-beta. binds to TbetaRII, which then recruits and phosphorylates TbetaRI. Activated TbetaRI then propagates the signal to downstream targets (Chen, F. and Weinberg. R. A. (1995) PNA892: 1565-1569; Wrana, J. L. *et al.* (1994) Nature 370: 341. The effect of TGF betas on signaling can be assayed by treating Primary BAECs transfected with a construct called p3TP-Lux, containing a TGF- beta responsive promoter fused to a reporter gene, and measuring luciferase gene expression (Wrana *et al.*, 1994, Nature 370: 341-347). Useful for treating cancer and to promote wound healing.
ZTGF-beta 9 GeneSeq Accession Y70654 WO0015798 SEQ ID NO:2 of WO0015798 (SEQ ID NO:192)	Members of the TGF-beta family of proteins initiate cell signaling by binding to heteromeric receptor complexes of type I (TbetaRI) and type II (TbetaRII) serine/threonine kinase receptors (reviewed by Massague, J. *et al.* (1994) Trends Cell Biol. 4: 172 178; Miyazono, K. *et al.* (1994) Adv. Immunol. 55: 181-220). Activation of this heteromeric receptor complex occurs when TGF-beta. binds to TbetaRII, which then recruits and phosphorylates TbetaRI. Activated TbetaRI then propagates the signal to downstream targets (Chen, F. and Weinberg. R. A. (1995) PNA892: 1565-1569; Wrana, J. L. *et al.* (1994) Nature 370: 341. The effect of TGF betas on signaling can be assayed by treating Primary BAECs transfected with a construct called p3TP-Lux, containing a TGF- beta responsive promoter fused to a reporter gene, and measuring luciferase gene expression (Wrana *et al.*, 1994, Nature 370: 341-347). Useful for treating cancer and to promote wound healing.
Anti-TGF beta family antibodies GB2305921	Members of the TGF-beta family of proteins initiate cell signaling by binding to heteromeric receptor complexes of type I (TbetaRI) and type II (TbetaRII) serine/threonine kinase receptors (reviewed by Massague, J. *et al.* (1994) Trends Cell Biol. 4: 172 178; Miyazono, K. *et al.* (1994) Adv. Immunol. 55: 181-220). Activation of this heteromeric receptor complex occurs when TGF-beta. binds to TbetaRII, which then recruits and phosphorylates TbetaRI. Activated TbetaRI then propagates the signal to downstream targets (Chen, F. and Weinberg. R. A. (1995) PNA892: 1565-1569; Wrana, J. L. *et al.* (1994) Nature 370: 341. The effect of TGF betas on signaling in the presence of an anti-TGF beta antibody, can be assayed by treating Primary BAECs transfected with a construct called p3TP-Lux, containing a TGF-beta responsive promoter fused to a reporter gene, and measuring luciferase gene expression (Wrana *et al.*, 1994, Nature 370: 341-347). Useful for control of fibrosis, immune, and inflammatory disease.
Latent TGF beta binding protein II GeneSeq Accession Y70552 WO0012551 Q14767/LTBP2_HUMAN Latent-transforming growth factor beta-binding protein 2 (SEQ ID NO:193)	Members of the TGF-beta family of proteins initiate cell signaling by binding to heteromeric receptor complexes of type I (TbetaRI) and type II (TbetaRII) serine/threonine kinase receptors (reviewed by Massague, J. *et al.* (1994) Trends Cell Biol. 4: 172 178; Miyazono, K. *et al.* (1994) Adv. Immunol. 55: 181-220). Activation of this heteromeric receptor complex occurs when TGF-beta. binds to TbetaRII, which then recruits and phosphorylates TbetaRI. Activated TbetaRI then propagates the signal to downstream targets (Chen, F. and Weinberg. R. A. (1995) PNA892: 1565-1569; Wrana, J. L. *et al.* (1994) Nature 370: 341. The effect of TGF betas on signaling in the presence of a TGF beta binding protein, can be assayed by treating Primary BAECs transfected with a construct called p3TP-Lux, containing a TGF-beta responsivepromoter fused to a reporter gene, and measuring luciferase

	gene expression (Wrana *et al.*, 1994, Nature 370: 341-347). Useful for inhibiting tissue or tumor growth.
MP52 GeneSeq Accession W36100 WO9741250 P43026/GDF5_HUMAN Growth/differentiation factor 5 (SEQ ID NO:194)	Members of the TGF-beta family of proteins initiate cell signaling by binding to heteromeric receptor complexes of type I (TbetaRI) and type II (TbetaRII) serine/threonine kinase receptors (reviewed by Massague, J. *et al.* (1994) Trends Cell Biol. 4: 172 178; Miyazono, K. *et al.* (1994) Adv. Immunol. 55: 181-220). Activation of this heteromeric receptor complex occurs when TGF-beta. binds to TbetaRII, which then recruits and phosphorylates TbetaRI. Activated TbetaRI then propagates the signal to downstream targets (Chen, F. and Weinberg. R. A. (1995) PNA892: 1565-1569; Wrana, J. L. *et al.* (1994) Nature 370: 341. The effect of TGF betas on signaling can be assayed by treating Primary BAECs transfected with a construct called p3TP-Lux, containing a TGF- beta responsive promoter fused to a reporter gene, and measuring luciferase gene expression (Wrana *et al.*, 1994, Nature 370: 341-347). Bone formation or Regeneration Abnormalities
b57 Protein GeneSeq Accession W69293 WO9837195 SEQ ID NO:2 of WO9837195 (SEQ ID NO:195)	BMPs are involved in the induction of bone formation. Specific antagonists are useful is preventing this activity from occurring. BMP activity, in the presence of b57 protein, can be determined using the following assays known in the art: Nat Genet. 2001 Jan; 27(1): 84-8; Eur J Biochem 1996 Apr 1; 237(1): 295-302; J Biol Chem, Vol. 274, Issue 16, 1089- 10902, Apr. 16, 1999; and Hogan, B. L. M. (1996) Genes Deve. 10, 1580-1594. BMP Antagonist useful for Osteosarcoma, abnormal bone growth.
Resistin GeneSeq Accession W69293 WO0064920 Q9HD89/RETN_HUMAN Resistin (isoform 1) (SEQ ID NO:196)	This gene belongs to the family defined by mouse FIZZI and FIZZ3/Resistin genes. The characteristic feature of this family is the C-terminal stretch of 10 cys residues with identical spacing. The mouse homolog of this protein is secreted by adipocytes, may be the hormone potentially linking obesity to type II diabetes. Ability of resistin to influence type II diabetes can be determined using assays known in the art: Pontoglio *et al.*, J Clin Invest 1998 May 15; 101(10): 2215-22. Type II diabetes and Syndrome X.
Galectin-4 GeneSeq Accession W11841 WO9703190 P56470/LEG4_HUMAN Galectin-4 (SEQ ID NO:197)	Galectins are a family of carbohydrate-binding proteins characterized by an affinity for beta- galactoside containing glycoconjugates. Ability of Galectin-4 polypeptides to bind lactose can be determined using assays known in the art: Wada, *et al.*, J Biol Chem 1997 Feb 28; 272(9): 6078- 86. Lactose intolerance.
APM-I; ACRP- 30; Famoxin GeneSeq Accession Y71035 W00026363 Q15848/ADIPO_HUMAN Adiponectin (SEQ ID NO:198)	ACPR30 gene is exclusively expressed in adipose tissue. ACRP30 is thought to increase fatty acid oxidation by muscle tissue. Ability of ACRP30 polypeptides to influence obesity and fat oxidation can be determined using assays known in the art: Fruebis *et al.*, Proc Nat'l Acad Sci USA 2001 Feb 13; 98(4): 2005-10. Obesity, Metabolic disorders, Lipid Metabolism; Hormone Secretion.
ACRP-30 Homologue; Complement Component Clq C GeneSeq Accession B30234 WO0063376 P02747/C1QC_HUMAN Complement C1q	ACPR30 gene is exclusively expressed in adipose tissue. ACRP30 is thought to increase fatty acid oxidation by muscle tissue. Ability of ACRP30 homologue polypeptides to influence obesity and fat oxidation can be determined using assays known in the art: Fruebis *et al.*, Proc Nat'l Acad Sci USA 2001 Feb 13; 98(4): 2005-10. Obesity, Metabolic disorders, Lipid Metabolism; Hormone Secretion.

subcomponent subunit C (SEQ ID NO:199)	
Calpain-10a GeneSeq Accession Y79567 WO0023603 Q9HC96/CAN10_HUMAN Calpain-10 (Isoform A) (SEQ ID NO:200)	Calpain is believed to play a role in insulin secretion and insulin activity, and therefore may be useful in the treatment of type II diabetes. Ability of Calpain-10 to influence type II diabetes can be determined using assays known in the art: Pontoglio *et al.*, J Clin Invest 1998 May 15; 101(10): 2215-22. Diabetes mellitus; Regulation of Insulin secretory response; Insulin mediated glucose transport disorders.
Calpain-10b GeneSeq Accession Y79568 WO0023603 Q9HC96-2/CAN10_HUMAN Isoform B of Calpain-10 (SEQ ID NO:201)	Calpain is believed to play a role in insulin secretion and insulin activity, and therefore may be useful in the treatment of type II diabetes. Ability of Calpain-10 to influence type II diabetes can be determined using assays known in the art: Pontoglio *et al.*, J Clin Invest 1998 May 15; 101(10): 2215-22. Diabetes mellitus; Regulation of Insulin secretory response; Insulin mediated glucose transport disorders.
Calpain-10c GeneSeq Accession Y79569 WO0023603 Q9HC96-3/CAN10_HUMAN Isoform C of Calpain-10 (SEQ ID NO:202)	Calpain is believed to play a role in insulin secretion and insulin activity, and therefore may be useful in the treatment of type II diabetes. Ability of Calpain-10 to influence type II diabetes can be determined using assays known in the art: Pontoglio *et al.*, J Clin Invest 1998 May 15; 101(10): 2215-22. Diabetes mellitus; Regulation of Insulin secretory response; Insulin mediated glucose transport disorders.
PDGF-D GeneSeq Accession Y71130 WO0027879 Q9GZP0/PDGFD_HUMAN Platelet-derived growth factor D (isoform 1) (SEQ ID NO:203)	Vascular Endothelial Growth Factor. Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266). Wound Healing; Atherosclermis.
FasL GeneSeq Accession Y28594 WO9936079 P48023/TNFL6_HUMAN Tumor necrosis factor ligand superfamily member 6 (isoform 1) (SEQ ID NO:204)	Activities associated with apoptosis and immune system functions. Activity can be determined using Apoptosis assays known in the art: Walczak *et al.* (1996) EMBOJ 16: 5386-5397. Apoptosis-related disorders; Auto- immune disorders; Graft v-Host disorders.
Chondro modulin-like protein GeneSeq Accession Y71262 WO0029579	Chondromodulin proteins are cartilage proteins thought to confer resistance to anglogeneis, and thus are useful as anti-angiogenic agents that may have utility in combating cancer. Ability of Chondromodulin-like protein to inhibit vascularization can be determined using assays known in the art: Hirakie *et al.*, J Biol Chem 1997 Dec

SEQ ID NO:2 from WO0029579 (SEQ ID NO:370)	19; 272(51): 32419-26. Antianglogenic agent; Osteoblast proliferation stimulator; prevents vascularization of cartilage tissue; Useful to treat cancer.
Patched GeneSeq Accession W72969 US Pat. No. 5,837,538 Q13635/PTC1_HUMAN Protein patched homolog 1 (isoform L) (SEQ ID NO:205)	Patched is a tumour-suppressor receptor for Sonic hedgehog (shh), which is a protein that controls developmental patterning and growth. Ability of soluble Patched to bind to and inhibit the activities of shh can be determined using assays known in the art: Stone *et al.*, Nature 1996 Nov 14; 384(6605): 129-34. Receptor for Hedgehog cellular proliferation signaling molecule. This receptor is useful as a means of preventing cellular proliferation via the shh signaling path- way, thus useful for cancers.
Patched-2 GeneSeq Accession Y43261 WO9953058 Q9Y6C5/PTC2_HUMAN Protein patched homolog 2 (isoform 1) (SEQ ID NO:206)	Patched is a tumour-suppressor receptor for Sonic hedgehog (shh), which is a protein that controls developmental patterning and growth. Ability of soluble Patched to bind to and inhibit the activities of shh can be determined using assays known in the art: Stone *et al.*, Nature 1996 Nov 14; 384(6605): 129-34. Receptor for Hedgehog cellular proliferation signaling molecule. This receptor is useful as a means of preventing cellular proliferation via the shh signaling path- way, thus useful for cancers.
Maspin; Protease Inhibitor 5 GeneSeq Accession R50938 WO9405804 P36952/SPB5_HUMAN Serpin B5 (isoform 1) (SEQ ID NO:207)	Maspin is a member of the serpin family of serine protease inhibitors that is thought to suppress tumor metastasis. The inhibitory effects of Maspin and other protease inhibitors can be assayed using methods known in the art such as a labeled protease substrate, for example, Universal Protease Substrate (casein, resorufin-labeled): Roche Molecular Biochemicals, Cat. No. 1080733. Tumor suppressor which is down-regulated in breast cancers. The maspin protein has tumour suppressing and invasion sup- pressing activity.
Endostatin GeneSeq Accession B28399 WO0064946 P39060/COIA1_HUMAN Collagen alpha-1(XVIII) chain (isoform 1) (SEQ ID NO:208)	Endostatin is believed to inhibit effects of capillary endothelial cell proliferation. The inhibitory effects of endostatin can be assayed using assays disclosed by Cao *et al.* (1996) J. Biol. Chem. 271 29461-29467. Anti-angiogenic activity. Useful in the prevention and/ or treatment of cancers.
aFGF; FGF-1 GeneSeq Accession P94037 EP298723 P05230/FGF1_HUMAN Fibroblast growth factor 1 (isoform 1) (SEQ ID NO:209)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents. Diabetes, Metabolic Disease, Obesity.
bFGF; FGF-2 GeneSeq	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988

Accession R06685 FR2642086 P09038/FGF2_HUMAN Fibroblast growth factor 2 (isoform 1) (SEQ ID NO:210)	Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-3; INT-2 GeneSeq Accession R07824 WO9503831 P11487/FGF3_HUMAN Fibroblast growth factor 3 (SEQ ID NO:211)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-4; HST-1; HBGF-4 GeneSeq Accession R07825 WO9503831 P08620/FGF4_HUMAN Fibroblast growth factor 4 (isoform 1) (SEQ ID NO:212)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-5 GeneSeq Accession W22600 WO9730155 P12034/FGF5_HUMAN Fibroblast growth factor 5 (isoform long) (SEQ ID NO:213)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-6; Heparin binding secreted transforming factor-2 GeneSeq Accession R58555 EP613946 P10767/FGF6_HUMAN Fibroblast growth factor 6 (SEQ ID NO:214)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-8 GeneSeq Accession R80783 WO9524928 P55075/FGF8_HUMAN Fibroblast growth factor 8 (isoform 8E) (SEQ ID NO:215)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-9; Gila activating	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988

factor GeneSeq Accession R70822 WO9503831 P31371/FGF9_HUMAN Fibroblast growth factor 9 (SEQ ID NO:216)	Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Hair growth. Antagonists may be useful as anti-cancer agents.
FGF-12; Fibroblast growth factor homologous factor-1 GeneSeq Accession W06309 WO9635708 P61328/FGF12_HUMAN Fibroblast growth factor 12 (isoform 1) (SEQ ID NO:217)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-19 GeneSeq Accession Y08582 WO9927100 O95750/FGF19_HUMAN Fibroblast growth factor 19 (SEQ ID NO:218)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Chronic liver disease. Primary biliary cirrhosis. Bile acid-induced liver damage. Antagonists may be useful as anti-cancer agents.
FGF-16 GeneSeq Accession Y05474 WO9918128 O43320/FGF16_HUMAN Fibroblast growth factor 16 (SEQ ID NO:219)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
FGF-18 GeneSeq Accession Y08590 WO9927100 O76093/FGF18_HUMAN Fibroblast growth factor 18 (SEQ ID NO:220)	Fibroblast Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266); Examples 23 and 39 disclosed herein. Promotion of growth and proliferation of cells, such as epithelial cells and keratinocytes. Antagonists may be useful as anti-cancer agents.
flt-3 ligand GeneSeq Accession R67541 EP627487 P49771|FLT3L_HUMAN Fms-related tyrosine kinase 3 ligand (isoform 1) (SEQ ID NO:221)	Stem Cell Progenitor Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Promotion of immune cell growth and/or differentiation.
VEGF-110 GeneSeq Accession Y69417 WO0013702	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of

SEQ ID NO:11 from WO0013702 (SEQ ID NO:222)	cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-121 GeneSeq Accession B50432 WO0071713 SEQ ID NO:2 from WO0071713 (SEQ ID NO:223)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-138 GeneSeq Accession Y43483 WO9940197 SEQ ID NO:4 of WO99/40197 (SEQ ID NO:371)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-145 GeneSeq Accession Y69413 WO0013702 SEQ ID NO:4 from WO0013702 (SEQ ID NO:224)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-162 GeneSeq Accession Y43484 W09940197 SEQ ID NO:8 of WO99/40197 (SEQ ID NO:372)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-165 GeneSeq Accession Y69414 WO0013702 SEQ ID NO:6 from WO0013702 (SEQ ID NO:225)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-182 GeneSeq Accession Y43483 W09940197 SEQ ID NO:6 of WO99/40197 (SEQ ID NO:373)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-189 GeneSeq	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be

Accession Y69415 WO0013702 SEQ ID NO:8 from WO0013702 (SEQ ID NO:226)	determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-206 GeneSeq Accession Y69416 W00013702 SEQ ID NO:10 from WO0013702 (SEQ ID NO:227)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-D GeneSeq Accession W53240 WO9807832 O43915/VEGFD_HUMAN Vascular endothelial growth factor D (SEQ ID NO:374)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF-E; VEGF-X GeneSeq Accession Y33679 WO9947677 SEQ ID NO:2 from WO9947677 (SEQ ID NO:228)	Promotes the growth and/or proliferation of endothelial cells. VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
VEGF Receptor; KDR; flk-1 GeneSeq Accession W69679 WO9831794 P35968/VGFR2_HUMAN Vascular endothelial growth factor receptor 2 (isoform 1) (SEQ ID NO:229)	Receptor for VEGF polypeptides VEGF activity, in the presence of flk-1 polypeptides, can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. VEGF Receptor. Fusion protein with the extracellular domain is useful as an anti-angiogenic agent. Antagonists may be useful in the promotion of angiogenesis.
Soluble VEGF Receptor GeneSeq Accession W47037 US Pat. No. 5,712,380 sVEGF-RI (Figure 3) of US Pat. No. 5,712,380 (SEQ ID NO:442) sVEGF-RII (Figure 11) of US Pat. No. 5,712,380	Receptor for VEGF polypeptides VEGF activity, in the presence of VEGF Receptor polypeptides, can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. VEGF Receptor. Fusion protein with the extracellular domain is useful as an anti-angiogenic agent. Antagonists may be useful in the promotion of angiogenesis.

(SEQ ID NO:443) sVEGF-RTMI (Figure 15) of US Pat. No. 5,712,380 (SEQ ID NO:444) sVEGF-RTMII (Figure 13) of US Pat. No. 5,712,380 (SEQ ID NO:445)	
flt-1 GeneSeq Accession Y70751 WO0021560 P17948/VGFR1_HUMAN Vascular endothelial growth factor receptor 1 (isoform 1) (SEQ ID NO:230)	Receptor for VEGF polypeptides VEGF activity, in the presence of flt-1 polypeptides, can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. VEGF Receptor. Fusion protein with the extracellular domain is useful as an anti-angiogenic agent. Antagonists may be useful in the promotion of angiogenesis.
VEGF R-3; flt-4 GeneSeq Accession B29047 WO0058511 P35916/VGFR3_HUMAN Vascular endothelial growth factor receptor 3 (isoform 1) (SEQ ID NO:231)	Receptor for VEGF polypeptides VEGF activity, in the presence of flt-4 polypeptides, can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. VEGF Receptor. Fusion protein with the extracellular domain is useful as an anti-angiogenic agent. Antagonists may be useful in the promotion of angiogenesis.
Neuropilin-1 GeneSeq Accession Y06319 WO9929858 O14786/NRP1_HUMAN Neuropilin-1 (isoform 1) (SEQ ID NO:232)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Neuropilin-2 GeneSeq Accession Y03618 WO9929858 O60462/NRP2_HUMAN Neuropilin-2 (isoform A22) (SEQ ID NO:233)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Human fast twitch skeletal muscle troponin C GeneSeq Accession W22597 W09730085	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis

P02585/TNNC2_HUMAN Troponin C, skeletal muscle (SEQ ID NO:234)	
Human fast twitch skeletal muscle troponin I GeneSeq Accession W18054 W09730085 P48788/TNNI2_HUMAN Troponin I, fast skeletal muscle (isoform 1) (SEQ ID NO:235)	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis
Human fast twitch skeletal muscle troponin T GeneSeq Accession W22599 W09730085 SEQ ID NO:3 of WO9730085 (SEQ ID NO:236)	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis
fragment. myofibrillar protein troponin I GeneSeq Accession W18053 W09719955 SEQ ID NO:3 of WO9719955 (SEQ ID NO:237)	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis
myofibrillar protein troponin I GeneSeq Accession W18054 WO9719955 SEQ ID NO:3 of WO9719955 (SEQ ID NO:237)	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis
Troponin peptides GeneSeq Accessions Y29581, Y29582, Y29583, Y29584, Y29585, and Y29586 WO9933874 Wildtype troponins provided as: Human fast twitch skeletal muscle troponin C	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis

GeneSeq Accession W22597 W09730085 P02585/TNNC2_HUMAN Troponin C, skeletal muscle (SEQ ID NO:234)
Human fast twitch skeletal muscle troponin I GeneSeq Accession W18054 W09730085 P48788/TNNI2_HUMAN Troponin I, fast skeletal muscle (isoform 1) (SEQ ID NO:235)
Human fast twitch skeletal muscle troponin T GeneSeq Accession W22599 W09730085 SEQ ID NO:3 of WO9730085 (SEQ ID NO:236)
fragment. myofibrillar protein troponin I GeneSeq Accession W18053 W09719955 SEQ ID NO:3 of WO9719955 (SEQ ID NO:237)
Human fast twitch skeletal muscle Troponin subunit C GeneSeq Accession B00134 WO0054770 SEQ ID NO:1 of WO0054770 (SEQ ID NO:375)
Human fast twitch skeletal muscle Troponin subunit I Protein GeneSeq Accession B00135

WO0054770 SEQ ID NO:2 of WO0054770 (SEQ ID NO:376) Human fast twitch skeletal muscle Troponin subunit T GeneSeq Accession B00136 WO0054770 SEQ ID NO:3 of WO0054770 (SEQ ID NO:377)	
Human fast twitch skeletal muscle Troponin subunit C GeneSeq Accession B00134 WO0054770 SEQ ID NO:1 of WO0054770 (SEQ ID NO:375)	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis
Human fast twitch skeletal muscle Troponin subunit I Protein GeneSeq Accession B00135 WO0054770 SEQ ID NO:2 of WO0054770 (SEQ ID NO:376)	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis
Human fast twitch skeletal muscle Troponin subunit T GeneSeq Accession B00136 WO0054770 SEQ ID NO:3 of WO0054770 (SEQ ID NO:377)	Troponins are contractile proteins that are thought to inhibit angiogenesis. High levels may contribute to the difficulty encountered in revascularizing the ischemic myocardium after cardiovascular injury. Ability of soluble Troponins to inhibit angiogenesis can be determined using assays known in the art:. Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis
Activator Inbibitor-1; PAI-1 GeneSeq Accession R08411 WO9013648 P05121/PAI1_HUMAN Plasminogen activator inhibitor 1 (isoform 1)	PAIs are believed to play a role in cancer, and cardiovascular disease and blood-clotting disorders. Methods that measure plasminogen activator inhibitor (PAI) activity are known in the art, for example, assay the ability of PAI to inhibit tissue plasminogen activator (tPA) or urokinase (uPA): J Biochem Biophys Methods 2000 Sep 11; 45(2): 127-40, Breast Cancer Res Treat 1996; 41(2): 141-6. Methods that measure anti- angiogenesis activity are known in the art, for example, Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis; blood-clotting disorders.

(SEQ ID NO:238)	
Plasminogen Activator Inhibitor-2; PAI-2 GeneSeq Accession P94160 DE3722673 P05120/PAI2_HUMAN Plasminogen activator inhibitor 2 (SEQ ID NO:239)	PAIs are believed to play a role in cancer, and cardiovascular disease and blood-clotting disorders. Methods that measure plasminogen activator inhibitor (PAI) activity are known in the art, for example, assay the ability of PAI to inhibit tissue plasminogen activator (tPA) or urokinase (uPA): J Biochem Biophys Methods 2000 Sep 11; 45(2): 127-40, Breast Cancer Res Treat 1996; 41(2): 141-6. Methods that measure anti- angiogenesis activity are known in the art, for example, Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis; blood-clotting disorders.
Activator Inhibitor-2; PAI-2 GeneSeq Accession R10921 WO9102057 P05120/PAI2_HUMAN Plasminogen activator inhibitor 2 (SEQ ID NO:239)	PAIs are believed to play a role in cancer, and cardiovascular disease and blood-clotting disorders. Methods that measure plasminogen activator inhibitor (PAI) activity are known in the art, for example, assay the ability of PAI to inhibit tissue plasminogen activator (tPA) or urokinase (uPA): J Biochem Biophys Methods 2000 Sep 11; 45(2): 127-40, Breast Cancer Res Treat 1996; 41(2): 141-6. Methods that measure anti- angiogenesis activity are known in the art, for example, Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis; blood-clotting disorders.
Human PAI-1 mutants GeneSeq Accessions R11755, R11756, R11757, R11758, R11759, R11760, R11761, R11762 and R11763 WO9105048 Wildtype PAI-1 is provided as P05121/PAI1_HUMAN Plasminogen activator inhibitor 1 (isoform 1) (SEQ ID NO:238)	PAIs are believed to play a role in cancer, and cardiovascular disease and blood-clotting disorders. Methods that measure plasminogen activator inhibitor (PAI) activity are known in the art, for example, assay the ability of PAI to inhibit tissue plasminogen activator (tPA) or urokinase (uPA): J Biochem Biophys Methods 2000 Sep 11; 45(2): 127-40, Breast Cancer Res Treat 1996; 41(2): 141-6. Methods that measure anti- angiogenesis activity are known in the art, for example, Proc Natl Acad Sci USA 1999 Mar 16; 96(6): 2645-50. Anti-angiogenesis; blood-clotting disorders.
CXCR3; CXC GeneSeq Accession Y79372 WO0018431 P49682|CXCR3_HUMAN C-X-C chemokine receptor type 3 (isoform 1) (SEQ ID NO:240)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Soluble CXCR3 polypeptides may be useful for inhibiting chemokine activities and viral infection.
Modified Rantes GeneSeq Accession W38129 WO9737005 Wildtype Rantes provided herein as P13501/CCL5_HUMAN C-C motif chemokine 5	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138:

(SEQ ID NO:241)	Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
RANTES GeneSeq Accession Y05299 EP905240 P13501/CCL5_HUMAN C-C motif chemokine 5 (SEQ ID NO:241)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
MCP-Ia GeneSeq Accession R73914 WO9509232 MCP-1 provided as P13500/CCL2_HUMAN C-C motif chemokine 2 (SEQ ID NO:337)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
MCP-Ib GeneSeq Accession Y26176 WO9929728 MCP-1 provided as P13500/CCL2_HUMAN C-C motif chemokine 2 (SEQ ID NO:337)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
MCP-I receptor GeneSeq Accession R79165 WO9519436 MCP-IA SEQ ID NO:2 of WO9519436 (SEQ ID NO:446) MCP-1B SEQ ID NO:4 of WO9519436 (SEQ ID NO:447)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Soluble MCP-1 Receptor polypep- tides may be useful for inhibiting chemokine activities and viral infection.
MCP-3 GeneSeq Accession R73915 W09509232 P80098/CCL7_HUMAN C-C motif chemokine 7	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined

(SEQ ID NO:336)	using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
MCP-4 receptor GeneSeq Accession W56689 WO9809171 SEQ ID NO:2 of WO9809171 (SEQ ID NO:378)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Soluble MCP-4 Receptor polypep- tides may be useful for inhibiting chemokine activities and viral infection.
RANTES receptor GeneSeq Accession W29588 US Pat. No. 5,652,133 SEQ ID NO:2 of US Pat. No. 5,652,133 (SEQ ID NO:379)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Soluble RANTES Receptor polypep- tides may be useful for inhibiting chemokine activities and viral infection.
CCR5 variant GeneSeq Accession W88238 WO9854317 Variants of wildtype CCR5 which has the sequence of : P51681|CCR5_HUMAN C-C chemokine receptor type 5 (SEQ ID NO:448)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Soluble CCR5 polypeptides may be useful for inhibiting chemokine activities and viral infection.
CCR7 GeneSeq Accession B50859 US Pat. No. 6,153,441 P32248/CCR7_HUMAN C-C chemokine receptor type 7 (SEQ ID NO:243)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Soluble CCR7 polypeptides may be useful for inhibiting chemokine activities and viral infection.
CXC3 GeneSeq Accession W23345 WO9727299	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The

P78423/X3CL1_HUMAN Fractalkine (SEQ ID NO:244)	chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
Eotaxin GeneSeq Accession W10099 WO9700960 P51671/CCL11_HUMAN Eotaxin (SEQ ID NO:245)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
Neurotactin GeneSeq Accessions Y77537, W34307, Y53259, and, Y77539 US Pat. No. 6,013,257 WO9742224 P78423/X3CL1_HUMAN Fractalkine (SEQ ID NO:244)	Neurotactin may play a role in chemotactic leukocyte migration and brain inflammation processes. Chemotactic leukocyte migration assays are known in the art, for example: J. Immunol. Methods 33, ((1980)); Nature 1997 Jun 5; 387(6633): 611-7. Immune disorders.
Human CKbeta-9 GeneSeq Accession B50860 US Pat. No. 6,153,441 SEQ ID NO:2 of US Pat. No. 6,153,441 (SEQ ID NO:246)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
Lymphotactin GeneSeq Accession B50052 WO0073320 P47992/XCL1_HUMAN Lymphotactin (SEQ ID NO:247)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
MIP-3 alpha GeneSeq Accession W44398 WO9801557 P78556/CCL20_HUMAN C-C motif chemokine 20 (isoform 1) (SEQ ID NO:248)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.

MIP-3 beta GeneSeq Accession W44399 WO9801557 Q99731/CCL19_HUMAN C-C motif chemokine 19 (SEQ ID NO:249)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
MIP-Gamma GeneSeq Accession R70798 WO2006135382 (SEQ ID NO:457)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
Stem Cell Inhibitory Factor GeneSeq Accession R11553 WO9104274 SCIF in Table I of WO9104274 (SEQ ID NO:380) SCIF in Table II of WO9104274 (SEQ ID NO:381)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Hematopoietic growth factors.
Thrombopoietin GeneSeq Accession R79905 WO9521920 P40225|TPO_HUMAN Thrombopoietin (isoform 1) (SEQ ID NO:250)	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Hematopoietic growth factors.
c-kit ligand; SCF; Mast cell growth factor; MGF; Fibrosarcoma- derived stem cell factor GeneSeq Accession Y53284, R83978 and R83977 EP992579 and EP676470 P21583|SCF_HUMAN Kit ligand (isoform 1) (SEQ ID NO:251)	C-kit ligan is thought to stimulate the proliferation of mast cells, and is able to augment the proliferation of both myeloid and lymphoid hematopoietic progenitors in bone marrow culture. C-kit ligand is also though to act synergistically with other cytokines. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Hematopoietic growth factors.

Platelet derived growth factor GeneSeq Accession B48653 WO0066736 PDGF-A P04085/PDGFA_HUMAN Platelet-derived growth factor subunit A (Isoform long) (SEQ ID NO:257) PDGF-B P01127/PDGFB_HUMAN Platelet-derived growth factor subunit B (isoform 1) (SEQ ID NO:258)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Melanoma inhibiting protein GeneSeq Accession R69811 WO9503328 (SEQ ID NO:458)	Melanoma inhibiting protein has melanoma-inhibiting activity and can be used to treat cancer (melanoma, glioblastoma, neuroblastoma, small cell lung cancer, neuroectodermal tumors) or as an immunosuppressant (it inhibits IL-2 or phytohaemagglutinin induced proliferation of peripheral blood lymphocytes. Tumor suppressor activity of melanoma inhibiting protein can be determined using assays known in the art: Matzuk *et al.*, Nature 1992 Nov 26; 360(6402): 313-9. Cancer; melanoma
Glioma-derived growth factor GeneSeq Accession R08120 EP399816	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Platelet derived growth factor precursor A GeneSeq Accession R84759 EP682110 PDGF-A precursor (variant D1) (SEQ ID NO:382) PDGF-A precursor (variant 13-1) (SEQ ID NO:383)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Platelet derived growth factor precursor B GeneSeq Accession R84760 EP682110, Figure 1 or Figure 2 Wildtype PDGF-B provided as: PDGF-B P01127/PDGFB_HUMAN	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.

Platelet-derived growth factor subunit B (isoform 1) (SEQ ID NO:258)	
Platelet derived growth factor Bvsis GeneSeq Accession P80595 and P80596 EP282317 Figure 1 of EP282317 (SEQ ID NO:384)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Placental Growth Factor GeneSeq Accessions R23059 and R23060 WO9206194 P49763-2/PLGF_HUMAN Isoform PlGF-1 of Placenta growth factor (isoform PlGF-1) (SEQ ID NO:252)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Placental Growth Factor- 2 GeneSeq Accession Y08289 DE19748734 P49763-3/PLGF_HUMAN Isoform PlGF-2 of Placenta growth factor (isoform PlGF-2) (SEQ ID NO:253)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer.
Thrombopoietin derivative1 GeneSeq Accession Y77244 WO0000612 (*e.g.* Table 3) Wildtype thrombopoietin provided as: P40225|TPO_HUMAN Thrombopoietin (isoform 1) (SEQ ID NO:250)	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Thrombocytopenia, cancer.
Thrombopoietin derivative2 GeneSeq Accession Y77255 WO0000612 (*e.g.* Table 3) Wildtype thrombopoietin provided as:	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Thrombocytopenia, cancer.

P40225|TPO_HUMAN Thrombopoietin (isoform 1) (SEQ ID NO:250)	
Thrombopoietin derivative 3 GeneSeq Accession Y77262 WO0000612 (*e.g.* Table 3) Wildtype thrombopoietin provided as: P40225|TPO_HUMAN Thrombopoietin (isoform 1) (SEQ ID NO:250)	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Thrombocytopenia, cancer.
Thrombopoietin derivative 4 GeneSeq Accession Y77267 WO0000612 (*e.g.* Table 3) Wildtype thrombopoietin provided as: P40225|TPO_HUMAN Thrombopoietin (isoform 1) (SEQ ID NO:250)	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Thrombocytopenia, cancer.
Thrombopoietin derivative 5 GeneSeq Accession Y77246 WO0000612 (*e.g.* Table 3) Wildtype thrombopoietin provided as: P40225|TPO_HUMAN Thrombopoietin (isoform 1) (SEQ ID NO:250)	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Thrombocytopenia, cancer.
Thrombopoietin derivative 6 GeneSeq Accession Y77253 WO0000612 (*e.g.* Table 3) Wildtype thrombopoietin provided as: P40225|TPO_HUMAN	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Thrombocytopenia, cancer.

Thrombopoietin (isoform 1) (SEQ ID NO:250)	
Thrombopoietin derivative 7 GeneSeq Accession Y77256 WO0000612 (*e.g.* Table 3) Wildtype thrombopoietin provided as: P40225|TPO_HUMAN Thrombopoietin (isoform 1) (SEQ ID NO:250)	Thrombopoietin is involved in the regulation of the growth and differentiation of megakaryocytes and preceptors thereof. Thrombopoietin (TPO) can be assayed to determine regulation of growth and differentiation of megakaryocytes. Mol Cell Biol 2001 Apr; 21(8): 2659-70; Exp Hematol 2001 Jan; 29(1): 51-8 and within. Thrombocytopenia, cancer.
Fractalkine GeneSeq Accession Y53255 US Pat. No. 6,043,086 P78423/X3CL1_HUMAN Fractalkine (SEQ ID NO:244)	Fractalkine is believed to play a role in chemotactic leukocyte migration and neurological disorders. Fractalkine activity can be determined using Chemotactic leukocyte migration assays known in the art, for example: J. Immunol. Methods 33, ((1980)); Nature 1997 Jun 5; 387(6633): 611-7. Immune disorders.
CXC3 GeneSeq Accession W23345 WO9757599 P78423/X3CL1_HUMAN Fractalkine (SEQ ID NO:244)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders.
CCR7 GeneSeq Accession B50859 US Pat. No. 6,153,441 P32248/CCR7_HUMAN C-C chemokine receptor type 7 (SEQ ID NO:243)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Soluble CCR7 polypeptides may be useful for inhibiting chemokine activities and viral infection.
Nerve Growth Factor-beta GeneSeq Accession R11474 EP414151 P01138/NGF_HUMAN Beta-nerve growth factor (SEQ ID NO:254)	Nerve Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266) Neurological disorders, cancer
Nerve Growth Factor-	Nerve Growth Factor Proliferation assay using NR6R 3T3 cells (Rizzino 1988 Cancer

beta2 GeneSeq Accession W69725 EP859056 Fig 1 of EP859056 (SEQ ID NO:465)	Res. 48: 4266 Neurological disorders, cancer
Neurotrophin-3 GeneSeq Accession W8889 WO9821234 P20783/NTF3_HUMAN Neurotrophin-3 (isoform 1) (SEQ ID NO:255)	Neurotrophins regulate neuronal cell survival and synaptic plasticity. Trk tyrosine kinase activation assays known in the art can be used to assay for neurotrophin activity, for example, Proc Natl Acad Sci USA 2001 Mar 13; 98(6): 3555-3560. Neurological disorders, cancer
Neurotrophin-4 GeneSeq Accession R47100 WO9325684 P34130/NTF4_HUMAN Neurotrophin-4 (SEQ ID NO:256)	Neurotrophins regulate neuronal cell survival and synaptic plasticity. Trk tyrosine kinase activation assays known in the art can be used to assay for neurotrophin activity, for example, Proc Natl Acad Sci USA 2001 Mar 13; 98(6): 3555-3560. Neurological disorders, cancer
Neurotrophin- 4a GeneSeq Accession R47101 WO9325684 Wildtype neurotrophin provided as: P34130/NTF4_HUMAN Neurotrophin-4 (SEQ ID NO:256)	Neurotrophins regulate neuronal cell survival and synaptic plasticity. Trk tyrosine kinase activation assays known in the art can be used to assay for neurotrophin activity, for example, Proc Natl Acad Sci USA 2001 Mar 13; 98(6): 3555-3560. Neurological disorders, cancer
Neurotrophin- 4b GeneSeq Accession R47102 WO9325684 P34130/NTF4_HUMAN Neurotrophin-4 (SEQ ID NO:256)	Neurotrophins regulate neuronal cell survival and synaptic plasticity. tyrosine kinases. Trk tyrosine kinase activation assays known in the art can be used to assay for neurotrophin activity, for example, Proc Natl Acad Sci USA 2001 Mar 13; 98(6): 3555-3560. Neurological disorders, cancer
Neurotrophin- 4c GeneSeq Accession R47103 WO9325684 P34130/NTF4_HUMAN Neurotrophin-4 (SEQ ID NO:256)	Neurotrophins regulate neuronal cell survival and synaptic plasticity. tyrosine kinases. Trk tyrosine kinase activation assays known in the art can be used to assay for neurotrophin activity, for example, Proc Natl Acad Sci USA 2001 Mar 13; 98(6): 3555-3560. Neurological disorders, cancer
Neurotrophin- 4d GeneSeq Accession R47102 WO9325684	Neurotrophins regulate neuronal cell survival and synaptic plasticity. tyrosine kinases. Trk tyrosine kinase activation assays known in the art can be used to assay for neurotrophin activity, for example, Proc Natl Acad Sci USA 2001 Mar 13; 98(6): 3555-

P34130/NTF4_HUMAN Neurotrophin-4 (SEQ ID NO:256)	3560. Neurological disorders, cancer
Platelet-Derived Growth Factor A chain GeneSeq Accession R38918 US Pat. No. 5,219,739 P04085/PDGFA_HUMAN Platelet-derived growth factor subunit A (Isoform long) (SEQ ID NO:257)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. W00045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Hematopoietic and immune dis- orders. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer
Platelet-Derived Growth Factor B chain GeneSeq Accession R38919 US Pat. No. 5,219,739 P01127/PDGFB_HUMAN Platelet-derived growth factor subunit B (isoform 1) (SEQ ID NO:258)	Vascular Endothelial Growth Factor VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. W00045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Hematopoietic and immune dis- orders. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer
Stromal Derived Factor- 1 alpha GeneSeq Accession Y39995 WO9948528 P48061-2/SDF1_HUMAN Isoform Alpha of Stromal cell-derived factor 1 (isoform alpha) (SEQ ID NO:259)	Stromal Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266) Hematopoietic, immune disorders, cancer
Stromal Derived Factor- 1 beta GeneSeq Accession R75420 CA2117953 P48061/SDF1_HUMAN Stromal cell-derived factor 1 (isoform beta) (SEQ ID NO:260)	Stromal Growth Factor Proliferation assay using NR6R-3T3 cells (Rizzino 1988 Cancer Res. 48: 4266) Hematopoietic, immune disorders, cancer
Tarc GeneSeq Accession W14917 WO9711969 Q92583/CCL17_HUMAN C-C motif chemokine 17 (SEQ ID NO:261)	Chemotactic for T lymphocytes. May play a role in T-cell development. Thought to bind CCR8 and CCR4 Chemotactic leukocyte migration assays are known in the art, for example: J. Immunol. Methods 33 ((1980)) Antiinflammatory. Immune disorders, cancer

Prolactin GeneSeq Accession R78691 WO9521625 P01236/PRL_HUMAN Prolactin (SEQ ID NO:262)	Prolactin is involved in immune cell proliferation and apoptosis. Immune coil proliferation and suppression of apoptosis by prolactin can be assayed by methods well-known in the art, for example, Buckley, AR and Buckley DJ, Ann N Y Acad Sci 2000; 917: 522-33, and within. Reproductive system disorders, cancer.
Prolactin2 GeneSeq Accession Y31764 US Pat. No. 5,955,346	Prolactin is involved in immune cell proliferation and apoptosis. Immune coil proliferation and suppression of apoptosis by prolactin can be assayed by methods well-known in the art, for example, Buckley, AR and Buckley DJ, Ann N Y Acad Sci 2000; 917: 522-33, and within. Reproductive system disorders, cancer.
Follicle stimulating hormone Alpha subunit GeneSeq Accession Y54160 EP974359 P01215/GLHA_HUMAN Glycoprotein hormones alpha chain (SEQ ID NO:263)	FSH stimulates secretion of interleukin-1 by cells isolated from women in the follicular phase FSH activities can be determined using assays known in the art; J Gend Specif Med 1999 Nov-Dec; 2(6): 30-4; Mol Cell Endocrinol. 1997 Nov 15; 134(2): 109-18. Reproductive system disorders, cancer.
Follicle stimulating hormone Beta subunit GeneSeq Accession Y54161 EP974359 P01225/FSHB_HUMAN Follitropin subunit beta (SEQ ID NO:264)	FSH stimulates secretion of interleukin-1 by cells isolated from women in the follicular phase FSH activities can be determined using assays known in the art; J Gend Specif Med 1999 Nov-Dec; 2(6): 30-4; Mol Cell Endocrinol. 1997 Nov 15; 134(2): 109-18. Reproductive system disorders, cancer.
Substance P (tachykinin) GeneSeq Accession B23027 WO0054053 (SEQ ID NO:385)	Substance P is associated with immunoregulation. Immuneregulation and bone marrow, cell proliferation by substance P can be assayed by methods well-known in the art, for example, Lai *et al.* Proc Natl Acad Sci USA 2001 Mar 27; 98(7): 3970-5; Jallat-Daloz *et al.* Allergy Asthma Proc 2001 Jan-Feb; 22(1): 17- 23; Kahler *et al.* Exp Lung Res 2001 Jan-Feb; 27(1): 25-46; and Adamus MA and Dabrowski ZJ. J Cell Biochem 2001; 81(3)499-506. diabetes mellitus, hypertension, cancer
Oxytocin (Neurophysin I) GeneSeq Accession B24085 and B24086 WO0053755 P01178/NEU1_HUMAN Oxytocin-neurophysin 1 (SEQ ID NO:265)	Oxytocin is involved in the induction of prostaglandin (E2) release as well as an increased amount of calcium release by smooth muscle cells. Oxytocin and prostaglandin E(2) release and Ocytocin (Ca2+) increase can be assayed by methods well-known in the art, for example, Pavan *et al.*, AM J Obset Gynecol 2000 Jul; 183(1): 76- 82 and Holda *et al.*, Cell Calcium 1996 Jul; 20(1): 43 51. inflammatory disorders immunologic disorders, cancer
Vasopressin (Neurophysin II) GeneSeq Accession B24085 and B24086 WO0053755 P01185/NEU2_HUMAN Vasopressin-neurophysin	Vasopressinis believed to have a direct antidiuretic action on the kidney, and it is thought to cause vasoconstriction of the peripheral vessels. Vasopressin activity can be determined using assays known in the art, for example, Endocr Regul 1996 Mar; 30(I): 13-17. inflammatory disorders immunologic disorders, cancer

2-copeptin (SEQ ID NO:266)	
IL-1 GeneSeq Accession P60326 EP165654 IL-1 alpha P01583|IL1A_HUMAN Interleukin-1 alpha (SEQ ID NO:269) IL-1 beta P01584|IL1B_HUMAN Interleukin-1 beta (SEQ ID NO:267)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarclio (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
IL-1 mature GeneSeq Accession R14855 EP456332 (mature truncated form wherein the precursor is cleaved between amino acids 116-117) (SEQ ID NO:386)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarclio (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
IL-1 beta GeneSeq Accession Y08322 WO9922763 P01584|IL1B_HUMAN Interleukin-1 beta (SEQ ID NO:267)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarclio (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
IL-3 variants GeneSeq Accession P80382, P80383, P80384, and P80381 WO8806161 Variants of wildtype IL-3 which has the sequence: P08700|IL3_HUMAN Interleukin-3 (SEQ ID NO:449)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Kitamura et al (1989) J Cell Physiol. 140 323-334. inflammatory disorders immunologic disorders, cancer
IL-4 GeneSeq Accession P70615 WO8702990 P05112/IL4_HUMAN Interleukin-4 (isoform 1)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132,

(SEQ ID NO:268)	287-295. inflammatory disorders immunologic disorders, cancer
IL-4 muteins GeneSeq Accession W52151 W52152 W52153 W52154 W52155 W52156 W52157 W52158 W52159 W52160 W52161 W52162 W52163 W52164 and W52165 WO9747744 Variants of wildtype IL-4 which has the sequence: P05112/IL4_HUMAN Interleukin-4 (isoform 1) (SEQ ID NO:268)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132, 287-295. inflammatory disorders immunologic disorders, cancer
IL-1 alpha GeneSeq Accession P90108 EP324447 P01583|IL1A_HUMAN Interleukin-1 alpha (SEQ ID NO:269)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarclio (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
IL-3 variants GeneSeq Accession R38561, R38562, R38563, R38564, R38565, R38566, R38567, R38568, R38569, R38570, R38571, and R38572 WO9307171 Variants of wildtype IL-3 which has the sequence: P08700|IL3_HUMAN Interleukin-3 (SEQ ID NO:449)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Aarden et al (1987) Eur. J. Immunol 17, 1411-16. inflammatory disorders immunologic disorders, cancer
IL-6 GeneSeq Accession R45717 and R45718 WO9402512 P05231/IL6_HUMAN Interleukin-6 (SEQ ID NO:270)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Aarden et al (1987) Eur. J. Immunol 17, 1411-16. inflammatory disorders immunologic disorders, cancer. Obesity. Metabolic Disease. Diabetes.
IL-13 GeneSeq Accession R48624 WO9404680 P35225/IL13_HUMAN	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity

Interleukin-13 (SEQ ID NO:271)	can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Boutelier et al (1995) J. Immunol. Methods 181, 29. inflammatory disorders immunologic disorders, cancer
IL-4 mutein GeneSeq Accession R47182 DE4137333 Variants of wildtype IL-4 which has the sequence: P05112/IL4_HUMAN Interleukin-4 (isoform 1) (SEQ ID NO:268)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132, 287-295. inflammatory disorders immunologic disorders, cancer
IL-4 mutein Y124X GeneSeq Accession R47183 DE4137333 Variants of wildtype IL-4 which has the sequence: P05112/IL4_HUMAN Interleukin-4 (isoform 1) (SEQ ID NO:268))	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132, 287-295. inflammatory disorders immunologic disorders, cancer
IL-4 mutein Y124G GeneSeq Accession R47184 DE4137333 Variants of wildtype IL-4 which has the sequence: P05112/IL4_HUMAN Interleukin-4 (isoform 1) (SEQ ID NO:268)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132, 287-295. inflammatory disorders immunologic disorders, cancer
Human Interleukin-10 (precursor) GeneSeq Accession R41664 WO9317698 P22301/IL10_HUMAN Interleukin-10 (precursor form is processed into a truncated mature form) (SEQ ID NO:272)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Thompson-Snipes et al (1991) J. Exp. Med. 173, 507-510. inflammatory disorders immunologic disorders, cancer

Human Interleukin-10 GeneSeq Accession R42642 WO9318783-A SEQ ID NO:3 of WO9318783-A (mature IL-10) (SEQ ID NO:273)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Thompson-Snipes et al (1991) J. Exp. Med. 173, 507-510. inflammatory disorders immunologic disorders, cancer
Human interleukin-1 beta precursor. GeneSeq Accession R42447 EP569042 P01584/IL1B_HUMAN Interleukin-1 beta (SEQ ID NO:274)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarclio (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
Interleukin- 1alpha GeneSeq Accession R45364 EP578278 P01583|IL1A_HUMAN Interleukin-1 alpha (SEQ ID NO:269)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
Human interleukin-3 variant GeneSeq Accession R22814 JP04063595 Variants of wildtype IL-3 which has the sequence: P08700|IL3_HUMAN Interleukin-3 (SEQ ID NO:449)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. inflammatory disorders immunologic disorders, cancer
IL-1i fragments GeneSeq Accession R35484 and R35485 EP541920	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarclio (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
IL-1 inhibitor (IL-Ii) GeneSeq Accession R35486 and R35484 EPS541920	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarclio (1989) inflammatory disorders immunologic disorders, cancer

ICE 22 kD subunit. GeneSeq Accession R33780 EP533350 SEQ ID NO:16 of EP533350 (SEQ ID NO:450)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
ICE 20 kD subunit. GeneSeq Accession R33781 EP533350 SEQ ID NO:17 of EP533350 (SEQ ID NO:451)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
ICE 10 kD subunit GeneSeq Accession R33782 EP533350 SEQ ID NO:18 of EP533350 (SEQ ID NO:452)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
Human Interleukin-10 (precursor) GeneSeq Accession R41664 WO9317698 P22301/IL10_HUMAN Interleukin-10 (precursor form is processed into a truncated mature form) (SEQ ID NO:272)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Thompson-Snipes et al (1991) J. Exp. Med. 173, 507-510. inflammatory disorders immunologic disorders, cancer
Human Interleukin-10 GeneSeq Accession R42642 WO9318783 SEQ ID NO:3 of WO9318783-A (mature IL-10) (SEQ ID NO:273)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Thompson-Snipes et al (1991) J. Exp. Med. 173, 507-510. inflammatory disorders immunologic disorders, cancer
Human Interleukin-1 beta precursor GeneSeq Accession R42447 EP569042 P01584/IL1B_HUMAN Interleukin-1 beta	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. inflammatory disorders immunologic disorders, cancer

(SEQ ID NO:274)	
Human interleukin-6 GeneSeq Accession R49041 WO9403492 P05231/IL6_HUMAN Interleukin-6 (SEQ ID NO:270)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Aarden et al (1987) Eur. J. Immunol 17, 1411-16. inflammatory disorders immunologic disorders, cancer
Mutant Interleukin 6 S176R GeneSeq Accession R54990 WO9411402 S176R variant of wildtype IL-6 which has the sequence: P05231/IL6_HUMAN Interleukin-6 (SEQ ID NO:270)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Aarden et al (1987) Eur. J. Immunol 17, 1411-16. inflammatory disorders immunologic disorders, cancer
Interleukin 6 GeneSeq Accession R55256 JP06145063 P05231/IL6_HUMAN Interleukin-6 (SEQ ID NO:270)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Aarden et al (1987) Eur. J. Immunol 17, 1411-16. inflammatory disorders immunologic disorders, cancer
Interleukin 8 (IL-8) receptor GeneSeq Accession R53932 JP06100595 GenBank: AAA59159.1 (SEQ ID NO:275)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Holmes et al (1991) Science 253, 1278-80. Soluble IL-8 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-7 GeneSeq Accession R59919 US Pat. No. 5,328,988 P13232/IL7_HUMAN Interleukin-7 (isoform 1) (SEQ ID NO:276)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Park et al (1990) J. Exp. Med. 171, 1073-79. inflammatory disorders immunologic disorders, cancer
IL-3 containing fusion protein. GeneSeq Accession R79342 and R79344 WO9521254 Fusions of wildtype IL-3	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington,

which has the sequence: P08700|IL3_HUMAN Interleukin-3 (SEQ ID NO:449)	D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. inflammatory disorders immunologic disorders, cancer
IL-3 mutant proteins GeneSeq Accession R79254, R79255, R79256, R79257, R79258, R79259, R79260, R79261, R79262, R79263, R79264, R79265, R79266, R79267, R79268, R79269, R79270, R79271, R79272, R79273, R79274, R79275, R79276, R79277, R79278, R79279, R79280, R79281, R79282, R79283, R79284, and R79285 ZA9402636 Variants of wildtype IL-3 which has the sequence: P08700|IL3_HUMAN Interleukin-3 (SEQ ID NO:449)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Giri et al (1994) EMBO J. 13 2822-2830. inflammatory disorders immunologic disorders, cancer
IL-12 p40 subunit. GeneSeq Accession R63018 AU9466072 P2946/|IL12B_HUMAN Interleukin-12 subunit beta (SEQ ID NO:277)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
AGF GeneSeq Accession R64240 WO9429344 Q8NI99/ANGL6_HUMAN Angiopoietin-related protein 6 (SEQ ID NO:278)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
Human interlaukin-12 40 kD subunit GeneSeq Accession R79187 WO9519786 P2946/|IL12B_HUMAN Interleukin-12 subunit beta (SEQ ID NO:277)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Hori et al (1987), Blood 70, 1069- 1078. inflammatory disorders immunologic disorders, cancer
Human interleukin-15	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes,

receptor from clone P1 GeneSeq Accession R90843 WO9530695 Q13261|I15RA_HUMAN Interleukin-15 receptor subunit alpha Isoform 1) (SEQ ID NO:453)	monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Giri et al (1994) EMBO J. 13 2822- 2830. Soluble IL-8 receptor polypep- tides may be useful for inhibiting interleukin activities. Obesity. Metabolic Disease. Diabetes. Enhancing secretion and stability of Interleukin 15
Human interleukin-7 GeneSeq Accession R92796 WO9604306 P13232/IL7_HUMAN Interleukin-7 (isoform 1) (SEQ ID NO:276)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Park et al (1990) J. Exp. Med. 171, 1073-79. inflammatory disorders immunologic disorders, cancer
interleukin-9 GeneSeq Accession R92797 WO9604306 P15248/IL9_HUMAN Interleukin-9 (SEQ ID NO:279)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. inflammatory disorders immunologic disorders, cancer
interleukin-3 GeneSeq Accession R92801 WO9604306 P08700|IL3_HUMAN Interleukin-3 (SEQ ID NO:280)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. inflammatory disorders immunologic disorders, cancer
Human interleukin-5 GeneSeq Accession R92802 WO9604306 P05113/IL5_HUMAN Interleukin-5 (SEQ ID NO:281)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. inflammatory disorders immunologic disorders, cancer
Recombinant interleukin-16 GeneSeq Accession W33373 DE19617202 Q14005/IL16_HUMAN Pro-interleukin-16 (isoform 1) (SEQ ID NO:282)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Lim et al (1996) J. Immunol. 156, 2566-70. inflammatory disorders immunologic disorders, cancer
Human IL-16 protein GeneSeq Accession	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of

W33234 DE19617202 Q14005/IL16_HUMAN Pro-interleukin-16 (isoform 1) (SEQ ID NO:282)	immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Lim et al (1996) J. Immunol. 156, 2566-70. inflammatory disorders immunologic disorders, cancer
Thrl 17 human interleukin 9 GeneSeq Accession W27521 WO9708321 P15248|IL9_HUMAN Interleukin-9 (SEQ ID NO:387)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
Metl 17 human interleukin 9 GeneSeq Accession W27522 WO9708321 (SEQ ID NO:388)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. inflammatory disorders immunologic disorders, cancer
Human intracellular IL- 1 receptor antagonist. GeneSeq Accession W77158 EP864585 (*e.g.* SEQ ID NOs:12 to 19, or 22 to 25 of this publication).	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
Human interleukin-18 protein (IL-18) GeneSeq Accession W77158 EP864585 Q14116/IL18_HUMAN Interleukin-18 (isoform 1) (SEQ ID NO:283)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and USHIO et al (1996) J. Immunol. 156, 4274-79. inflammatory disorders immunologic disorders, cancer
Human interleukin-18 GeneSeq Accession W77077 EP861663 Q14116/IL18_HUMAN Interleukin-18 (isoform 1) (SEQ ID NO:283)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and USHIO et al (1996) J. Immunol. 156, 4274-79. inflammatory disorders immunologic disorders, cancer
Human interleukin 18 derivatives GeneSeq Accessions W77083,	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis

W77084, W77085, W77086, W77087, W77088, and W77089 EP861663 Variants of wildtype IL18 which is provided as: Q14116/IL18_HUMAN Interleukin-18 (isoform 1) (SEQ ID NO:283)	of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Ushio et al (1996) J. Immunol, 156, 4274-79. inflammatory disorders immunologic disorders, cancer
Interleukin-9 (IL-9) mature protein (Thr117 version). GeneSeq Accession W68158 WO9827997 Figure 2 of WO9827997 (SEQ ID NO:389)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. inflammatory disorders immunologic disorders, cancer
IL-9 mature protein variant (Met117 version) GenSeq Accession W68157 WO9827997 Figure 3 of WO9827997 (SEQ ID NO:390)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. inflammatory disorders immunologic disorders, cancer
Human IL-9 receptor protein variant #3. GeneSeq Accession W64058 WO9824904 Wildtype IL-9R is provided as: Q01113/IL9R_HUMAN Interleukin-9 receptor (isoform 1) (SEQ ID NO:303)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. inflammatory disorders immunologic disorders, cancer
Human IL-9 receptor protein variant fragment GenSeq Accession W64060 WO9824904 Wildtype IL-9R is provided as: Q01113/IL9R_HUMAN Interleukin-9 receptor (isoform 1)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. Soluble IL-9 receptor polypep- tides may be useful for inhibiting interleukin activities.

(SEQ ID NO:303)	
Human IL-9 receptor protein variant #3. GeneSeq Accession W64061 WO9824904 Wildtype IL-9R is provided as: Q01113/IL9R_HUMAN Interleukin-9 receptor (isoform 1) (SEQ ID NO:303)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. Soluble IL-9 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human Interleukin-12 p40 protein GeneSeq Accession W51311 WO9817689 P2946/IL12B_HUMAN Interleukin-12 subunit beta (SEQ ID NO:277)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Hori et al (1987), Blood 70, 1069- 1078. inflammatory disorders immunologic disorders, cancer
Human Interleukin-12 p35 protein GeneSeq Accession W51312 WO9817689 P29459/IL12A_HUMAN Interleukin-12 subunit alpha (SEQ ID NO:284)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Hori et al (1987), Blood 70, 1069- 1078. inflammatory disorders immunologic disorders, cancer
Human protein with IL-16 activity GeneSeq Accession W63753 DE19649233-	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Lim et al (1996) J. Immunol. 156, 2566-70. inflammatory disorders immunologic disorders, cancer
Human protein with IL-16 activity GeneSeq Accession W59425 DE19649233-	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Lim et al (1996) J. Immunol. 156, 2566-70. inflammatory disorders immunologic disorders, cancer
Human interleukin-15 GeneSeq Accession W53878 US Pat. No.	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis

5,747,024 P40933/IL15_HUMAN Interleukin-15 (isoform IL15-S48AA) (SEQ ID NO:285)	of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Giri et al (1994) EMBO J. 13 2822- 2830. inflammatory disorders immunologic disorders, cancer. Obesity. Metabolic Disease. Diabetes.
Human wild- type interleukin-4 (hIL-4) protein GeneSeq Accession W52149 WO9747744 P05112/IL4_HUMAN Interleukin-4 (isoform 1) (SEQ ID NO:286)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132, 287-295. inflammatory disorders immunologic disorders, cancer
interleukin-4 muteins GeneSeq Accessions W52150, W52151, W52153, W52154, W52155, W52156, W52157, W52158, W52159, W52160, W52161, W52162, W52163, W52164, W52165, W52166, and W52167 WO9747744 Variants of wildtype IL-4 which has the sequence: P05112/IL4_HUMAN Interleukin-4 (isoform 1) (SEQ ID NO:268)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132, 287-295. inflammatory disorders immunologic disorders, cancer
Human interleukin 1 delta GeneSeq Accession Y28408 WO9935268 SEQ ID NO:4 of WO9935268 (SEQ ID NO:287)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer
Human interleukin-1 receptor antagonist beta GeneSeq Accession Y24395 WO9935268	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. inflammatory disorders immunologic disorders, cancer

Human EDIRF II protein sequence GeneSeq Accession Y22199 WO9932632 SEQ ID NO:6 of WO9932632 (SEQ ID NO:391)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
Human EDIRF I protein sequence GeneSeq Accession Y22197 WO9932632 SEQ ID NO:2 of WO9932632 (SEQ ID NO:392)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
Human IL- 1RD10 protein sequence GeneSeq Accession Y14131 WO9919480 SEQ ID NO:20 of WO9919480	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. Soluble IL-1RD10 receptor polypep- tides may be useful for inhibiting interleukin activites.
Human IL- 1RD9 GeneSeq Accession Y14122 WO9919480 SEQ ID NOS:6, 8, 10 of WO9919480	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. Soluble IL-1RD10 receptor polypep- tides may be useful for inhibiting interleukin activites.
Human DNAX interleukin-40 GeneSeq Accession Y09196 WO9919491 SEQ ID NO: 2 or 4 of WO9919491 (SEQ ID NO:454)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
(DIL-40) alternative sequence GeneSeq Accession Y09197 WO9919491 SEQ ID NO: 4 of WO9919491 (SEQ ID NO:455)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
IL-11 GeneSeq Accession R50176 WO9405318	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of

P2080/IL11_HUMAN Interleukin-11 (isoform 1) (SEQ ID NO:288)	immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Lu et al (1994) J immunol. Methods 173, 19. inflammatory disorders immunologic disorders, cancer
Human adipogenesis inhibitory factor GeneSeq Accession R43260 EP566410 (also known as IL-11) P2080/IL11_HUMAN Interleukin-11 (isoform 1) (SEQ ID NO:288)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
IL-11 GeneSeq Accession W02202 JP08127539 P2080/IL11_HUMAN Interleukin-11 (isoform 1) (SEQ ID NO:288)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Lu et al (1994) J immunol. Methods 173, 19. inflammatory disorders immunologic disorders, cancer
IL-14 GeneSeq Accession R55800 WO9416074 P40222/TXLNA_HUMAN Alpha-taxilin (SEQ ID NO:289)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Ambrus et al (1993) PNAS 90, 63330-34. inflammatory disorders immunologic disorders, cancer
IL-17 receptor GeneSeq Accession B03807 US Pat. No. 6,072,033 Q96F46/I17RA_HUMAN Interleukin-17 receptor A (SEQ ID NO:290)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yao et al (1995) J. Immunol. 155, 5483-86. Soluble IL-17 receptor polypep- tides may be useful for inhibiting interleukin activites.
IL-17 GeneSeq Accession R76573 WO9518826 Q16552/IL17_HUMAN Interleukin-17A (SEQ ID NO:291)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yao et al (1995) J. Immunol. 155, 5483-86. inflammatory disorders immunologic disorders, cancer
CTLA-8 GeneSeq Accession W13651	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of

WO9704097 (also known as IL-17) Q16552/IL17_HUMAN Interleukin-17A (SEQ ID NO:291)	immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. inflammatory disorders immunologic disorders, cancer
IL-19 GeneSeq Accession W37935 WO9808870 Q9UHD0|IL19_HUMAN Interleukin-19 (isoform 1) (SEQ ID NO:292)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Gallagher et al (2000) Genes Immun. 1, 442-50. inflammatory disorders immunologic disorders, cancer
IL-21 (TIF) GeneSeq Accession Y92879 WO0024758 Q9HBE4/IL21_HUMAN Interleukin-21 (isoform 1) (SEQ ID NO:293)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Parrish-Novak et al (2000) Nature 408, 57-63. inflammatory disorders immunologic disorders, cancer
IL-8 receptor GeneSeq Accession R33420 WO9306229 IL-8RA P25024/CXCR1_HUMAN C-X-C chemokine receptor type 1 (SEQ ID NO:294) IL-8RB P25025/CXCR2_HUMAN C-X-C chemokine receptor type 2 (SEQ ID NO:295)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Holmes et al (1991) Science 253, 1278-80. Soluble IL-8 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human type II interleukin-1 receptor GeneSeq Accession R85480 US Pat. No. 5,464,937 P27930/IL1R2_HUMAN Interleukin-1 receptor type 2 (SEQ ID NO:296)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. Soluble type II interleukin-1 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-12 receptor GeneSeq	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of

Accession R69632 EP638644 IL-12 receptor B1 P42701|I12R1_HUMAN Interleukin-12 receptor subunit beta-1 (isoform 1) (SEQ ID NO:393) IL-12 receptor B2 Q99665|I12R2_HUMAN Interleukin-12 receptor subunit beta-2 (isoform 1) (SEQ ID NO:394)	immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Hori et al (1987), Blood 70, 1069- 1078. Soluble IL-12 receptor polypep- tides may be useful for inhibiting interleukin activities.
Interleukin 8 receptor B GeneSeq Accession R80758 US Pat. No. 5,440,021 IL-8RB P25025/CXCR2_HUMAN C-X-C chemokine receptor type 2 (SEQ ID NO:295)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Holmes et al (1991) Science 253, 1278-80. Soluble IL-8 receptor B polypep- tides may be useful for inhibiting interleukin activities.
Human IL-8 receptor protein hIL8RA GeneSeq Accession B09989 JP08103276 IL-8RA P25024/CXCR1_HUMAN C-X-C chemokine receptor type 1 (SEQ ID NO:294)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Holmes et al (1991) Science 253, 1278-80. Soluble IL-8 receptor A polypep- tides may be useful for inhibiting interleukin activities.
Human IL-8 receptor protein hIL8R GeneSeq Accession B09990 JP08103276 IL-8RA P25024/CXCR1_HUMAN C-X-C chemokine receptor type 1 (SEQ ID NO:294) IL-8RB P25025/CXCR2_HUMAN C-X-C chemokine receptor	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Holmes et al (1991) Science 253, 1278-80. Soluble IL-8 receptor polypep- tides may be useful for inhibiting interleukin activities.

type 2 (SEQ ID NO:295)	
Interleukin-2 receptor associated protein p43 GeneSeq Accession R97569 WO9621732- SEQ ID NO:2 of WO9621732 (SEQ ID NO:395)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferons: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Gillis et al (1978) J. Immunol. 120, 2027. Soluble IL-2 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-17 receptor GeneSeq Accession W04185 WO9629408 Q96F46/I17RA_HUMAN Interleukin-17 receptor A (SEQ ID NO:290)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yao et al (1995) J. Immunol. 155, 5483-86. Soluble IL-17 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-11 receptor GeneSeq Accession R99090 WO9619574 Q14626/I11RA_HUMAN Interleukin-11 receptor subunit alpha (SEQ ID NO:297)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Lu et al (1994) J immunol. Methods 173, 19. Soluble IL-11 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-1 receptor accessory protein GeneSeq Accession W01911 WO9623067 Human IL1R Acp SEQ ID NO:3 of WO9623067 (SEQ ID NO:396) Soluble Human IL1R Acp SEQ ID NO:9 of WO9623067 (SEQ ID NO:397)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. Inflammatory disorders immunologic disorders, cancer
AGF Protein GeneSeq Accession R92749 US Pat. No. 5,488,032 Q8NI99/ANGL6_HUMAN Angiopoietin-related	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington,

protein 6 (SEQ ID NO:278)	D.C. 1987, pp. 221-225. Inflammatory disorders immunologic disorders, cancer
Human interleukin-1 type-3 receptor GeneSeq Accession R91064 W09607739 SEQ ID NO:2 and 4 of WO9607739 (SEQ ID NO:398 and SEQ ID NO:399, respectively)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Orencole & Dinarello (1989) Cytokine 1, 14-20. Soluble IL-type-3 receptor polypep- tides may be useful for inhibiting interleukin activities
Human interleukin-13 beta receptor GeneSeq Accession W24972 WO9720926 SEQ ID NO:2 from WO9720926 (SEQ ID NO:400)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Boutelier et al (1995) J. Immunol. Methods 181, 29. Soluble IL-13 beta receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-13 alpha receptor GeneSeq Accession W24973 WO9720926 IL-13RA1 P78552/I13R1_HUMAN Interleukin-13 receptor subunit alpha-1 (isoform 1) (SEQ ID NO:298) IL-13RA2 Q14627/I13R2_HUMAN Interleukin-13 receptor subunit alpha-2 (SEQ ID NO:299)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Boutelier et al (1995) J. Immunol. Methods 181, 29. Soluble IL-13 alpha receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-4 receptor GeneSeq Accession W13499 US Pat. No. 5,599,905 P24394/IL4RA_HUMAN Interleukin-4 receptor subunit alpha (isoform 1) (SEQ ID NO:300)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Siegel & Mostowski (1990) J Immunol Methods 132, 287-295. Soluble IL-4 receptor polypep- tides may be useful for inhibiting interleukin activities.

Human interleukin-12 beta-2 receptor GeneSeq Accession W12771 EP759466 Q9966/I12R2_HUMAN Interleukin-12 receptor subunit beta-2 (isoform 1) (SEQ ID NO:301)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Hori et al (1987), Blood 70, 1069- 1078. Soluble IL-12 beta-2 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-12 beta-1 receptor. GeneSeq Accession W12772 EP759466 P4270/I12R1_HUMAN Interleukin-12 receptor subunit beta-1 (isoform 1) (SEQ ID NO:302)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Hori et al (1987), Blood 70, 1069- 1078. Soluble IL-12 beta-1 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human IL-9 receptor protein GeneSeq Accessions W64055, W64056, and W64057 WO9824904 Q01113/IL9R_HUMAN Interleukin-9 receptor (isoform 1) (SEQ ID NO:303)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yang et al (1989) Blood 74, 1880- 84. Soluble IL-9 receptor polypep- tides may be useful for inhibiting interleukin activities.
IL-10 receptor GeneSeq Accession W41804 US Pat. No. 5,716,804 IL-10RA Q13651/I10R1_HUMAN Interleukin-10 receptor subunit alpha (SEQ ID NO:304) IL-10RB Q0833/I10R2_HUMAN Interleukin-10 receptor subunit beta (SEQ ID NO:305)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Thompson-Snipes et al (1991) J. Exp. Med. 173, 507-510. Soluble IL-10 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human IL-6 receptor GeneSeq Accession Y30938 JP11196867	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity

P08887/IL6RA_HUMAN Interleukin-6 receptor subunit alpha (isoform 1) (SEQ ID NO:306)	can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Aarden et al (1987) Eur. J. Immunol 17, 1411-16. Soluble IL-6 receptor polypep- tides may be useful for inhibiting interleukin activities.
Il-17 receptor GeneSeq Accession Y97181 US Pat. No. 6,096,305 Q96F46/I17RA_HUMAN Interleukin-17 receptor A (SEQ ID NO:290)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yao et al (1995) J. Immunol. 155, 5483-86. Soluble IL-17 receptor polypep- tides may be useful for inhibiting interleukin activities.
Il-17 receptor GeneSeq Accession Y97131 US Pat. No. 6,100,235 Q96F46/I17RA_HUMAN Interleukin-17 receptor A (SEQ ID NO:290)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Yao et al (1995) J. Immunol. 155, 5483-86. Soluble IL-17 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human interleukin-3 receptor GeneSeq Accession R25300 EP509826 P26951/IL3RA_HUMAN Interleukin-3 receptor subunit alpha (isoform 1) (SEQ ID NO:307)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. Soluble IL-3 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human GM- CSF receptor GeneSeq Accession R10919 WO9102063 GM-CSF receptor A P15509/CSF2R_HUMAN Granulocyte-macrophage colony-stimulating factor receptor subunit alpha (isoform 1) (SEQ ID NO:308) GM-CSF receptor B P32927/IL3RB_HUMAN Cytokine receptor common subunit beta (isoform 1) (SEQ ID NO:309)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. Soluble GM-CSF receptor polypep- tides may be useful for inhibiting interleukin activities.

Human IL-5 receptor alpha chain GeneSeq Accession R25064 EP492214 Q01344/IL5RA_HUMAN Interleukin-5 receptor subunit alpha (isoform 1) (SEQ ID NO:310)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. Soluble IL-5 receptor alpha polypeptides may be useful for inhibiting interleukin activities.
Il-5 receptor GeneSeq Accession W82842 WO9847923 Q01344/IL5RA_HUMAN Interleukin-5 receptor subunit alpha (isoform 1) (SEQ ID NO:310)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; Kitamura et al (1989) J Cell Physiol. 140 323-334. Soluble IL-5 receptor polypep- tides may be useful for inhibiting interleukin activities.
Il-6 receptor GeneSeq Accession R37215 JP05091892 P08887/IL6RA_HUMAN Interleukin-6 receptor subunit alpha (isoform 1) (SEQ ID NO:306)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Aarden et al (1987) Eur. J. Immunol 17, 1411-16. Soluble IL-6 receptor polypep- tides may be useful for inhibiting interleukin activities.
Human B cell stimulating factor-2 receptor GeneSeq Accession P90525 AU8928720 P08887/IL6RA_HUMAN Interleukin-6 receptor subunit alpha (isoform 1) (SEQ ID NO:306)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225. Soluble B cell stimulating factor-2 receptor polypep- tides may be useful for inhibiting interleukin activities.
IL-7 receptor clone GeneSeq Accession R08330 EP403114 P1687/|IL7RA_HUMAN Interleukin-7 receptor subunit alpha (isoform 1) (SEQ ID NO:311)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Park et al (1990) J. Exp. Med. 171, 1073-79. Soluble IL-7 receptor polypep- tides may be useful for inhibiting interleukin activities.
EPO receptor; EPOR GeneSeq Accession R06512 WO9008822	EPO Receptor is involved in the proliferation and differentiation of erythroblasts. EPO Receptor activity can be determined using assays known in the art, such as, J Biol Chem 2001 Mar 23; 276(12: 8995-9002; JAK2 protein tyrosine kinase activity: Blood

P19235/EPOR_HUMAN Erythropoietin receptor (isoform EPOR-F) (SEQ ID NO:312)	1994 Sep 1; 84(5): 1501-7 and Mol Cell Biol. 1994 Oct; 14(10: 6506-14. Inflammatory disorders, immunologic disorders, cancer, erythroblast proliferation and differentiation
IL-15 receptor GeneSeq Accession R90843 WO9530695 Q1326/Il15RA_HUMAN Interleukin-15 receptor subunit alpha (isoform 1) (SEQ ID NO:313)	Interleukins are a group of multi- functional cytokines synthesized by lymphocytes, monocytes, and macrophages. Known functions include stimulating proliferation of immune cells (*e.g.*, T helper cells, B cells, eosinophils, and lymphocytes), chemotaxis of neutrophils and T lymphocytes, and/or inhibition of interferons. Interleukin activity can be determined using assays known in the art: Matthews *et al.*, in *Lymphokines and Interferens: A Practical Approach*, Clemens *et al.*, eds, IRL Press, Washington, D.C. 1987, pp. 221-225; and Giri et al (1994) EMBO J. 13 2822- 2830. Soluble IL-15 receptor polypep- tides may be useful for inhibiting interleukin activities. Obesity. Metabolic Disease. Diabetes. Enhancing secretion and stability of Interleukin 15
CD137; 4-1BB Receptor Protein GeneSeq Accession R70977 WO9507984 Q07011/TNR9_HUMAN Tumor necrosis factor receptor superfamily member 9 (SEQ ID NO:314)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble 4-1BB receptor polypep- tides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
BCMA GeneSeq Accession Y71979 WO0068378 Q02223/TNR17_HUMAN Tumor necrosis factor receptor superfamily member 17 (isoform 1) (SEQ ID NO:315)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble BCMA receptor polypep- tides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
CD27 GeneSeq Accession R20814 WO9201049 P26842/CD27_HUMAN CD27 antigen (SEQ ID NO:316)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble CD27 polypeptides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
CD30 GeneSeq Accession R35478 DE4200043 P28908/TNR8_HUMAN Tumor necrosis factor receptor superfamily member 8 (isoform 1)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble CD30 polypeptides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.

(SEQ ID NO:317)	
CD40 GeneSeq Accession Y33499 WO9945944 P25942/TNR5_HUMAN Tumor necrosis factor receptor superfamily member 5 (isoform 1) (SEQ ID NO:318)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble CD40 polypeptides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
EDAR Genbank Accession AAD50077 Q9UNE0|EDAR_HUMAN Tumor necrosis factor receptor superfamily member EDAR (isoform 1) (SEQ ID NO:319)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Immune Disorders, Lymphomas, X- linked hypohidrotic ectodermal dysplasia
OX40; ACT-4 GeneSeq Accession R74737 WO9512673 P43489/TNR4_HUMAN Tumor necrosis factor receptor superfamily member 4 (SEQ ID NO:320)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Immune Disorders, Lymphomas, T cell disorders
TACI GeneSeq Accession W75783 WO9839361 O14836/TR13B_HUMAN Tumor necrosis factor receptor superfamily member 13B (isoform 1) (SEQ ID NO:321)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble TACI receptor polypep- tides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
TNF-R GeneSeq Accession R10986 AU9058976 P19438/TNR1A_HUMAN Tumor necrosis factor receptor superfamily member 1A (isoform 1) (SEQ ID NO:322)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble TNF-R receptor polypep- tides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
TNF-RII; TNF p75 receptor; Death Receptor	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-

GeneSeq Accession R11141 EP418014 P20333/TNR1B_HUMAN Tumor necrosis factor receptor superfamily member 1B (isoform 1) (SEQ ID NO:323)	stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble TNFR-II receptor polypep- tides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
hAPO-4; TROY GeneSeq Accession W93581 WO9911791 Q9NS68/TNR19_HUMAN Tumor necrosis factor receptor superfamily member 19 (isoform 1) (SEQ ID NO:324)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Immune Disorders, Cancers
TNF-alpha precursor GeneSeq Accession P60074 EP205038	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
Human TNF- alpha GeneSeq Accession R62463 EP619372 P01375/TNFA_HUMAN Tumor necrosis factor (SEQ ID NO:325)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
Human TNF- alpha GeneSeq Accession R42679 EP563714 P01375/TNFA_HUMAN Tumor necrosis factor (SEQ ID NO:325)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
Human TNF- beta (LT-alpha) GeneSeq Accession B37799 WO0064479 P01374/TNFB_HUMAN Lymphotoxin-alpha (SEQ ID NO:326)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
LT-alpha GeneSeq Accession P70107	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-

EP250000 P01374/TNFB_HUMAN Lymphotoxin-alpha (SEQ ID NO:326)	stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
LT-beta GeneSeq Accession R56869 WO9413808 Q06643/TNFC_HUMAN Lymphotoxin-beta (isoform 1) (SEQ ID NO:327)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
OPGL GeneSeq Accession W83195 WO9846751 O14788/TNF11_HUMAN Tumor necrosis factor ligand superfamily member 11 (isoform 1) (SEQ ID NO:328)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer, loss of bone mass
FasL GeneSeq Accession W98071 WO9903999 P48023/TNFL6_HUMAN Tumor necrosis factor ligand superfamily member 6 (isoform 1) (SEQ ID NO:329)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
FasL GeneSeq Accession W95041 WO9903998 P48023/TNFL6_HUMAN Tumor necrosis factor ligand superfamily member 6 (isoform 1) (SEQ ID NO:329)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
CD27L GeneSeq Accession R50121 WO9405691 P32970/CD70_HUMAN CD70 antigen (isoform 1)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer

(SEQ ID NO:330)	
CD30 ligand GeneSeq Accession R45007 WO9324135 P32971/TNFL8_HUMAN Tumor necrosis factor ligand superfamily member 8 (SEQ ID NO:331)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
CD40L GeneSeq Accession R85486 WO9529935 P29965/CD40L_HUMAN CD40 ligand (SEQ ID NO:332)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
4-1BB ligand GeneSeq Accession W26657 US Pat. No. 5,674,704 P41273/TNFL9_HUMAN Tumor necrosis factor ligand superfamily member 9 (SEQ ID NO:333)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
FAS Ligand Inhibitory Protein (DcR3) GeneSeq Accession B19335 WO0058465 O95407/TNF6B_HUMAN Tumor necrosis factor receptor superfamily member 6B (SEQ ID NO:334)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Soluble DcR3 polypeptides may be useful for inhibiting apoptosis, NF-kB activation, and/or co-stimulation of immune cells such as B and T cells.
OX40L GeneSeq Accession R79903 WO9521915 P23510/TNFL4_HUMAN Tumor necrosis factor ligand superfamily member 4 (isoform 1) (SEQ ID NO:335)	Activities associated with apoptosis, NF-kB activation, and co- stimulation of immune cells such as T and B cells. Apoptosis activity, NF-kB activation, and B and T cell co-stimulation can be determined using assays known in the art: Moore *et al.*, 1999, Science, 285(5425): 260-3; Song HY *et al.*, 1997 Proc Natl Acad Sci USA 94(18): 9792- 6; Epsevik and Nissen-Meyer, 1986, J. Immunol. Methods. Inflammatory disorders immunologic disorders, cancer
Protease inhibitor peptides GeneSeq Accessions R12435, R12436, R12437,	Peptides that inhibit the function/binding of HIV HIV protease activities are known in the art: HIV protease assays: EP0387231. One can modify the assay to look for inhibition using any of the disclosed protease inhibitor polypeptides. HIV,

R12438, R12439, R12440, and R1244 WO9106561	inflammatory disorders, immuno- logic disorders, cancer, viral infections
Retroviral protease inhibitors GeneSeq Accessions R06660, R06661, R06662, R06663, R06664, R06665, R06666, R06667, R06668, R06669, R06670, R06671, R06672, R06673, R06674, R06675, and R06676 EP387231	Peptides that inhibit the function/binding of HIV HIV protease activities are known in the art: HIV protease assays: EP0387231. One can modify the assay to look for inhibition using any of the disclosed protease inhibitor polypeptides. HIV, inflammatory disorders, immuno- logic disorders, cancer, viral infections
HIV protease inhibiting peptides GeneSeq Accessions R59293, R59294, R59295, R59296, R59297, R59298, R59299, R592300, R59301, R59302, R59301, R59302, R59303, R59304, R59305, R59306, R59307, R59308, R59309, R59310, R59311, R59312, R59313, R59314, R59315, R59316, R59317 R59318, R59319, R59320, R59321, R59322, R59323, R59324, R59325, R59326, R59327, R59328, R59329, R59330, R59331, R59332, R59333, R59334, R59335, R59336, R59337, R59338, R59339, R59340, R59341, R59342, R59343, R59344, R59345, R59346, R59347, R59348, R59349, and R59350 WO9301828	Peptides that inhibit the function/binding of HIV HIV protease activities are known in the art: HIV protease assays: EP0387231. One can modify the assay to look for inhibition using any of the disclosed protease inhibitor polypeptides. HIV, inflammatory disorders, immuno- logic disorders, cancer, viral infections
HIV-1 protease inhibitors GeneSeq Accessions R86326, R86327, R86328, R86329, R86330, R86331, R86332, R86333, R86334, R86335, R86336, R86337, R86338, R86339, R86340, R86341, R86342, R86343, R86344, R86345, R86346, R86347, R86348, R86349, R86350, R86351, R86352, R86353, R86354, R86355, R86356, R86357, R86358,	Peptides that inhibit the function/binding of HIV HIV protease activities are known in the art: HIV protease assays: EP0387231. One can modify the assay to look for inhibition using any of the disclosed protease inhibitor polypeptides. HIV, inflammatory disorders, immuno- logic disorders, cancer, viral infections

R86359, R86360, R86361, R86362, R86363, R86364, R86365, R86366, R86367, R86368, R86369, R86370, and R86371 DE4412174	
HIV Inhibitor Peptide GeneSeq Accession Y89687 WO9959615	Peptides that inhibit the function/binding of HIV HIV protease activities are known in the art: HIV protease assays: EP0387231. One can modify the assay to look for inhibition using any of the disclosed protease inhibitor polypeptides. HIV, inflammatory disorders, immuno- logic disorders, cancer, viral infections
HIV Inhibitor Peptide GenSeq Accession Y31955 WO9948513	Peptides that inhibit the function/binding of HIV HIV protease activities are known in the art: HIV protease assays: EP0387231. One can modify the assay to look for inhibition using any of the disclosed protease inhibitor polypeptides. HIV, inflammatory disorders, immuno- logic disorders, cancer, viral infections
HIV Inhibitor Peptide Science 291, 884 (2001); Published online 12 Jan. 2001; 10.1126/science.1057453	Peptides that inhibit the function/binding of HIV HIV protease activities are known in the art: HIV protease assays: EP0387231. One can modify the assay to look for inhibition using any of the disclosed protease inhibitor polypeptides. HIV, inflammatory disorders, immuno- logic disorders, cancer, viral infections
Human monocyte chemoattractant factor hMCP-3 GeneSeq Accession R73915 WO9509232 P80098/CCL7_HUMAN C-C motif chemokine 7 (SEQ ID NO:336)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, particularly useful for treating bacterial and/or viral menigitis
Human monocyte chemoattractant factor hMCP-1 GeneSeq Accession R73914 WO9509232 P13500/CCL2_HUMAN C-C motif chemokine 2 (SEQ ID NO:337)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, particularly useful for treating bacterial and/or viral menigitis
Human gro-beta chemokine GeneSeq Accessions R66699 and W17671 WO9429341 P19875/CXCL2_HUMAN C-X-C motif chemokine 2	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138:

(SEQ ID NO:338)	Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, inflammatory dis- orders, blood-related disorders, stem cell transplantation, cancer
Human gro-gamma chemokine GeneSeq Accessions R66700 and W17672 WO9429341 P19876/CXCL3_HUMAN C-X-C motif chemokine 3 (SEQ ID NO:339)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, inflammatory dis- orders, blood-related disorders, stem cell transplantation, cancer
Human gro-alpha chemokine GeneSeq Accessions R66698 and W18024 WO9429341 P09341/GROA_HUMAN Growth-regulated alpha protein (SEQ ID NO:340)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, inflammatory dis- orders, blood-related disorders, stem cell transplantation, cancer
Human eosinophil-expressed chemokine (EEC) GeneSeq Accession W05186 WO9632481 SEQ ID NO:2 of WO9632481 (SEQ ID NO:401)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, particularly treatment of eosinophilia, inflammation, allergies, asthma, leukaemia and lymphoma
Chemokine-like protein PF4-414 Full-Length and Mature GeneSeq Accessions R92318 and R99809 WO9613587 Figure 3C of WO9613587 (SEQ ID NO:402)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and blood- related disorders, particularly myelosuppression
Chemokine-like protein IL-8M3 GeneSeq Accession R99812 WO9613587	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined

	using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Cancer and blood- related disorders, particularly myelosuppression
Human interleukin-8 (IL-8) GeneSeq Accession R99814 WO9613587 P10145/IL8_HUMAN Interleukin-8 (isoform 1) (SEQ ID NO:341)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Cancer and blood- related disorders, particularly myelosuppression
Chemokine-like protein IL-8M1 Full-Length and Mature GeneSeq Accessions R99815 and R99803 WO9613587 Figure 4B of WO9613587 (SEQ ID NO:403)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Cancer and blood- related disorders, particularly myelosuppression
Chemokine-like protein IL-8M8 Full-Length and Mature GeneSeq Accessions R99816 and R99805 WO9613587 Figure 4C of WO9613587 (SEQ ID NO:404)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Cancer and blood- related disorders, particularly myelosuppression
Chemokine-like protein IL-8M8 Full-Length and Mature GeneSeq Accessions R99817 and R99806 WO9613587 Figure 4C of WO9613587 (SEQ ID NO:404)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Cancer and blood- related disorders, particularly myelosuppression.
Chemokine-like protein IL-8M8 Full-Length and Mature GeneSeq Accessions R99818 and R99804 WO9613587	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which

Figure 4C of WO9613587 (SEQ ID NO:404)	bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Cancer and blood- related disorders, particularly myelosuppression.
Chemokine-like protein IL-8M8 Full-Length and Mature GeneSeq Accessions R99819 and R99807 WO9613587 Figure 4C of WO9613587 (SEQ ID NO:404)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and blood- related disorders, particularly myelosuppression.
Chemokine-like protein IL-8M8 Full-Length and Mature GeneSeq Accessions R99822 and R9807 WO9613587 Figure 4C of WO9613587 (SEQ ID NO:404)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and blood- related disorders, particularly myelosuppression.
Human foetal spleen expressed chemo-kine, FSEC GeneSeq Accession R98499 WO9622374 SEQ ID NO:2 of WO9622374 (SEQ ID NO:405)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders
Liver expressed chemokine- 1(LVEC-1) GeneSeq Accession R95689 WO9616979 SEQ ID NO:2 of WO9616979 (SEQ ID NO:406)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammation of the liver
Liver expressed chemokine- 2(LVEC-2) GeneSeq Accession R95690 WO9616979 SEQ ID NO:4 of WO9616979	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined

(SEQ ID NO:407)	using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammation of the liver
Pituitary expressed chemokine (PGEC) GeneSeq Accession R95691 WO9616979 SEQ ID NO:6 of WO9616979 (SEQ ID NO:408)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammation, particularly of the liver
Adenoid- expressed chemokine (ADEC) GeneSeq Accession R97664 WO9617868 SEQ ID NO:2 of WO9617868 (SEQ ID NO:409)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammation, angiogenesis, tumorigenesis, musculoskeletal disorders
Human chemokine CC-2 GeneSeq Accession W38170 WO9741230 Q16663/CCL15_HUMAN C-C motif chemokine 15 (SEQ ID NO:342)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cell migration, proliferation, and differentiation disorders
Human chemokine HCC-1 GeneSeq Accession W38171 WO9741230 Q16627/CCL14_HUMAN C-C motif chemokine 14 (SEQ ID NO:343)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cell migration, proliferation, and differentiation disorders
Human chemokine CC- 3 GeneSeq Accession W38172 WO9741230 Q16627/CCL14_HUMAN C-C motif chemokine 14 (SEQ ID NO:343)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138:

	Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cell migration, proliferation, and differentiation
Novel betachemokine designated PTEC GeneSeq Accession W27271 WO9739126 SEQ ID NO:2 of WO9739126 (SEQ ID NO:410)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, vascular disorders, cancer
Human CX3C 111 amino acid chemokine GeneSeq Accession W23344 WO9727299 SEQ ID NO:2 of WO9727299 (SEQ ID NO:411)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, inflammatory diseases, abnormal proliferation, regeneration, degeneration, and atrophy
Human CCF18 chemokine GeneSeq Accession W25942 WO9721812 SEQ ID NO:4 of WO9721812 (SEQ ID NO:412)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Abnormal physiology and development disorders, can also be used as an anti- viral agent
Human beta- chemokine H1305 (MCP-2) GeneSeq Accession W26655 WO9725427 P80075/CCL8_HUMAN C-C motif chemokine 8 (SEQ ID NO:344)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Chemotaxis, blood- related disorders, viral infection, HIV, wound healing, cancer
Human eosinocyte CC type chemokine eotaxin GeneSeq Accession W14990 WO9712914 P51671/CCL11_HUMAN Eotaxin	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138:

(SEQ ID NO:245)	Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammatory and immune disorders
Human thymus and activation regulated cytokine (TARC) GeneSeq Accession W14018 WO9711969 Q92583/CCL17_HUMAN C-C motif chemokine 17 (SEQ ID NO:261)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in molecular Biology, 2000, vol. 138: Chemokine Protocols, Edited by A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power Humana Press Inc., Totowa, NJ Inflammatory and immune disorders
Human chemokine beta-8 short forms GeneSeq Accession W16315 WO9712041 Wildtype chemokine beta-8 provided as: P55773|CCL23_HUMAN C-C motif chemokine 23 (SEQ ID NO:459)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, wound healing, immune disorders
Microphage derived chemokine, MDC GeneSeq Accession W20058 WO9640923 O00626/CCL22_HUMAN C-C motif chemokine 22 (SEQ ID NO:345)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammatory diseases, wound healin, angiogenesis
Human chemokine ZSIG-35 GeneSeq Accession W30565 WO9844117 SEQ ID NO:2 of WO WO9844117 (SEQ ID NO:413)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammatory and immune diseases
Primate CC chemokine "ILINCK" GeneSeq Accesssion W69990 WO98328658 SEQ ID NO:4 from WO9832858 (SEQ ID NO:414)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders, abnormal proliferation, regen- eration, generation and atrophy disorders
Primate CXC chemokine	Chemokines are a family of related small, secreted proteins involved in biological

"IBICK" GeneSeq Accession W69989 WO9832858 SEQ ID NO:2 from WO9832858 (SEQ ID NO:415)	processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders, abnormal proliferation, regen- eration, generation and atrophy disorders
Human CC-type chemokine protein designated SLC (secondary lymphoid chemokine) GeneSeq Accession W69163 WO9831809 O00585/CCL21_HUMAN C-C motif chemokine 21 (SEQ ID NO:346)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune, inflammatory, and infectious disorders, cancer
Human CC chemokine ELC protein GeneSeq Accession W62542 WO9826071 Q99731/CCL19_HUMAN C-C motif chemokine 19 (SEQ ID NO:249)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and infectious diseases, particularly herpes virus
Human DVic-1 C-C chemokine GeneSeq Accession W60649 WO9823750 SEQ ID NO:2 of WO9823750 (SEQ ID NO:416)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Abnormal prolifera- tion, regeneration, degeneration, and atrophy disorders, including cancer
Human C-C chemokine DGWCC GeneSeq Accession W60650 WO9823750 SEQ ID NO:6 of WO9823750 (SEQ ID NO:417)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cell proliferation disorders,

	cancer
Human STCP-1 GeneSeq Accession W62783 WO9824907 O00626/CCL22_HUMAN C-C motif chemokine 22 (SEQ ID NO:345)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, particularly T cell related disorders, viral infection, and inflammation, especially joint
Exodus protein GeneSeq Accession W61279 WO9821330 P78556/CCL20_HUMAN C-C motif chemokine 20 (isoform 1) (SEQ ID NO:248)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders, angiogenesis, cancer, and proliferation disorders, particularly myeloproliferative diseases
Human Chr19kine protein GeneSeq Acession W50887 WO9814581 SEQ ID NO:10 of WO9814581 (SEQ ID NO:418)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and de- generative disorders
Human T cell mixed lymphocyte reaction expressed chemokine (TMEC) GeneSeq Accession W58703 US Pat. No. 5,780,268 SEQ ID NO:2 of US Pat. No. 5,780,268 (SEQ ID NO:460)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune, inflammatory, and infectious disorders, cancer
Human 6CKine protein GeneSeq Accession W50885 W09814581 SEQ ID NO:8 of WO9814581 (SEQ ID NO:419)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and de- generative disorders

human liver and activation regulated chemokine (LARC) GeneSeq Accession W57475 WO9817800 P78556/CCL20_HUMAN C-C motif chemokine 20 (isoform 1) (SEQ ID NO:248)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune, inflammatory, and infectious disorders, cancer
RANTES peptide GeneSeq Accession W29538 WO9744462 Wildtype Rantes provided herien as P13501/CCL5_HUMAN C-C motif chemokine 5 (SEQ ID NO:241)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Infectious diseases, particularly HIV
RANTES 8-68 GeneSeq Accession W29529 WO9744462 Wildtype Rantes provided herien as P13501/CCL5_HUMAN C-C motif chemokine 5 (SEQ ID NO:241)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Infectious diseases, particularly HIV
RANTES 9-68 GeneSeq Accession W29528 WO9744462 Wildtype Rantes provided herien as P13501/CCL5_HUMAN C-C motif chemokine 5 (SEQ ID NO:241)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Infectious diseases, particularly HIV
Human chemokine protein 331D5 GeneSeq Accession W59433 WO9811226 SEQ ID NO:12 of WO9811226 (SEQ ID NO:420)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Abnormal prolifera- tion, regeneration, degeneration, or atrophy, including cancer
Human chemokine protein 61164 GeneSeq	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking.

Accession W59430 WO9811226 SEQ ID NO:6 of WO9811226 (SEQ ID NO:421)	Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Abnormal prolifera- tion, regeneration, degeneration, or atrophy, including cancer
Chemokine MCP-4 GeneSeq Accession W56690 WO9809171 Q99616/CCL13_HUMAN C-C motif chemokine 13 (SEQ ID NO:347)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune, Inflammatory, and infectious diseases
Human stromal cell-derived chemokine, SDF-1 GeneSeq Accession W50766 FR2751658 P48061/SDF1_HUMAN Stromal cell-derived factor 1 (isoform beta) (SEQ ID NO:260)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. HIV infections
Thymus expressed chemokine (TECK) GeneSeq Accession W44397 WO9801557 O15444/CCL25_HUMAN C-C motif chemokine 25 (SEQ ID NO:348)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders
Human chemokine MIP-3alpha GeneSeq Accession W44398 WO9801557 P78556/CCL20_HUMAN C-C motif chemokine 20 (isoform 1) (SEQ ID NO:248)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders
Human chemokine MIP-3beta GeneSeq Accession W44399 WO9801557	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The

Q99731/CCL19_HUMAN C-C motif chemokine 19 (SEQ ID NO:249)	chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders
Human monocyte chemotactic proprotein (MCPP) sequence GeneSeq Accession W42072 WO9802459 SEQ ID NO:1 of WO9802459 (SEQ ID NO:456)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, respiratory disorders, cancer
Macrophage- derived chemokine (MDC) GeneSeq Accessions W40811 and Y24414 US Pat. No. 5,688,927/US Pat. No. 5,932,703 O00626/CCL22_HUMAN C-C motif chemokine 22 (SEQ ID NO:345)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune, and inflammatory disorders, cancer
Macrophage derived chemokine analogue MDC-eyfy GeneSeq Accession Y24416 US Pat. No. 5,932,703 ("eyfy" disclosed as SEQ ID NO: 546) Wildtype MDC is SEQ ID NO:2 of 5,932,703 (SEQ ID NO:422)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders
Macrophage derived chemokine analogue MDC (n + 1) GeneSeq Accession Y24413 US Pat. No. 5,932,703	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders
Macrophage derived chemokine analogue MDC- yl GeneSeq Accession Y24415 US Pat. No. 5,932,703	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-

	protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and inflammatory disorders
Human type CC chemokine eotaxin 3 protein sequence GeneSeq Accession Y43178 JP11243960 Q9Y258/CCL26_HUMAN C-C motif chemokine 26 (SEQ ID NO:349)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Allergic diseases and HIV infection
Human MCP-3 and human Muc-1 core epitope (VNT) fusion protein GeneSeq Acession Y29893 WO9946392 Wildtype MCP-3 has the sequence: P80098/CCL7_HUMAN C-C motif chemokine 7 (SEQ ID NO:336) Wildtype Muc-1 has the sequence: P15941|MUC1_HUMAN Mucin-1 (isoform 1) (SEQ ID NO:461)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and immune disorders, particularly HIV infection
Human IP-10 and human Muc-1 core epitope (VNT) fusion protein GeneSeq Accession Y29894 WO9946392 Wildtype IP10 has the sequence: P02778/CXL10_HUMAN C-X-C motif chemokine 10 (SEQ ID NO:242) Wildtype Muc-1 has the sequence:	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and immune disorders, particularly HIV infection

P15941|MUC1_HUMAN Mucin-1 (isoform 1) (SEQ ID NO:461)	
Human IP-10 and HIV-1 gp 120 hyper- variable region fusion protein GeneSeq Accession Y29897 W09946392 Wildtype IP10 has the sequence: P02778/CXL10_HUMAN C-X-C motif chemokine 10 (SEQ ID NO:242) Wildtype gp120 has the sequence: P03378|32-509 (cleaved product of gp160) (SEQ ID NO:462)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and immune disorders, particularly HIV infection
Human mammary associated chemokine (MACK) protein Full-Length and Mature GeneSeq Accessions Y29092 and Y29093 WO9936540 Full-length: SEQ ID NO:1 of WO9936540 (SEQ ID NO:423) Mature Form: SEQ ID NO:2 of WO9936540 (SEQ ID NO:424)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Breast disease, including cancer
Tim-1 protein GeneSeq Accession Y28290 WO9933990 SEQ ID NO:2 of WO9933990 (SEQ ID NO:350)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammation due to stimuli such as heart attacks and stroke, infection, physical trauma, UV or ionizing radiation, burns, frostbite or

	corrosive chemicals
Human Lkn-1 Full-Length and Mature protein GeneSeq Accessions Y17280, Y17274, Y17281, and Y17275 WO9928473 and WO9928472 Q16663/CCL15_HUMAN C-C motif chemokine 15 (SEQ ID NO:342)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. HIV infection and cancer, particularly leukemia
N-terminal modified chemokine met- hSDF-1 alpha GeneSeq Accession Y05818 WO9920759 SEQ ID NO:10 of WO9920759 (SEQ ID NO:425)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inhibit or stimulate angiogenesis, inhibit the binding of HIV
N-terminal modified chemokine met- hSDF-1 beta GeneSeq Accession Y05819 WO9920759 SEQ ID NO:11 of WO9920759 (SEQ ID NO:426)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inhibit or stimulate angiogenesis, inhibit the binding of HIV, antiinflammatory; immunosuppressant
N-terminal modified chemokine GroHEK/hSDF- 1alpha GeneSeq Accession Y05820 WO9920759 SEQ ID NO:12 of WO9920759 (SEQ ID NO:427)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inhibit or stimulate angiogenesis, inhibit the binding of HIV, antiinflammatory; immunosuppressant
N-terminal modified chemokine GroHEK/hSDF- 1beta. GeneSeq Accession Y05821 WO9920759 SEQ ID NO:13 of WO9920759	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power.

(SEQ ID NO:428)	Humana Press Inc., Totowa, NJ. Inhibit or stimulate angiogenesis, inhibit the binding of HIV, antiinflammatory; immunosuppressant
Chemokine Eotaxin GeneSeq Accession Y14230 WO9912968 P51671/CCL11_HUMAN Eotaxin (SEQ ID NO:245)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Increase or enhance an inflammatory response, an immune response orhaematopoietic cell-associated activity; treat a vascular indication; Cancer; enhance wound healing, to prevent or treat asthma, organ transplant rejction, rheumatoid arthritis or allergy
Chemokine hMCP1a GeneSeq Accession Y14225 WO9912968	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, Vascular disorders, Wound healing, cancer, prevent organ transplant rejection, Increase or enhance an inflammatory response,
Chemokine hMCP1b GeneSeq Accession Y14226 WO9912968	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, Vascular disorders, Wound healing, cancer, prevent organ transplant rejection, Increase or enhance an inflammatory response,
Chemokine hSDF1b GeneSeq Accession Y14228 WO9912968 P48061/SDF1_HUMAN Stromal cell-derived factor 1 (isoform beta) (SEQ ID NO:260)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, Vascular disorders, Wound healing, cancer, prevent organ transplant rejection, Increase or enhance an inflammatory response,
Chemokine hIL-8 GeneSeq Accession Y14229 WO9912968	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies

P10145/IL8_HUMAN Interleukin-8 (isoform 1) (SEQ ID NO:341)	including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Immune disorders, Vascular disorders, Wound healing, cancer, prevent organ transplant rejection, Increase or enhance an inflammatory response,
Chemokine hMCP1 GeneSeq Accession Y14222 WO9912968 P13500/CCL2_HUMAN C-C motif chemokine 2 (SEQ ID NO:337)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, Vascular disorders, Wound healing, cancer, prevent organ transplant rejection, Increase or enhance an inflammatory response,
Chemokine hMCP2 GeneSeq Accession Y14223 WO9912968 P80075/CCL8_HUMAN C-C motif chemokine 8 (SEQ ID NO:344)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, Vascular disorders, Wound healing, cancer, prevent organ transplant rejection, Increase or enhance an inflammatory response,
Chemokine hMCP3 GeneSeq Accession Y14224 WO9912968 P80098/CCL7_HUMAN C-C motif chemokine 7 (SEQ ID NO:336)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, Vascular disorders, Wound healing, cancer, prevent organ transplant rejection, Increase or enhance an inflammatory response,
C-C chemokine, MCP2 GeneSeq Accession Y05300 EP905240 P80075/CCL8_HUMAN C-C motif chemokine 8 (SEQ ID NO:344)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power.

	Humana Press Inc., Totowa, NJ. Inflammatory, Immune and infectious diseases; pulmonary diseases and skin disorders; tumours, and angiogenesis-and haematopoiesis- related diseases
Wild type monocyte chemotactic protein 2 GeneSeq Accession Y07233 EP906954 P80075/CCL8_HUMAN C-C motif chemokine 8 (SEQ ID NO:344)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammatory, Immune and infectious diseases; pulmonary diseases and skin disorders; tumours, and angiogenesis-and haematopoiesis- related diseases
Truncated monocyte chemotactic protein 2 (6-76) GeneSeq Accession Y07234 EP906954 Figure 1 of EP905241 and EP906954 (SEQ ID NO:429)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Inflammatory, Immune and infectious diseases; pulmonary diseases and skin disorders; tumours, and angiogenesis-and haematopoiesis- related diseases
Truncated RANTES protein (3-68) GeneSeq Accessions Y07236 and Y07232 EP905241; EP906954 Figure 1 of EP906954 (SEQ ID NO:430)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Inflammatory, immune and infectious diseases; pulmonary diseases and skin disorders; tumours, and angiogenesis-and haematopoiesis- related diseases
Wild type monocyte chemotactic protein 2 GeneSeq Accession Y07237 EP905241 P80075/CCL8_HUMAN C-C motif chemokine 8 (SEQ ID NO:344)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Inflammatory, immune and infectious diseases; pulmonary diseases and skin disorders; tumours, and angiogenesis-and haematopoiesis- related diseases
Truncated monocyte chemotactic protein 2 (6-76) GeneSeq Accession	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies

Y07238 EP905241 Figure 1 of EP905241 and EP906954 (SEQ ID NO:429)	including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Inflammatory, immune and infectious diseases; pulmonary diseases and skin disorders; tumours, and angiogenesis-and haematopoiesis- related diseases
A partial CXCR4B protein GeneSeq Accession W97363 EP897980 SEQ ID NO:2 of EP897980 (sEQ ID NO:431)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Soluble CXCR4B receptor polypep- tides may be useful for inhibiting chemokine activities and viral infection.
Interferon gamma-inducible protein (IP-10) GeneSeq Accession W96709 US Pat. No. 5,871,723 P02778/CXL10_HUMAN C-X-C motif chemokine 10 (SEQ ID NO:242)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
A monokine induced by gamma- interferon (MIG) GeneSeq Accession W96710 US Pat. No. 5,871,723 Q07325/CXCL9_HUMAN C-X-C motif chemokine 9 (SEQ ID NO:351)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Interleukin-8 (IL-8) protein. GeneSeq Accession W96711 US Pat. No. 5,871,723 P10145/IL8_HUMAN Interleukin-8 (isoform 1) (SEQ ID NO:341)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ; and Holmes et al (1991) Science 253, 1278-80. Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders

Epithelial neutrophil activating protein-78 (ENA-78) GeneSeq Accession W96712 US Pat. No. 5,871,723 P42830/CXCL5_HUMAN C-X-C motif chemokine 5 (SEQ ID NO:352)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Growth related oncogene-alpha (GRO-alpha). GeneSeq Accession W96713 US Pat. No. 5,871,723 P09341/GROA_HUMAN Growth-regulated alpha protein (SEQ ID NO:340)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power, Humana Press Inc., Totowa, NJ Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Growth related oncogene-beta (GRO-beta). GeneSeq Accession W96714 US Pat. No. 5,871,723 P19875/CXCL2_HUMAN C-X-C motif chemokine 2 (SEQ ID NO:338)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Growth related oncogene-gamma (GRO-gamma) GeneSeq Accession W96715 US Pat. No. 5,871,723 P19876/CXCL3_HUMAN C-X-C motif chemokine 3 (SEQ ID NO:339)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
A platelet basic protein (PBP) GeneSeq Accession W96716 US Pat. No. 5,871,723 P02775/CXCL7_HUMAN Platelet basic protein (SEQ ID NO:353)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Angiogenesis, Cancer, Inflammatory and Immune

	disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Connective tissue activating protein-III (CTAP-III) GeneSeqAccession S96717 US Pat. No. 5,871,723 SEQ ID NO:9 of U.S. Patent NO. 5,871,723 (SEQ ID NO:354)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Beta-thrombo- globulin protein (beta-TG) GeneSeq Accession W96718 US Pat. No. 5,871,723 SEQ ID NO:10 of U.S. Patent NO. 5,871,723 (SEQ ID NO:355)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Neutrophil activating peptide-2 (NAP-2) GeneSeq Accession W96719 US Pat. No. 5,871,723 SEQ ID NO:11 of U.S. Patent NO. 5,871,723 (SEQ ID NO:356)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Granulocyte chemotactic protein-2 (GCP-2) GeneSeq Accession W96720 US Pat. No. 5,871,723 P80162/CXCL6_HUMAN C-X-C motif chemokine 6 (SEQ ID NO:357)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Angiogenesis, Cancer, Inflammatory and Immune disorders, Cardio- Vascular disorders, Musco-skeletal disorders
Human chemokine MIG-beta protein GeneSeq Accession W90124 EP887409 (SEQ ID NO:463)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power.

	Humana Press Inc., Totowa, NJ. Immune disorders, viral, parasitic, fungal or bacterial infections, Cancer; autoimmune diseases or transplant rejection
Human ZCHEMO-8 GeneSeq Accession W82716 WO9854326 SEQ ID NO:2 of WO9854326 (SEQ ID NO:432)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cancer, myelopoietic disorders, autoimmune disorders and immunodeficiencies, Inflammatory and infectious diseases, Vascular disorders, wound healing
Human Act-2 protein GeneSeq Accession W82717 WO9854326 P13236/CCL4_HUMAN C-C motif chemokine 4 (SEQ ID NO:358)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cancer, myelopoietic disorders, autoimmune disorders and immunodeficiencies, Inflammatory and infectious diseases, Vascular disorders, wound healing
Human SISD protein GeneSeq Acession W82720 WO9854326 P13501/CCL5_HUMAN C-C motif chemokine 5 (SEQ ID NO:241)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cancer, myelopoietic disorders, autoimmune disorders and immunodeficiencies, Inflammatory and infectious diseases, Vascular disorders, wound healing
Human MI10 protein GeneSeq Accession W82721 WO9854326 SEQ ID NO:37 of WO9854326 (SEQ ID NO:433)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cancer, myelopoietic disorders, autoimmune disorders and immunodeficiencies, Inflammatory and infectious diseases, Vascular disorders, wound healing
Human MI1A protein GeneSeq Accession W82722 W09854326	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The

SEQ ID NO:38 of WO9854326 (SEQ ID NO:434)	chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cancer, myelopoietic disorders, autoimmune disorders and immunodeficiencies, Inflammatory and infectious diseases, Vascular disorders, wound healing
Human CCC3 protein GeneSeq Accession W82723 WO9854326 SEQ ID NO:39 of WO9854326 (SEQ ID NO:435)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune disorders, cancer, myelopoietic disorders, autoimmune disorders and immunodeficiencies, Inflammatory and infectious diseases, Vascular disorders, wound healing
A human L105 chemokine designated huL105_3. GeneSeq Accession W87588 WO9856818 SEQ ID NO:2 of WO9856818 (SEQ ID NO:436)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, wound healing
A human L105 chemokine designated huL105_7. GeneSeq Accession W87589 WO9856818 SEQ ID NO:4 of WO9856818 (SEQ ID NO:437)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, wound healing
Human mature gro-alpha polypeptide used to treat sepsis GeneSeq Accession W81498 WO9848828 P09341/GROA_HUMAN Growth-regulated alpha protein (SEQ ID NO:340)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Infectious diseases, sepsis
Human mature gro-gamma polypeptide used to treat sepsis GeneSeq	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies

Accession W81500 WO9848828 P19876/CXCL3_HUMAN C-X-C motif chemokine 3 (SEQ ID NO:339)	including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Infectious diseases, sepsis
Human thymus expressed chemokine TECK and TECK variant GeneSeq Accessions B19607 and B19608 WO0053635 Wildtype TECK provided as: O15444/CCL25_HUMAN C-C motif chemokine 25 (SEQ ID NO:348)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Inflammatory disorders, cancer, Immune and vascular disorders
Human chemokine SDF1alpha GeneSeq Accession B15791 WO0042071 P48061-2/SDF1_HUMAN Isoform Alpha of Stromal cell-derived factor 1 (isoform alpha) (SEQ ID NO:259)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine GRO-alpha GeneSeq Accession B15793 WO0042071 P09341/GROA_HUMAN Growth-regulated alpha protein (SEQ ID NO:340)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine eotaxin GeneSeq Accession B15794 WO0042071 P51671/CCL11_HUMAN Eotaxin (SEQ ID NO:245)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders

Human chemokine MIG GeneSeq Accession B15803 WO0042071 Q07325/CXCL9_HUMAN C-X-C motif chemokine 9 (SEQ ID NO:351)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine PF4 GeneSeq Accession B15804 WO0042071 P02776/PLF4_HUMAN Platelet factor 4 (SEQ ID NO:359)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine I- 309 GeneSeq Accession B15805 WO0042071 P22362/CCL1_HUMAN C-C motif chemokine 1 (SEQ ID NO:360)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine HCC-1 GeneSeq Accession B15806 WO0042071 Q16627/CCL14_HUMAN C-C motif chemokine 14 (SEQ ID NO:361)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine C10 GeneSeq Accession B15807 WO0042071 SEQ ID NO:49 of WO0042071 (SEQ ID NO:438)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and

	Inflammatory disorders
Human chemokine CCR-2 GeneSeq Accession B15808 WO0042071 P41597/CCR2_HUMAN C-C chemokine receptor type 2 (isoform A) (SEQ ID NO:362)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine ENA-78 GeneSeq Accession B15809 WO0042071 P42830/CXCL5_HUMAN C-X-C motif chemokine 5 (SEQ ID NO:352)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine GRObeta GeneSeq Accession B15810 WO0042071 P19875/CXCL2_HUMAN C-X-C motif chemokine 2 (SEQ ID NO:338)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine IP-10 GeneSeq Accession B15811 WO0042071 P02778/CXL10_HUMAN C-X-C motif chemokine 10 (SEQ ID NO:242)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine SDF1beta GeneSeq Accession B15812 WO0042071 P48061/SDF1_HUMAN Stromal cell-derived factor 1 (isoform beta)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power.

(SEQ ID NO:260)	Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine GRO alpha GeneSeq Accession B15813 WO0042071 P09341/GROA_HUMAN Growth-regulated alpha protein (SEQ ID NO:340)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
Human chemokine MIP1beta GeneSeq Accession B15831 WO0042071 P13236/CCL4_HUMAN C-C motif chemokine 4 (SEQ ID NO:358)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Autoimmune disorders, Immune, Vascular and Inflammatory disorders
A human C-C chemokine designated exodus GeneSeq Accession B07939 US Pat. No. 6,096,300 P78556/CCL20_HUMAN C-C motif chemokine 20 (isoform 1) (SEQ ID NO:248)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer
Human chemokine L105_7 GeneSeq Accession Y96922 US Pat. No. 6,084,071 SEQ ID NO:4 of WO9856818 (SEQ ID NO:437)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Chemotaxis, Gene Therapy, Wound healing
Human chemokine L105_3 GeneSeq Accession Y96923 US Pat. No. 6,084,071 SEQ ID NO:2 of WO9856818 (SEQ ID NO:436)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power.

	Humana Press Inc., Totowa, NJ. Chemotaxis, Gene Therapy, Wound healing
Human secondary lymphoid chemokine (SLC) GeneSeq Accession B01434 WO0038706 O00585/CCL21_HUMAN C-C motif chemokine 21 (SEQ ID NO:346)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, Vascular and Immune disorders
Human non- ELR CXC chemokine H174 GeneSeq Accession Y96310 WO0029439 O14625/CXL11_HUMAN C-X-C motif chemokine 11 (SEQ ID NO:363)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and Inflammatory disorders, Cancer, Haemostatic and thrombolytic activity
Human non- ELR CXC chemokine IP10 GeneSeq Accession Y96311 WO0029439 P02778/CXL10_HUMAN C-X-C motif chemokine 10 (SEQ ID NO:242)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and Inflammatory disorders, Cancer, haemostatic and thrombolytic activity
Human non- ELR CXC chemokine Mig GeneSeq Accession Y96313 WO0029439 Q07325/CXCL9_HUMAN C-X-C motif chemokine 9 (SEQ ID NO:351)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Immune and Inflammatory disorders, Cancer, haemostatic and thrombolytic activity
Human chemokine Ckbeta-7 GeneSeq Accession Y96280 WO0028035 Figure1 of WO0028035 (SEQ ID NO:439)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, wound healing, inflammatory and

	immunoregulatory disorders
Human chemokine MIP-1alpha GeneSeq Accession Y96281 WO0028035 P10147/CCL3_HUMAN C-C motif chemokine 3 (SEQ ID NO:364)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, wound healing, inflammatory and immunoregulatory disorders
Human mature chemokine Ckbeta-7 (optionally truncated) GenSeq Accession Y96282 WO0028035 Figure1 of WO0028035 (SEQ ID NO:440)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, wound healing, inflammatory and immunoregulatory disorders
Human chemokine receptor CXCR3 GeneSeq Accession Y79372 WO0018431 P49682|CXCR3_HUMAN C-X-C chemokine receptor type 3 (isoform 1) (SEQ ID NO:240)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Soluble CXCR3 polypeptides may be useful for inhibiting
Human neurotactin chemokine like domain GeneSeq Accession Y53259 US Pat. No. 6,043,086 P78423/X3CL1_HUMAN Fractalkine (SEQ ID NO:244)	hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. chemokine activities and viral infection.
Human CC type chemokine interleukin C GeneSeq Accession Y57771 JP11302298	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer and infectious diseases

Human CKbeta- 9 GeneSeq Accession B50860 US Pat. No. 6,153,441 O00585/CCL21_HUMAN C-C motif chemokine 21 (SEQ ID NO:346)	Chemokines are a family of related small, secreted proteins involved in biological processes ranging from hematopoiesis, angiogenesis, and leukocyte trafficking. Members of this family are involved in a similarly diverse range of pathologies including inflammation, allergy, tissue rejection, viral infection, and tumor biology. The chemokines exert their effects by acting on a family of seven transmembrane G-protein coupled receptors. Over 40 human chemokines have been described, which bind to ~17 receptors thus far identified. Chemokine activities can be determined using assays known in the art: Methods in Molecular Biology, 2000, vol. 138: Chemokine Protocols. Edited by: A. E. I. Proudfoot, T. N. C. Wells, and C. A. Power. Humana Press Inc., Totowa, NJ. Cancer, Auto- immune and inflammatory disorders, Cardiovascular disorders
Preproapolipo- protein "paris" variant GeneSeq Accession W08602 WO9637608 (SEQ ID NO:466)	Apoa-1 participates in the reverse transport of cholesterol from tissues to the liver for excretion by promoting cholesterol efflux from tissues and by acting as a cofactor for the lecithin cholesterol acyltransferase (lcat). Lipid binding activity can be determined using assays known in the art, such as, for example, the Cholesterol Efflux Assays of Takahaski *et al.*, P. N. A. S., Vol. 96, Issue 20, 11358-11363, Sep. 28, 1999. Useful for cardio- vascular disorders, cholesterol disorders, and Hyperlipidaemia
Preproapolipo- protein "milano" variant 5,721,114 SEQ ID NO:6 of U.S. Patent No. 5,721,114 (SEQ ID NO:441)	Apoa-1 participates in the reverse transport of cholesterol from tissues to the liver for excretion by promoting cholesterol efflux from tissues and by acting as a cofactor for the lecithin cholesterol acyltransferase (lcat). Lipid binding activity can be determined using assays known in the art, such as, for example, the Cholesterol Efflux Assays of Takahaski *et al.*, P. N. A. S., Vol. 96, Issue 20, 11358-11363, Sep. 28, 1999. Useful for cardio- vascular disorders, cholesterol disorders, and Hyperlipidaemia
Glycodelin-A; Progesterone- associated endometrial protein GeneSeq Accession W00289 WO9628169 P09466/PAEP_HUMAN Glycodelin (SEQ ID NO:365)	Naturally produced female contraceptive that is removed rapidly from the body following 2-3 days production. Uses include contraception Glycodelin-A activity can be determined using the hemizona assay as described in Oehninger, S., Coddington, C. C., Hodgen, G. D., and Seppala, M (1995) Fertil. Steril. 63, 377-383. Naturally derived contraceptive useful for the prevention of pregnancy.
NOGO-A Genbank Accession CAB99248 (SEQ ID NO:366)	NOGO polypeptides are potent inhibitors of neurite growth. Inhibition of Neurite outgrowth. Antagonists to NOGO polypeptides may promote the outgrowth of neurites, thus inducing regeneration of neurons. NOGO-A polypep- tide antagonists are useful for the pro- motion of neural growth, which could be useful in the treatment of neural disorders and dys- function due to de- generative diseases or trauma; useful in the treatment of neo- plastic diseases of the CNS; induce regeneration of neurons or to promote the structural plasticity of the CNS.
NOGO-B Genbank Accession CAB99249 (SEQ ID NO:367)	NOGO polypeptides are potent inhibitors of neurite growth. Inhibition of Neurite outgrowth. Antagonists to NOGO polypeptides may promote the outgrowth of neurites, thus inducing regeneration of neurons. NOGO-B polypep- tide antagonists are useful for the pro- motion of neural growth, which could be useful in the treatment of neural disorders and dys- function due to de- generative diseases or trauma; useful in the treatment of neo- plastic diseases of the CNS; induce regeneration of neurons or to promote the structural plasticity of the CNS.
NOGO-C Genbank Accession CAB99250 (SEQ ID NO:368)	NOGO polypeptides are potent inhibitors of neurite growth. Inhibition of Neurite outgrowth. Antagonists to NOGO polypeptides may promote the outgrowth of neurites, thus inducing regeneration of neurons. NOGO-C polypep- tide antagonists are useful for the pro- motion of neural growth, which could be useful in the treatment of neural disorders and dys- function due to de- generative diseases or trauma; useful in the treatment of neo- plastic diseases of the CNS; induce regeneration of neurons

	or to promote the structural plasticity of the CNS.
NOGO-66 Receptor Genbank Accession AAG53612 (SEQ ID NO:369)	NOGO polypeptides are potent inhibitors of neurite growth, and are thought to mediate their effects through the NOGO-66 Receptor. Inhibition of Neurite outgrowth by mediating the biological effects of NOGO polypeptides. Soluble NOGO- 66 receptor polypeptides may promote the outgrowth of neurites, thus inducing regeneration of neurons. NOGO-66 receptor polypeptides are useful for the promotion of neural growth, which could be useful in the treatment of neural disorders and dys- function due to de- generative diseases or trauma; useful in the treatment of neo- plastic diseases of the CNS; induce regeneration of neurons or to promote the structural plasticity of the CNS.
Antibodies specific for collapsin US Pat. No. 5,416,197 Wildtype collapsin has the sequence: SEQ ID NO:2 of 5,416,197 (SEQ ID NO:464)	These antibodies are useful for the promotion of neurite outgrowth Collapsin activity, which is thought to inhibit the outgrowth of neurites, can be assayed in the presence of antibodies specific for collapsing using assays known in the art, such as, for example, the collapse assay disclosed by Luo *et al.*, Cell 1993 Oct 22; 75(2): 217-27 Useful for the pro- motion of neural growth, which could be useful in the treatment of neural disorders and dys- function due to de- generative diseases or trauma.
Humanized Anti-VEGF Antibodies, and fragments thereof WO9845331	These agents have anti-inflammatory and anti-cancer applications VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer
Humanized Anti-VEGF Antibodies, and fragments thereof WO0029584	These agents have anti-inflammatory and anti-cancer applications VEGF activity can be determined using assays known in the art, such as those disclosed in International Publication No. WO0045835, for example. Promotion of growth and proliferation of cells, such as vascular endothelial cells. Hematopoietic and immune dis- orders. Antagonists may be useful as anti-angiogenic agents, and may be applicable for cancer
Membrane bound proteins GeneSeq. Accession Y66631-Y66765 WO9963088	Cancer, Immune Disorders These proteins can be used for linking bioactive molecules to cells and for modulating biological activities of cells, using the polypeptides for specific targeting. The polypeptide targeting can be used to kill the target cells, *e.g.* for the treatment of cancers. These proteins are useful for the treatment of immune system disorders. Activities can be determined using assay known in the art, such as, for example, the assays disclosed in International Publication No.WO0121658.
Secreted and Transmembrane polypeptides GeneSeq Accession B44241-B44334 WO0053756	Cancer, Immune Disorders These proteins can be used for linking bioactive molecules to cells and for modulating biological activities of cells, using the polypeptides for specific targeting. The polypeptide targeting can be used to kill the target cells, *e.g.* for the treatment of cancers. These proteins are useful for the treatment of immune system disorders. Activities can be determined using assay known in the art, such as, for example, the assays disclosed in International Publication No.WO0121658.
Secreted and Transmembrane polypeptides GeneSeq Accession Y41685-Y41774 WO9946281	Cancer, Immune Disorders These proteins can be used for linking bioactive molecules to cells and for modulating biological activities of cells, using the polypeptides for specific targeting. The polypeptide targeting can be used to kill the target cells, *e.g.* for the treatment of cancers. These proteins are useful for the treatment of immune system disorders. Activities can be determined using assay known in the art, such as, for example, the assays disclosed in International Publication No. WO0121658.

Interleukin 2 (IL-2) SEQ ID NO:548	Metabolic Disease, Type 1 diabetes, Graft-versus-host disease.
Interleukin 15_vA (IL-15_vA) SEQ ID NO:549	Obesity, Metabolic Disease, Diabetes.
Interleukin 15_vB (IL-15_vB) SEQ ID NO:550	Obesity, Metabolic Disease, Diabetes.
Interleukin 15_vC (IL-15_vC) SEQ ID NO:551	Obesity, Metabolic Disease, Diabetes.
Interleukin 15_vD (IL15_vD) SEQ ID NO:552	Obesity, Metabolic Disease, Diabetes.
Interleukin 15_vE (IL15_vE) SEQ ID NO:553	Obesity, Metabolic Disease, Diabetes.
Interleukin 15_vF (IL15_vF) SEQ ID NO:565	Obesity, Metabolic Disease, Diabetes.
Interleukin 22 (IL22) SEQ ID NO:554	Metabolic Disease, Diabetic Ulcers, Inflamatory Bowel Diseases.
Fibroblast Growth Factor 1 (FGF1) SEQ ID NO:555	Diabetes, Metabolic Disease, Obesity.
Fibroblast Growth Factor 1_vA (FGF1_vA) SEQ ID NO:556	Diabetes, Metabolic Disease, Obesity. See Nature 513, 436–439 (18 September 2014) doi:10.1038/nature13540.
Fibroblast Growth Factor 1_vB (FGF1_vB)	Diabetes, Metabolic Disease, Obesity. See Proc Natl Acad Sci U S A. 1991 Apr 1; 88(7): 2893–2897.

SEQ ID NO:557	
Fibroblast Growth Factor 1_vC (FGF1_vC) SEQ ID NO:566	Diabetes, Metabolic Disease, Obesity.
Fibroblast Growth Factor 19_vA (FGF19_vA) SEQ ID NO:558	Chronic liver disease, primary biliary cirrhosis, bile acid-induced liver damage. See Cancer Res. 2014 Jun 15;74(12):3306-16. doi: 10.1158/0008-5472.CAN-14-0208. Epub 2014 Apr 11. Regulates bile acid metabolism without tumorigenicity.
Fibroblast Growth Factor 21 (FGF21) SEQ ID NO:559	Metabolic Disease, Fibrotic Diseases.
Fibroblast Growth Factor 23 (FGF23) SEQ ID NO:560	Hyperphosphatemic familial tumoral calcinosis.
Brain-Derived Neurotrophic Factor (BDNF) SEQ ID NO:561	Neurological diseases (including Alzheimer's Disease, Autism, Huntington's Disease, Parkinson's Disease, and Depression), obesity, metabolic disease.
Serpin Family A Member 1 (SERPINA1) SEQ ID NO: 584, SEQ ID NO: 585	alpha-1-antitrypsin deficiency.
Serpin Peptidase Inhibitor, Clade B (Ovalbumin), Member 1 (SERPINB1) SEQ ID NO:562	Diabetes.
CASPASE1 SEQ ID NO:563	Diabetes.
Leukemia Inhibitory Factor (LIF) SEQ ID NO:564	Muscular dystrophy, atherosclerosis, kidney disease

Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1) SEQ ID NO:567	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 2 (PCSK2) SEQ ID NO:568	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 3 (PCSK3) SEQ ID NO:569	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 3 Sol (PCSK3_SOL) SEQ ID NO:570	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 4 (PCSK4) SEQ ID NO:571	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 5 (PCSK5) SEQ ID NO:572	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 6 (PCSK6) SEQ ID NO:573	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type (PCSK7) SEQ ID NO:574	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 8 (PCSK8) SEQ ID NO:575	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) SEQ ID NO:576	Cardiovascular disease, hypercholesterolemia, heterozygous familial hypercholesterolemia (HeFH), atherosclerotic cardiovascular disease such as heart attacks or strokes, increasing the amount of a functional protein, polypeptide or peptide
Membrane-Bound Transcription Factor Peptidase, Site 2	IFAP syndrome, increasing the amount of a functional protein, polypeptide or peptide

(MBTPS2) SEQ ID NO:577	
Carboxypeptidase E (CPE) SEQ ID NO:578	Endocrine disorders, such as, for example, obesity and infertility; hyperproinsulinemia; metabolic syndrome, increasing the amount of a functional protein, polypeptide or peptide

In various embodiments, the nucleic acid drug, including synthetic RNA, is administered is a manner that it effects one or more of keratinocytes and fibroblasts (*e.g.* causes these cells to express one or more therapeutic proteins). For example, present methods allow for methods in which a patient's cells are used to generate a therapeutic protein and the levels of such protein are tailored by synthetic RNA dosing.

In a specific embodiment, the synthetic RNA targets a soluble protein. In some embodiments, the synthetic RNA targets a protein of one or more of the following families of proteins: transforming growth factor (TGF) beta, bone morphogenetic proteins (BMPs), Fibroblast growth factors (FGFs), vascular endothelial growth factors (VEGFs), and interleukins. The terms "family", "superfamily", and "subfamily" can be used interchangeably

In a specific embodiment, the synthetic RNA targets a member of the TGF beta family. TGF-β superfamily proteins comprise cytokines characterized by six-conserved cysteine residues (Lander *et al.*, (2001) Nature, 409:860-921). The human genome contains at least about 42 open reading frames encoding TGF-β superfamily proteins. TGF-β superfamily proteins can at least be divided into the BMP subfamily and the TGF-β subfamily based on sequence similarity and the specific signaling pathways that they activate. In various embodiments, the synthetic RNA targets one or more of TGFs (*e.g.*, TGF-β1, TGF-β2, and TGF-β3), activins (*e.g.*, activin A) and inhibins, macrophage inhibitory cytokine-1 (MIC-1), Mullerian inhibiting substance, anti-Mullerian hormone, and glial cell line derived neurotrophic factor (GDNF).

The TGF-β superfamily comprises a subset of the cysteine knot cytokine superfamily. Additional members of the cysteine knot cytokine superfamily include, but are not limited to, platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), placenta growth factor (P1GF), Noggin, neurotrophins (BDNF, NT3, NT4, and βNGF), gonadotropin, follitropin, lutropin, interleukin-17, and coagulogen. This family of proteins is also among the targets encompassed by the present invention.

In various embodiments, the present invention relates to targeting a TGF beta family member for treatment or prevention of various immunological disorders, cancer, bronchial asthma, lung fibrosis, heart disease, diabetes, hereditary hemorrhagic telangiectasia, Marfan syndrome, Vascular Ehlers-Danlos syndrome, Loeys–Dietz syndrome, Parkinson's disease, chronic kidney disease, multiple sclerosis and AIDS.

In a specific embodiment, the synthetic RNA targets a member of the BMP family. The BMP subfamily includes, but is not limited to, BMP-2, BMP-3 (osteogenin), BMP-3b (GDF-10), BMP-4 (BMP-2b), BMP-5, BMP-6, BMP-7 (osteogenic protein-1 or OP-1), BMP-8 (OP-2), BMP-8B (OP-3), BMP-9 (GDF-2), BMP-10, BMP-11 (GDF-11),

BMP-12 (GDF-7), BMP-13 (GDF-6, CDMP-2), BMP-15 (GDF-9), BMP-16, GDF-1, GDF-3, GDF-5 (CDMP-1), and GDF-8 (myostatin). In various embodiments, the synthetic RNA targets one or more of BMP-2, BMP-3 (osteogenin), BMP-3b (GDF-10), BMP-4 (BMP-2b), BMP-5, BMP-6, BMP-7 (osteogenic protein-1 or OP-1), BMP-8 (OP-2), BMP-8B (OP-3), BMP-9 (GDF-2), BMP-10, BMP-11 (GDF-11), BMP-12 (GDF-7), BMP-13 (GDF-6, CDMP-2), BMP-15 (GDF-9), BMP-16, GDF-1, GDF-3, GDF-5 (CDMP-1), and GDF-8 (myostatin). BMPs are sometimes referred to as Osteogenic Protein (OPs), Growth Differentiation Factors (GDFs), or Cartilage-Derived Morphogenetic Proteins (CDMPs). In a specific embodiment, the synthetic RNA targets one or more BMP fusions (*e.g.* as described in US Patent Publication No. 2009/0202638, the entire contents of which are hereby incorporated by reference) and/or one or more BMP mutants (*e.g.* as described in US Patent Publication No. 2011/0039773, the entire contents of which are hereby incorporated by reference).

In various embodiments, the present invention relates to targeting a BMP family member for regenerative medicine or metabolic applications, including without limitation orthopedic applications such as spinal fusions, nonunions and oral surgerie, metabolic disease, prediabetes, diabetes, thermogenesis, insulin sensitivity, insulin resistance, and adipogenesis, including brown-fat adipogenesis. Various other metabolic applications are described elesewhere herein. In various embodiments, the present invention relates to targeting a BMP family member, including BMP-7, for treatment of chronic kidney disease (CKD) and/or to reverse the loss of glomeruli due to sclerosis.

In various embodiments, the present invention relates to targeting a BMP family member to induce proliferation of bone and cartilage in a variety of locations in the body. For example, repair of joints such as knee, elbow, ankle, and finger joints are contemplated by the invention. For example, targeting a BMP family member may result in regenerating cartilage in patients suffering from arthritis or other cartilage degenerating diseases. Further, the invention pertains to treating tears in cartilage due to injury. In addition, the invention is useful for inducing bone growth in patients, for instance, by way of non-limitation, for use in treating patients suffering from bone fractures or breaks, osteoporosis, or patients in need of spinal fusion or for repair of the spine, vertebrae or the like.

In various embodiments, the present invention relates to targeting a BMP family member to induce a developmental cascade of bone morphogenesis and tissue morphogenesis for a variety of tissues in mammals different from bone or bone cartilage. This morphogenic activity includes the ability to induce proliferation and differentiation of progenitor cells, and the ability to support and maintain the differentiated phenotype through the progression of events that results in the formation of bone, cartilage, non-mineralized skeletal or connective tissues, and other adult tissues.

For example, the present invention may be used for treatment to prevent loss of and/or increase bone mass in metabolic bone diseases. General methods for treatment to prevent loss of and/or increase bone mass in metabolic bone diseases using osteogenic proteins are disclosed in US Pat. No. 5,674,844, the entire contents of which are hereby incorporated by reference. Further the present compositions and methods find use in

replacing or repairing bone or cartilage at injury sites such as bone breaks, bone fractures, and cartilage tears, periodontal tissue regeneration (*e.g.* general methods for periodontal tissue regeneration using osteogenic proteins are disclosed in US Pat. No. 5,733,878, the entire contents of which are hereby incorporated by reference), liver regeneration, including following a partial hepatectomy (*see, e.g.*, US Pat. No. 5,849,686, the entire contents of which are hereby incorporated by reference), treatment of chronic renal failure (*see, e.g.,* US. Pat. No. 6,861,404, the entire contents of which are hereby incorporated by reference), enhancing functional recovery following central nervous system ischemia or trauma (*see, e.g.* US Pat. No. 6,407,060, the entire contents of which are hereby incorporated by reference), inducing dendritic growth (*see, e.g.,* US Pat. No. 6,949,505, the entire contents of which are hereby incorporated by reference), inducing neural cell adhesion (*see, e.g.,* US Pat. No. 6,800,603, the entire contents of which are hereby incorporated by reference), and treatment and prevention of Parkinson's disease (*see, e.g.,* US Pat. No. 6,506,729, the entire contents of which are hereby incorporated by reference). As another example, the present compositions and methods, including when targeting one or more BMPs, can be used to induce dentinogenesis. To date, the unpredictable response of dental pulp tissue to injury is a basic clinical problem in dentistry. Using standard dental surgical procedures, small areas (*e.g.*, 2 mm) of dental pulps can be surgically exposed by removing the enamel and dentin immediately above the pulp (by drilling) of sample teeth, performing a partial amputation of the coronal pulp tissue, inducing hemostasis, application of the pulp treatment, and sealing and filling the cavity by standard procedures.

In various embodiments, the present invention relates to targeting a BMP family member for the treatment of one or more metabolic-related disorders as described herein.

In a specific embodiment, the synthetic RNA targets a member of the FGF family. FGFs are a family of growth factors, with members involved in angiogenesis, wound healing, embryonic development and various endocrine signaling pathways. In various embodiments, any one of the following FGFs are targets of the invention: FGF1, FGF2, FGF3, FGF4, FGF5, FGF6, FGF7, FGF8, FGF9, FGF10, FGF11, FGF12, FGF13, FGF14 (FGF11, FGF12, FGF13, and FGF14 being FGF homologous factors 1-4 (FHF1-FHF4)), FGF16, FGF17, FGF18, FGF19 (aka FHF15/19), FGF20, FGF21, FGF22 and FGF22. In some embodiments, the synthetic RNA targets a cognate receptor of any of the above FGFs. In various embodiments, the present invention relates to targeting a FGF family member to a treat or prevent disease or disorder associated with abnormal function and/or expression of an FGF, a metabolic disease or disorder (*e.g.*, diabetes, obesity, dyslipidemia, hyperglycemia, hyperinsulinemia, hypertension, hepatosteaotosis such as non-alcoholic steatohepatitis (NASH) *etc.*), cancer, a disease or disorder associated with impaired lipid metabolism a disease or disorder associated with impaired renal function, a disease or disorder associated with impaired hepatic function, abnormal cell proliferation, a vascular disease or disorder (*e.g.*, coronary artery disease, peripheral artery disease, atherosclerosis, abdominal aortic aneurysm, a blood clot, deep vein thrombosis, venous stasis disease, phlebitis, varicose veins *etc.*), angiogenesis, atherosclerosis, a cardiovascular disease or disorder, a disease or disorder associated with impaired blood vessel formation, a disease or disorder associated with impaired cell signaling, a disease or

disorder associated with impaired kinase activity, and a disease or disorder associated with impaired uptake of glucose into adipocytes.

In a specific embodiment, the synthetic RNA targets a member of the VEGF family. In some embodiments, the target is one or more of VEGF-A (including all isoforms, *e.g.* VEGF121, VEGF165 and VEGF189), placenta growth factor (PGF, including all isoforms, *e.g.* PGF-1, PGF-2, and PGF-3), VEGF-B, VEGF-C and VEGF-D, and any variants thereof (see, *e.g.* US Patent No. 9,078,860, the entire contents of which are hereby incorporated by reference). In some embodiments, the synthetic RNA targets a cognate receptor of any of the above VEGFs. The present invention also encompasses as targets VEGF-related proteins including orf virus-encoded VEGF-like proteins referred to as VEGF-E and a series of snake venoms referred to as VEGF-F. VEGFs and VEGF-related proteins are members of the Platelet Derived Growth Factor (PDGF) supergene family of cystine knot growth factors. All members of the PDGF supergene family share a high degree of structural homology with PDGF.

In various embodiments, the present invention relates to targeting a VEGF family member to treat diseases and conditions associated with angiogenesis, including but not limited to, solid tumor cancers, hemangiomas, rheumatoid arthritis, osteoarthritis, septic arthritis, asthma, atherosclerosis, idiopathic pulmonary fibrosis, vascular restenosis, arteriovenous malformations, meningiomas, neovascular glaucoma, psoriasis, Kaposi's Syndrome, angiofibroma, hemophilic joints, hypertrophic scars, Osler-Weber syndrome, pyogenic granuloma, retrolental fibroplasias, scleroderma, trachoma, von Hippel-Lindau disease, vascular adhesion pathologies, synovitis, dermatitis, neurological degenerative diseases, preeclampsia, unexplained female infertility, endometriosis, unexplained male infertility, pterygium, wounds, sores, skin ulcers, gastric ulcers, and duodenal ulcers. In various embodiments, the present invention relates to targeting a VEGF family member to treat angiogenesis-associated eye diseases, including without limitation any eye disease associated with abnormal intraocular neovascularization, including but not limited to retinopathy of prematurity, diabetic retinopathy, retinal vein occlusion, and age-related macular degeneration, as well diabetic macular edema and retinal vein occlusion. In an embodiment, the present compositions and methods relate to the treatment of wet age-related macular degeneration.

In a specific embodiment, the synthetic RNA targets a member of the interleukin family. The interleukins represent a large group of cytokines with diverse functions and were first characterized by expression in leukocytes and have since been shown to be expressed in a wide variety of cells, for example macrophages, TH-1 and TH-2 cells, T- lymphocytes, monocytes and bone marrow stroma. Broadly, the function of the immune system depends in a large part on the expression and function of the interleukins. In some embodiments, the target is one or more of interleukins 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31 , 32, 33, 35 and 36, and, within each species of interleukin, various isotypes and/or interleukin receptors (*e.g.*, IL-1R, IL-2R, IL-3R, IL-4R, IL-5R, IL-6R, IL-7R, IL-8R, IL-9R, IL-10R, IL-11R, IL-12R, IL-13R, IL-14R, IL-15R, IL-16R, IL-17R, IL-18R, IL-19R, IL-20R, IL-21R, IL-22R, IL-23R, IL-24R, IL-25R, IL-26, IL-27R, IL-28R, IL-29R, IL-30R, IL-31R, IL-32R, IL-33R, IL-34R, IL-35R, and IL-36R). In a specific embodiment, both IL-15 and IL-15R (*e.g.*, IL-15RA) are targeted. Without wishing to be bound by theory, it is believed that the

targeting of both interleukin (*e.g.*, IL-15) and its cognitive interleukin receptor (*e.g.*, IL-15RA) results in synergistic beneficial effects. In various embodiments, the present invention relates to targeting a member of the interleukin family to treat cancer, inflammatory, respiratory, autoimmune, cardiovascular, neurological, metabolic, and/or proliferative diseases, disorders, and/or conditions in a subject or organism, as described herein. In a specific embodiment, the present invention relates to targeting a member of the interleukin family to treat cancer. In a specific embodiment, the present invention relates to targeting a member of the interleukin family to treat rheumatoid arthritis.

In a specific embodiment, the synthetic RNA targets an EPO gene or a derivative thereof (*e.g.* SEQ ID NO: 164, SEQ ID NO: 165, SEQ ID NO: 166, and SEQ ID NO: 167). Some embodiments are related to NOVEPOETIN protein (SEQ ID NO: 167). Other embodiments are related to NOVECRIT (SEQ ID NO: 168).

Erythropoietin can stimulate erythropoiesis in anemic patients with chronic renal failure in whom the endogenous production of erythropoietin is impaired. Without being bound by theory, because of the length of time often required for erythropoiesis (several days for erythroid progenitors to mature and be released into the circulation), a clinically significant increase in hemoglobin is usually not observed in less than two weeks and may require up to ten weeks in some patients. The present methods and compositions provide, in some embodiments, more rapid therapeutic effect. The present methods and compositions provide, in some embodiments, more rapid therapeutic effect, for instance, when compared to wild type EPO and/or EPO without non-canonical nucleotides and/or EPO delivered as a protein biologic. The present methods and compositions provide, in some embodiments, a sustained therapeutic effect. The present methods and compositions provide, in some embodiments, a sustained therapeutic effect, for instance, when compared to wild type EPO and/or EPO without non-canonical nucleotides and/or EPO delivered as a protein biologic.

For instance, for EPO, the present methods and compositions provide a clinically significant increase in hematocrit in less than about 6 weeks, or less than about 5 weeks, or less than about 4 weeks, or less than about 3 weeks, or less than about 2 weeks, or less than about 1 week. In some embodiments, the present methods and compositions provide a clinically significant increase in hematocrit in about 2 weeks, or about 10 days, or about 1 week, or about 3 days, or about 1 day. In various embodiments, the present methods and compositions accelerate the process by which erythroid progenitors mature and are released into the circulation.

In some embodiments, the present EPO-related compositions find use in decreasing the dose and/or frequency of administration when compared to wild type EPO and/or EPO without non-canonical nucleotides and/or EPO delivered as a protein biologic. For instance, the present EPO-related compositions may find use in treatment regimens for the diseases disclosed herein (including, without limitation, one or more anemias) that involve administration on a monthly, or biweekly, or weekly basis. In some embodiments, therefore, the present EPO-related compositions reduce the need for daily, or, in some embodiments, weekly, administration. In some embodiments, the present EPO-related compositions require lower maintenance doses as compared to wild type EPO and/or EPO without non-canonical nucleotides and/or EPO delivered as a protein biologic. Certain

embodiments are particularly useful for treating chemotherapy-induced anemia. Other embodiments are particularly useful for treating anemia associated with inflammation, including, but not limited to, rheumatoid arthritis.

In some embodiments, the present the present methods and compositions provide a fast and robust response that obviates the need for RBC transfusion. For instance, in some embodiments, the present methods and compositions allow for treatment of patients do not consent to transfusions.

In some embodiments, the present methods and compositions increase the rate of increase in hematocrit. In some embodiments, the present methods and compositions maintain elevated hematocrits (*e.g.* of 25%, or 30%, or 35%, or 40% or more) for a sustained period (*e.g.* about 1 month, or about 2 months, or about 3 months, or about 4 months, or about 5 months, or about 6 months, or about 9 months).

In some embodiments, the present methods and compositions stimulate red blood cell production. In some embodiments, the present methods and compositions stimulate division and differentiation of committed erythroid progenitors in the bone marrow.

In some embodiments, including, without limitation, when targeting EPO, the present invention relates to the treatment of one or more of anemia, including anemia resulting from resulting from chronic kidney disease (*e.g.* from dialysis) and/or chemotherapy and/or HIV treatment (*e.g.* Zidovudine (INN) or azidothymidine (AZT)), inflammatory bowel disease (*e.g.* Crohn's disease and ulcer colitis), anemia linked to inflammatory conditions (*e.g.* arthritis, lupus, IBD), anemia linked to diabetes, schizophrenia, cerebral malaria, as aplastic anemia, and myelodysplasia from the treatment of cancer (*e.g.* chemotherapy and/or radiation), and various myelodysplastic syndrome diseases (*e.g.* sickle cell anemia, hemoglobin SC disease, hemoglobin C disease, alpha- and beta-thalassemias, neonatal anemia after premature birth, and comparable conditions).

In some embodiments, including, without limitation, when targeting EPO, the present invention relates to the treatment of, or a patient having one or more of cancer, heart failure, autoimmune disease, sickle cell disease, thalassemia, blood loss, transfusion reaction, diabetes, vitamin B12 deficiency, collagen vascular disease, Shwachman syndrome, thrombocytopenic purpura, Celiac disease, endocrine deficiency state such as hypothyroidism or Addison's disease, autoimmune disease such as Crohn's Disease, systemic lupus erythematosis, rheumatoid arthritis or juvenile rheumatoid arthritis, ulcerative colitis immune disorders such as eosinophilic fasciitis, hypoimmunoglobulinemia, or thymoma/thymic carcinoma, graft vs. host disease, preleukemia, Nonhematologic syndrome (*e.g.* Down's, Dubowwitz, Seckel), Felty syndrome, hemolytic uremic syndrome, myelodysplasic syndrome, nocturnal paroxysmal hemoglobinuria, osteomyelofibrosis, pancytopenia, pure red-cell aplasia, Schoenlein-Henoch purpura, malaria, protein starvation, menorrhagia, systemic sclerosis, liver cirrhosis, hypometabolic states, congestive heart failure, chronic infections such as HIV/ AIDS, tuberculosis, oseomyelitis, hepatitis B, hepatitis C, Epstein-barr virus or parvovirus, T cell leukemia virus, bacterial overgrowth syndrome, fungal or parasitic infections, and/or red cell membrane disorders such as hereditary spherocytosis,

hereditary elliptocytosis, heriditray pyrpoikilocytosis, hereditary stomatocytosis, red cell enzyme defects, hypersplenism, immune hemolysis or paroxysmal nocturnal hemoglobinuria.

In some embodiments, including, without limitation, when targeting EPO, the present invention relates to the treatment of, or a patient having anemia, *i.e.* a condition in which the number of red blood cells and/or the amount of hemoglobin found in the red blood cells is below normal. In various embodiments, the anemia may be acute or chronic. For example, the present anemias include but are not limited to iron deficiency anemia, renal anemia, anemia of chronic diseases/inflammation, pernicious anemia such as macrocytic achylic anemia, juvenile pernicious anemia and congenital pernicious anemia, cancer-related anemia, chemotherapy-related anemia, radiotherapy-related anemia, pure red cell aplasia, refractory anemia with excess of blasts, aplastic anemia, X-lined siderobalstic anemia, hemolytic anemia, sickle cell anemia, anemia caused by impaired production of ESA, myelodysplasia syndromes, hypochromic anemia, microcytic anemia, sideroblastic anemia, autoimmune hemolytic anemia, Cooley's anemia, Mediterranean anemia, Diamond Blackfan anemia, Fanconi's anemia and drug-induced immune hemolytic anemia. Anemia may cause serious symptoms, including hypoxia, chronic fatigue, lack of concentration, pale skin, low blood pressure, dizziness and heart failure.

In some embodiments, the anemia is induced by chemotherapy is one cause of anemia. For instance, the chemotherapy may be any myelosuppressive chemotherapy. In some embodiments, the chemotherapy is one or more platinum-based drugs including cisplatin (*e.g.* PLATINOL) and carboplatin (*e.g.* PARAPLATIN). In some embodiments, the chemotherapy is any one of the agents described herein. In some embodiments, the chemotherapy is any agent described in Groopman *et al.* J Natl Cancer Inst (1999) 91 (19): 1616-1634, the contents of which are hereby incorporated by reference in their entireties. In some embodiments, the present compositions and methods are used in the treatment of chemotherapy-related anemia in later stage cancer patients (*e.g.* a stage IV, or stage III, or stage II cancer). In some embodiments, the present compositions and methods are used in the treatment of chemotherapy-related anemia in cancer patients receiving dose-dense chemotherapy or other aggressive chemotherapy regimens.

In some embodiments, the present invention relates to the treatment of anemia in a patient having one or more blood-based cancers, such as leukemia, lymphoma, and multiple myeloma. Such cancers may affect the bone marrow directly. Further, the present invention relates to metastatic cancer that has spread to the bone or bone marrow. In some embodiments, the present invention relates to the treatment of anemia in a patient undergoing radiation therapy. Such radiation therapy may damage the bone marrow, lowering its ability to make red blood cells. In further embodiments, the present invention relates to the treatment of anemia in a patient having a reduction or deficiency of one or more of iron, vitamin B12, and folic acid. In further embodiments, the present invention relates to the treatment of anemia in a patient having excessive bleeding including without limitation, after surgery or from a tumor that is causing internal bleeding. In further embodiments, the present invention relates to the treatment of anemia in a patient having anemia of chronic disease.

In some embodiments, the present invention relates to the treatment of anemia resulting from chronic renal failure. In some embodiments, the present invention relates to the treatment of anemia resulting from the use of one or more renal replacement therapies, inclusive of dialysis, hemodialysis, peritoneal dialysis, hemofiltration, hemodiafiltration, and renal transplantation.

In some embodiments, the present invention relates to the treatment of anemia in patients with chronic kidney disease who are not on dialysis. For instance, the present invention relates to patients in stage 1 CKD, or stage 2 CKD, or stage 3 CKD, or stage 4 CKD, or stage 5 CKD. In some embodiments, the present patient is stage 4 CKD or stage 5 CKD. In some embodiments, the present patient has undergone a kidney transplant. In some embodiments, the present invention relates to the treatment of anemia is a patient having an acute kidney injury (AKI).

In various embodiments, the present compositions and methods are used to reduce or eliminate fatigue, dizziness, and shortness of breath in a patient.

In various embodiments, the present compositions and methods are used to treat a patient presenting with hyporesponse or resistance to erythropoiesis stimulating agent therapy. In some embodiments, hyporesponsiveness to erythropoietin or ESA-resistant anemia refers to the presence of at least one of the following conditions: i) a significant decrease in hemoglobin levels at a constant dose of ESA treatment, ii) a significant increase in the ESA dose requirement to achieve or maintain a certain hemoglobin level, iii) a failure to raise the hemoglobin level to the target range despite the ESA dose equivalent to erythropoietin greater than 150 IU/kg/week or 0.75 mg/kg/week of darbepoeitn-alpha or continued need for such high dose of ESA to maintain the target hemoglobin level. For example, approximately 5-10% of patients with CDK demonstrate hyporesponsiveness to ESA, defined as a continued need for greater than 300 IU/kg per week erythropoietin or 1.5 ng/kg per week darbepoetin administered by the subcutaneous route.

In various embodiments, the present compositions and methods mitigate the need for dose-escalation of the erythropoiesis stimulating agent therapy and therefore, optionally, avoid side effects (*e.g.* flu-like symptoms such as joint pains, weakness, dizziness and tiredness, skin irritation, increased risk of adverse cardiovascular complications).

In various embodiments, the present compositions and methods are used to maintain a hemoglobin level of about 12.5 to 13 g/dL. In various embodiments, the present compositions and methods are used in patients having hemoglobin levels of below about 12 g/dL, or about 11 g/dL, or about 10 g/dL, or about 9 g/dL, or about 8 g/dL, or about 7 g/dL, or about 6 g/dL, or about 5 g/dL. In various embodiments, the present compositions and methods are used in patients having iron blood test scores that indicate blood pathology, *e.g.* a ferritin score of below about 200 ng/L and/or a transferrin saturation score below about 30%.

In various embodiments, the present compositions and methods are used to increase or maintain hemoglobin levels at a target level ranging from 9 to 10 g/dL, at a target level ranging from 9 g/dL to 11 g/dL, at a target level

ranging from 9 g/dL to 12 g/dL, at a target level ranging from 9 g/dL to 14 g/dL, at a target level ranging from 10 g/dL to 14 g/dL, or at a target level ranging from 12 g/dL to 14 g/dL.

In various embodiments, the present compositions and methods are used to bring a patient's hemoglobin levels to normal. In various embodiments, normal hemoglobin ranges for humans are about 14-18 g/dl for men and 12-16 for women g/dl with the average hemoglobin value for men at about 16 g/dL and for women at about 14 g/dL.

In some embodiments, for instance when targeting EPO, the present invention relates to the treatment of anemia of one or more of the following toxicity grading criteria (*e.g.* NCI Common Toxicity Criteria): grade 1 (mild), 10.0 g hemoglobin/dL to within normal limits; grade 2 (moderate), 8.0-10.0 g of hemoglobin/dL; grade 3 (serious or severe), 6.5-7.9 g of hemoglobin/dL; and grade 4 (life threatening), less than 6.5 g of hemoglobin/dL. In various embodiments, the present invention brings an increase in toxicity grading criteria by about 1 point, or about 2 points, or about 3 points, or about 4 points. In various embodiments, the present invention results in a patient having a level of 0 or 1. In various embodiments, the present compositions and methods improve anemia as assessed by one or more scales described in Groopman *et al.* J Natl Cancer Inst (1999) 91 (19): 1616-1634, the entire contents of which are hereby incorporated by reference in their entireties.

In some embodiments, when targeting EPO, the present invention relates to combination therapy with one or more EPOs. For example, the present compositions may provide a sustained effect that can supplement a fast action of another EPO. In some embodiments, the present compositions are used as an adjuvant to other EPOs. In some embodiments, the present compositions are used as a maintenance therapy to other EPOs Other EPOs include the following: epoetin alfa, including without limitation, DARBEPOETIN (ARANESP), EPOCEPT (LUPIN PHARMA), NANOKINE (NANOGEN PHARMACEUTICAL), EPOFIT (INTAS PHARMA), EPOGEN (AMGEN), EPOGIN, EPREX, (JANSSEN-CILAG), BINOCRIT (SANDOZ), PROCRIT; epoetin beta, including without limitation, NEORECORMON (HOFFMANN–LA ROCHE), RECORMON, Methoxy polyethylene glycol-epoetin beta (MIRCERA, ROCHE); epoetin delta, including without limitation, DYNEPO (erythropoiesis stimulating protein, SHIRE PLC); epoetin omega, including without limitation, EPOMAX; epoetin zeta, including without limitation, SILAPO (STADA) and RETACRIT (HOSPIRA) and other EPOs, including without limitation, EPOCEPT (LUPIN PHARMACEUTICALS), EPOTRUST (PANACEA BIOTEC LTD), ERYPRO SAFE (BIOCON LTD.), REPOITIN (SERUM INSTITUTE OF INDIA LIMITED), VINTOR (EMCURE PHARMACEUTICALS), EPOFIT (INTAS PHARMA), ERYKINE (INTAS BIOPHARMACEUTICA), WEPOX (WOCKHARDT BIOTECH), ESPOGEN (LG LIFE SCIENCES), RELIPOIETIN (RELIANCE LIFE SCIENCES), SHANPOIETIN (SHANTHA BIOTECHNICS LTD), ZYROP (CADILA HEALTHCARE LTD.), EPIAO (RHUEPO) (SHENYANG SUNSHINE PHARMACEUTICAL CO. LTD), CINNAPOIETIN (CINNAGEN).

In some embodiments, when targeting EPO, the present invention relates to combination therapy with a blood transfusion. For instance, the present compositions may supplement a blood transfusion. In some embodiments, when targeting EPO, the present invention relates to combination therapy with iron supplements.

In some embodiments, the present invention also relates to the following protein targets, *e.g.* in the treatment of disease: growth hormone (GH) *e.g.* human and bovine growth hormone, growth hormone-releasing hormones; interferon including α-, β-, or γ-interferons, *etc.*, interleukin-I; interleukin-II; erythropoietin including α- and β-erythropoietin (EPO), granulocyte colony stimulating factor (GCSF), granulocyte macrophage colony stimulating factor (GM-CSF), anti-agiogenic proteins (*e.g.*, angiostatin, endostatin) PACAP polypeptide (pituitary adenylate cyclase activating polypeptide), vasoactive intestinal peptide (VIP), thyrotrophin releasing hormone (TRH), corticotropin releasing hormone (CRH), vasopressin, arginine vasopressin (AVP), angiotensin, calcitonin, atrial naturetic factor, somatostatin, adrenocorticotropin, gonadotropin releasing hormone, oxytocin, insulin, somatotropin, plasminogen tissue activator, coagulation factors including coagulation factors VIII and IX, glucosylceramidase, sargramostim, lenograstin, filgrastin, dornase-α, molgramostim, PEG-L-asparaginase, PEG-adenosine deaminase, hirudin, eptacog-α (human blood coagulation factor VIIa) nerve growth factors, transforming growth factor, epidermal growth factor, basic fibroblast growth factor, VEGF; heparin including low molecular weight heparin, calcitonin; antigens; monoclonal antibodies; vancomycin; desferrioxamine (DFO); parathyroid hormone, an immunogen or antigen, and an antibody such as a monoclonal antibody.

In some embodiments, the present methods allow for effective additional therapeutic agent (*e.g.* those described herein) activity and/or targeting to a cell and/or tissue of interest. For example, the present synthetic RNA can lead to increased expression of one or more targeting molecules that direct an additional therapeutic to the location of therapy. For example, the additional therapeutic agent may have a binding partner that the synthetic RNA encodes. For example, the synthetic RNA may induce the expression of an antigen that directs the therapeutic activity of an antibody that may be used in combination (*e.g.* herceptin, rituxan, campath, gemtuzumab, herceptin, panorex, rituximab, bexxar, edrecolomab, alemtuzumab, mylotrag, IMC-C225, smartin 195, and mitomomab). In some embodiments, the synthetic RNA can be injected directly into one or more of the tumors described herein and home the therapeutic antibody to the tumor.

In some embodiments, the present methods allow for effective additional therapeutic agent generation, especially when the additional therapeutic agent is a prodrug, for example, to produce an active form of the drug. In some embodiments, the synthetic RNA can be injected directly into one or more of the tumors described herein and home the prodrug to the tumor. For instance, the synthetic RNA may encode an enzyme that catalyzes the localized conversion of a non-toxic, systemically delivered agent into a potent chemotherapeutic agent. By way of illustration (note that any of the prodrugs or drugs listed herein are additional agents as used herein):

Enzyme	Prodrug	Drug
aldehyde oxidases	5-Ethynyl-2(1H)-pyrimidinone	5-Ethynyluracil
aldehyde oxidases	IPdR	IUdR
aldehyde oxidases	5-FP	5-FU
amino acid oxidases	d-alanine	Hydrogen peroxide
amino acid oxidases	SeCys conjugates	Selenols and hydrogen peroxide
cytochrome P450 reductase	Menadione	Semiquinone radical
cytochrome P450 reductase	Mitomycin C	Quinone methide intermediate
cytochrome P450 reductase	Tirapazamine	Nitroxide radical
cytochrome P450 reductase	EO9	Unidentified semiquinone radical

DT-diaphorase	Streptonigrin	Unidentified
DT-diaphorase	Mitomycin C	Quinone methide intermediate
DT-diaphorase	CB 1954	5-(Aziridin-1-yl)-4-hydroxyl-amino-2-nitrobenzamide
DT-diaphorase	Diaziquone	Semiquinone radical[a]
cytochrome P450	Ipomeanol	Unidentified (possibly furan epoxide)
cytochrome P450	Ftorafur (tegafur)	5-FU
cytochrome P450	Dacarbazine	HHMTIC
cytochrome P450	Trofosfamide	Trofosfamide mustard
cytochrome P450	Ifosfamide	Isophosphamide mustard
cytochrome P450	Cyclophosphamide	Phosphoramide mustard
cytochrome P450	AQ4N	AQ4
tyrosinase	2,4-Dihydroxyphenylalanine	6-Hydroxydopa
tyrosinase	4-S-CAP	BQ
tyrosinase	GHB	GBQ
tyrosinase	Substituted phenols	Orthoquinones
tyrosinase	Phenyl mustards	Phenol mustard
tyrosinase	Urea mustards	Unidentified
glutathione S-transferase	TER286	Aziridinium agent
glutathione S-transferase	S-CPHC-ethylsulfoxide	S-CPHC-glutathione
glutathione S-transferase	PTA	6-MP
carboxylesterase	CPT-11	SN-38
carboxylesterase	Paclitaxel-2-ethylcarbonate	Paclitaxel
carboxylesterase	Capecitabine	5'-Deoxy-5-fluorocytidine (5-FU)
carboxylesterase	Tertiary amidomethyl esters	Carboxylic acids and amines[a]
alkaline phosphatase	Amifostine	WR-1065
alkaline phosphatase	3-AP phosphate	3-AP
β-glucuronidase	BHAMG	pHAM
β-glucuronidase	Epirubicin-glucuronide	Epirubicin
β-glucuronidase	HMR 1826	Doxorubicin
β-glucuronidase	DNR-GA3	Daunorubicin
β-glucuronidase	DOX-GA3	Doxorubicin
β-glucuronidase	Paclitaxel glucuronide	Paclitaxel
β-glucuronidase	5-FU glucuronide	5-FU
cysteine conjugate β-lyase	PC	6-MP
cysteine conjugate β-lyase	GC	6-Thioguanine
cysteine conjugate β-lyase	SeCys conjugate	Selenol
Nitroreductase	CB 1954	5-(Aziridin-1-yl)-4- hydroxyl-amino-2-nitro- benzamide
Cytochrome P450	4-Ipomeanol	Unidentified (furan epoxide is speculated)
Cytochrome P450	Ifosfamide	Isophosphoramide mustard
Cytochrome P450	Cyclophosphamide	Phosphoramide mustard
Purine-nucleoside phosphorylase	Fludarabine	2-Fluoroadenine
Purine-nucleoside phosphorylase	MeP-dR	MeP
Thymidine kinase	Ganciclovir	Ganciclovir-triphosphate nucleotide
Alkaline phosphatase	Etoposide phosphate	Etoposide
Alkaline phosphatase	Mitomycin C phosphate	Mitomycin C
Alkaline phosphatase	POMP	POM
Alkaline phosphatase	N-(4-phosphonooxy)-phenylacetyl)doxorubicin	Doxorubicin

β-Glucuronidase	Glucuronidated Nornitrogen mustard	Oxazolidinone
β-Glucuronidase	Glucuronidated 9-amino-camptothecin	9-Aminocamptothecin
β-Glucuronidase	Glucuronide mustard	Mustard
Carboxypeptidase	Methotrexate-amino acids	Methotrexate
Carboxypeptidase	CMDA	Benzoic acid mustard
Penicillin amidase	DPO	Doxorubicin
Penicillin amidase	MelPO	Melphalan
Penicillin amidase	NHPAP	Palytoxin
Penicillin amidase	N-(phenylacetyl) doxorubicin	Doxorubicin
Penicillin amidase	N-(phenylacetyl) melphalan	Melphalan
β-Lactamase	LY 266070	DAVLBHYD
β-Lactamase	C-DOX	Doxorubicin
β-Lactamase	PRODOX	Doxorubicin
β-Lactamase	CM	Phenylenediamine mustard
β-Lactamase	CCM	Phenylenediamine mustard
β-Lactamase	Cephalosporin-DACCP	DACCP
β-Lactamase	PROTAX	Taxol
β-Lactamase	Cephalosporin mitomycin C	Mitomycin C
β-Lactamase	C-Mel	Melphalan
Cytosine deaminase	5-Fluorocytosine	5-Fluorouracil
Methionine γ-lyase	Selenomethionine	Methylselenol
Methionine γ-lyase	Trifluoromethionine	CSF_2

In certain embodiments, the synthetic RNA may encode an enzyme that catalyzes the conversion of 5-FU and/or Doxorubicin from various prodrugs, as illustrated by the examples below:

5-FU Prodrugs and Enzymes	
5-FP	Aldehyde oxidase
Ftorafur	P450
5'-DFUR	Thymidine phosphorylase
5-FU glucuronide	β-Glucuronidase
5-FC	Cytosine deaminase
Doxorubicin Prodrugs and Enzymes	
N-(4-phosphono- oxy)-phenylacetyl) doxorubicin	Alkaline phosphatase
HMR 1826	β-Glucuronidase
DOX-GA3	β-Glucuronidase
DPO	Penicillin amidase
N-(phenyacetyl) doxorubicin	Penicillin amidase
C-DOX	β-Lactamase
PRODOX	β-Lactamase

In some embodiments, the nucleic acid drugs at the doses and regimens described herein may be used in combination with one or more additional agents (aka adjuvant therapy or combination agent). In some embodiments, the nucleic acid drugs at the doses and regimens described herein may be used in a human patient undergoing treatment with one or more additional agents. In some embodiments, the nucleic acid drug is used as an adjuvant or neoadjuvant to any of the additional agents described herein. In some embodiments, the invention pertains to co-administration and/or co-formulation. Any of the compositions described herein may be

co-formulated and/or co-administered. In some embodiments, any nucleic acid drug described herein acts synergistically when co-administered with another agent and may be administered at doses that are lower than the doses commonly employed when such agents are used as monotherapy.

In some embodiments, any nucleic acid drug described herein may include derivatives that are modified, *i.e.*, by the covalent attachment of any type of molecule to the composition such that covalent attachment does not prevent the activity of the composition. For example, but not by way of limitation, derivatives include composition that have been modified by, *inter alia*, glycosylation, lipidation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, *etc.* Any of numerous chemical modifications can be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of turicamycin, *etc.* Additionally, the derivative can contain one or more non-classical amino acids. In various embodiments, one or more additional agents (aka adjuvant therapy or combination agent) may be conjugated to any nucleic acid drug described herein.

Contacting a cell with a steroid can suppress the innate immune response to foreign nucleic acids, and can increase the efficiency of nucleic acid delivery and translation. Certain embodiments are therefore directed to contacting a cell with a steroid. Other embodiments are directed to administering a steroid to a patient. Illustrative steroids include corticosteroid steriods. In some embodiments, the steroid is one or more of cortisone, hydrocortisone, prednisone, prednisolone, dexamethasone, triamcinolone, and betamethasone. In one embodiment, the steroid is hydrocortisone. In another embodiment, the steroid is dexamethasone.

Other embodiments are directed to administering to a patient a member of the group: an antibiotic, an antimycotic, and an RNAse inhibitor.

Botulinum toxin type A has been approved by the US Food and Drug Administration (FDA) for the treatment of essential blepharospasm, strabismus and hemifacial spasm in patients over the age of twelve, cervical dystonia, glabellar line (facial) wrinkles and for treating hyperhydrosis and botulinum toxin type B has been approved for the treatment of cervical dystonia. The present compositions may be combined with these toxins in the treatment of these diseases and related diseases. Some embodiments are directed to a nucleic acid drug targeting a neurotoxin. In various embodiments, the neurotoxin is a botulinum toxin or a biologically active fragment, variant, analogue or family-member thereof.

Further the combination of any one of the aforementioned toxins may be used in combination with the present compositions for various cosmetic procedures, including, without limitation, facial wrinkles, hyperkinetic skin lines, glabellar lines, crow's feet, marionette lines, skin disorders, nasolabial folds, blepharospasm, strabismus, hemifacial spasms and sweating disorders. Alternatively, the present compositions may be used to in these cosmetic procedures as a monotherapy.

Certain embodiments are directed to a combination therapy comprising one or more of the therapeutic or cosmetic compositions of the present invention and one or more adjuvant therapies or cosmetic treatments. In

certain embodiments, one or more of the therapeutic or cosmetic compositions of the present invention are administered to a subject which is undergoing treatment with one or more adjuvant therapies or cosmetic treatments. Example adjuvant therapies and cosmetic treatments are set forth in Table 3 and Table 5 of US Provisional Application No. 61/721,302, the contents of which are hereby incorporated by reference, and are given by way of example, and not by way of limitation.

Table 3. *Illustrative Adjuvant Therapies*

Therapy/Treatment Class	Disease/Condition	Example Therapy/Treatment
Acetylcholinesterase inhibitors	Myasthenia gravis, Glaucoma, Alzheimer's disease, Lewy body dementia, Postural tachycardia syndrome	Edrophonium
Angiotensin-converting-enzyme inhibitor	Hypertension, Congestive heart failure	Perindopril
Alkylating agents	Cancer	Cisplatin
Angiogenesis inhibitors	Cancer, Macular degeneration	Bevacizumab
Angiotensin II receptor antagonists	Hypertension, Diabetic nephropathy, Congestive heart failure	Valsartan
Antibiotics	Bacterial infection	Amoxicillin
Antidiabetic drugs	Diabetes	Metformin
Antimetabolites	Cancer, Infection	5-fluorouracil (5FU)
Antisense oligonucleotides	Cancer, Diabetes, Amyotrophic lateral sclerosis (ALS), Hypercholesterolemia	Mipomersen
Cytotoxic antibiotics	Cancer	Doxorubicin
Deep-brain stimulation	Chronic pain, Parkinson's disease, Tremor, Dystonia	N/A
Dopamine agonists	Parkinson’s disease, Type II diabetes, Pituitary tumors	Bromocriptine
Entry/Fusion inhibitors	HIV/AIDS	Maraviroc
Glucagon-like peptide-1 agonists	Diabetes	Exenatide
Glucocorticoids	Asthma, Adrenal insufficiency, Inflammatory diseases, Immune diseases, Bacterial meningitis	Dexamethasone
Immunosuppressive drugs	Organ transplantation, Inflammatory diseases, Immune diseases	Azathioprine
Insulin/Insulin analogs	Diabetes	NPH insulin
Integrase inhibitors	HIV/AIDS	Raltegravir
MAO-B inhibitors	Parkinson's disease, Depression, Dementia	Selegiline
Maturation inhibitors	HIV/AIDS	Bevirimat
Nucleoside analog reverse-transcriptase inhibitors	HIV/AIDS, Hepatitis B	Lamivudine
Nucleotide analog reverse-transcriptase inhibitors	HIV/AIDS, Hepatitis B	Tenofovir
Non-nucleoside reverse-transcriptase inhibitors	HIV/AIDS	Rilpivirine
Pegylated interferon	Hepatitis B/C, Multiple sclerosis	Interferon beta-1a
Plant alkaloids/terpenoids	Cancer	Paclitaxel

Protease inhibitors	HIV/AIDS, Hepatitis C, Other viral infections	Telaprevir
Radiotherapy	Cancer	Brachytherapy
Renin inhibitors	Hypertension	Aliskiren
Statins	Hypercholesterolemia	Atorvastatin
Topoisomerase inhibitors	Cancer	Topotecan
Vasopressin receptor antagonist	Hyponatremia, Kidney disease	Tolvaptan
Dermal filler	Wrinkles, aged skin	Hyaluronic Acid
Botulinum toxin	Wrinkles, aged skin	botulinum toxin type A
Induction of skin repair	Acne scars, aged skin	Laser treatment, dermabrasion

In some embodiments, the additional agent is a cytotoxic agent, comprising, in illustrative embodiments, a toxin, a chemotherapeutic agent, a radioisotope, and an agent that causes apoptosis or cell death.

Illustrative cytotoxic agents include, but are not limited to, methotrexate, aminopterin, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine; alkylating agents such as mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU), mitomycin C, lomustine (CCNU), 1-methylnitrosourea, cyclothosphamide, mechlorethamine, busulfan, dibromomannitol, streptozotocin, mitomycin C, cis-dichlorodiamine platinum (II) (DDP) cisplatin and carboplatin (paraplatin); anthracyclines include daunorubicin (formerly daunomycin), doxorubicin (adriamycin), detorubicin, carminomycin, idarubicin, epirubicin, mitoxantrone and bisantrene; antibiotics include dactinomycin (actinomycin D), bleomycin, calicheamicin, mithramycin, and anthramycin (AMC); and antimytotic agents such as the vinca alkaloids, vincristine and vinblastine. Other cytotoxic agents include paclitaxel (taxol), ricin, pseudomonas exotoxin, gemcitabine, cytochalasin B, gramicidin D, ethidium bromide, emetine, etoposide, tenoposide, colchicin, dihydroxy anthracin dione, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, puromycin, procarbazine, hydroxyurea, asparaginase, corticosteroids, mytotane (O,P'-(DDD)), interferons, and mixtures of these cytotoxic agents.

Further cytotoxic agents include, but are not limited to, chemotherapeutic agents such as carboplatin, cisplatin, paclitaxel, gemcitabine, calicheamicin, doxorubicin, 5-fluorouracil, mitomycin C, actinomycin D, cyclophosphamide, vincristine, bleomycin, VEGF antagonists, EGFR antagonists, platins, taxols, irinotecan, 5-fluorouracil, gemcytabine, leucovorine, steroids, cyclophosphamide, melphalan, vinca alkaloids (*e.g.*, vinblastine, vincristine, vindesine and vinorelbine), mustines, tyrosine kinase inhibitors, radiotherapy, sex hormone antagonists, selective androgen receptor modulators, selective estrogen receptor modulators, PDGF antagonists, TNF antagonists, IL-1 antagonists, interleukins (*e.g.* IL-12 or IL-2), IL-12R antagonists, Toxin conjugated monoclonal antibodies, tumor antigen specific monoclonal antibodies, Erbitux, Avastin, Pertuzumab, anti-CD20 antibodies, Rituxan, ocrelizumab, ofatumumab, DXL625, HERCEPTIN, or any combination thereof. Toxic enzymes from plants and bacteria such as ricin, diphtheria toxin and Pseudomonas toxin may be conjugated to the therapeutic agents (*e.g.* antibodies) to generate cell-type-specific-killing reagents (Youle, *et al.*, Proc. Nat'l

Acad. Sci. USA 77:5483 (1980); Gilliland, *et al.*, Proc. Nat'l Acad. Sci. USA 77:4539 (1980); Krolick, *et al.*, Proc. Nat'l Acad. Sci. USA 77:5419 (1980)).

Other cytotoxic agents include cytotoxic ribonucleases as described by Goldenberg in US Pat. No. 6,653,104. Embodiments of the invention also relate to radioimmunoconjugates where a radionuclide that emits alpha or beta particles is stably coupled to the antibody, or binding fragments thereof, with or without the use of a complex-forming agent. Such radionuclides include beta-emitters such as Phosphorus-32, Scandium-47, Copper-67, Gallium-67, Yttrium-88, Yttrium-90, Iodine-125, Iodine-131, Samarium-153, Lutetium-177, Rhenium-186 or Rhenium-188, and alpha-emitters such as Astatine-211, Lead-212, Bismuth-212, Bismuth-213 or Actinium-225.

Illustrative detectable moieties further include, but are not limited to, horseradish peroxidase, acetylcholinesterase, alkaline phosphatase, beta-galactosidase and luciferase. Further exemplary fluorescent materials include, but are not limited to, rhodamine, fluorescein, fluorescein isothiocyanate, umbelliferone, dichlorotriazinylamine, phycoerythrin and dansyl chloride. Further exemplary chemiluminescent moieties include, but are not limited to, luminol. Further exemplary bioluminescent materials include, but are not limited to, luciferin and aequorin. Further exemplary radioactive materials include, but are not limited to, Iodine-125, Carbon-14, Sulfur-35, Tritium and Phosphorus-32.

The dosage of any additional agent described herein as well as the dosing schedule can depend on various parameters, including, but not limited to, the human patient's general health, and the administering physician's and/or human patient's discretion. Co-administration may be simultaneous or sequential. Any additional agent described herein, can be administered prior to (*e.g.*, about 5 minutes, about 15 minutes, about 30 minutes, about 45 minutes, about 1 hour, about 2 hours, about 4 hours, about 6 hours, about 12 hours, about 24 hours, about 48 hours, about 72 hours, about 96 hours, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 5 weeks, about 6 weeks, 8 weeks, or about 12 weeks before), concurrently with, or subsequent to (*e.g.,* about 5 minutes, about 15 minutes, about 30 minutes, about 45 minutes, about 1 hour, about 2 hours, about 4 hours, about 6 hours, about 12 hours, about 24 hours, about 48 hours, about 72 hours, about 96 hours, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 5 weeks, about 6 weeks, about 8 weeks, or about 12 weeks after) the administration of the nucleic acid drug to a human patient in need thereof. In various embodiments any agent described herein is administered about 1 minute apart, about 10 minutes apart, about 30 minutes apart, less than about 1 hour apart, about 1 hour apart, about 1 hour to about 2 hours apart, about 2 hours to about 3 hours apart, about 3 hours to about 4 hours apart, about 4 hours to about 5 hours apart, about 5 hours to about 6 hours apart, about 6 hours to about 7 hours apart, about 7 hours to about 8 hours apart, about 8 hours to about 9 hours apart, about 9 hours to about 10 hours apart, about 10 hours to about 11 hours apart, about 11 hours to about 12 hours apart, no more than about 24 hours apart or no more than about 48 hours apart.

In a specific embodiment, the combination regimen is designed to exploit the finding that the nucleic acid drug dosing and formulation of the present invention has potent effects quickly (*e.g.* in about 6, or about 12, or about 24, or about 30, or about 36, or about 48 hours) and the effects can last about 7 days, or longer.

The dose of a nucleic acid drug is disclosed herein. In general, the dose of any additional agent that is useful is known to those in the art. For example, doses may be determined with reference *Physicians' Desk Reference*, 66th Edition, PDR Network; 2012 Edition (December 27, 2011), the contents of which are incorporated by reference in its entirety. In some embodiments, the present invention allows a patient to receive doses that exceed those determined with reference *Physicians' Desk Reference*. The dosage of any additional agent described herein can depend on several factors including the severity of the condition, whether the condition is to be treated or prevented, and the age, weight, and health of the human patient to be treated. Additionally, pharmacogenomic (the effect of genotype on the pharmacokinetic, pharmacodynamic or efficacy profile of a therapeutic) information about a particular human patient may affect dosage used. Furthermore, the exact individual dosages can be adjusted somewhat depending on a variety of factors, including the specific combination of the agents being administered, the time of administration, the route of administration, the nature of the formulation, the rate of excretion, the particular disease being treated, the severity of the disorder, and the anatomical location of the disorder. Some variations in the dosage can be expected.

Cells, tissues, organs, and organisms, including, but not limited to, humans, have several characteristics that can inhibit or prevent the delivery of nucleic acids, including, for example, the stratum corneum, which can serve as a barrier to foreign organisms and nucleic acids. These characteristics can thus inhibit the effects of therapeutics and cosmetics comprising nucleic acids. It has now been discovered that many of these characteristics can be circumvented or overcome using a patch comprising a flexible membrane and a plurality of needles, and that such a patch can serve as an effective and safe article for the delivery of nucleic acids. Certain embodiments are therefore directed to a nucleic acid delivery patch. In one embodiment, the nucleic acid delivery patch comprises a flexible membrane. In another embodiment, the nucleic acid delivery patch comprises a plurality of needles. In yet another embodiment, the plurality of needles are attached to the flexible membrane. In some embodiments, the patch comprises a nucleic acid. In one embodiment, the nucleic acid is present in solution. In one embodiment, the plurality of needles include one or more needles having a lumen. In another embodiment, the patch further comprises a second flexible membrane. In yet another embodiment, the flexible membrane and the second flexible membrane are arranged to form a cavity. In a further embodiment, the cavity contains a nucleic acid. In a still further embodiment, the membrane comprises one or more holes through which a nucleic acid can pass. In a still further embodiment, one or more holes and one or more needles having a lumen are arranged to allow the passage of a solution containing a nucleic acid through at least one of the one or more holes and through at least one of the one or more needles having a lumen. In some embodiments, the patch is configured to deliver a solution to the skin. In one embodiment, the solution comprises a nucleic acid. In another embodiment, the solution comprises a vehicle. In yet another embodiment, the vehicle is a lipid or lipidoid. In a still further embodiment, the vehicle is a lipid-based transfection reagent.

The cell membrane can serve as a barrier to foreign nucleic acids. It has now been discovered that combining the patch of the present invention with an electric field can increase the efficiency of nucleic acid delivery. Certain embodiments are therefore directed to a nucleic acid delivery patch comprising a plurality of needles, wherein at least two needles form part of a high-voltage circuit. Certain embodiments are directed to an implantable "tattoo" for microneedle delivery (*see, e.g. Nature Materials* 12, pp 367–376 (2013), the contents of which are hereby incorporated by reference in their entirety). In one embodiment, the high-voltage circuit generates a voltage greater than about 10V. In another embodiment, the high-voltage circuit generates a voltage greater than about 20V. In yet another embodiment, an electric field is produced between two of the needles. In a further embodiment, the magnitude of the electric field is at least about 100V/cm. In a still further embodiment, the magnitude of the electric field is at least about 200V/cm. In some embodiments, the patch is configured to deliver a nucleic acid to the epidermis. In other embodiments, the patch is configured to deliver a nucleic acid to the dermis. In still other embodiments, the patch is configured to deliver a nucleic acid to sub-dermal tissue. In still other embodiments, the patch is configured to deliver a nucleic acid to muscle. Certain embodiments are directed to a nucleic acid delivery patch comprising a plurality of electrodes. In one embodiment, the plurality of electrodes is attached to a flexible membrane. Other embodiments are directed to a nucleic acid delivery patch comprising a rigid structure. In one embodiment, a plurality of electrodes are attached to the rigid structure.

In some embodiments, the compositions described herein are administered using an array of needles covering an affected area of the subject. In some embodiments, the treatment area is mechanically massaged after administration. In some embodiments, the treatment area is exposed to electric pulses after administration. In some embodiments, the electric pulses are between about 10V and about 200V for from about 50 microseconds to about 1 second. In some embodiments, the electric pulses are generated around the treatment area by a multielectrode array.

In some embodiments, the present invention provides a patch delivery system, comprising a non-viral RNA transfection composition enclosed within a membrane, and an array of delivery needles delivering from about 10 ng to about 2000 ng of RNA per treatment area of about 100 cm^2 or less, or about 50 cm^2 or less, or about 10 cm^2 or less, or about 5 cm^2 or less, or about 1 cm^2 or less, or about 0.5 cm^2 or less, or about 0.2 cm^2 or less. In some embodiments, the non-viral transfection composition contains from about 10 ng to about 2000 ng per injection volume of about 20 µL to about 1 ml. In some embodiments, each needle delivers an injection volume of between 1 µL and 500 µL.

In some embodiments, the delivery patch comprises an acrylic reservoir that holds the nucleic acid drug. In some embodiments, a silicon adhesive is added to create a semisolid suspension of microscopic, concentrated drug cells. Further, some embodiments pride a patch that is associated with one or more enhancers (these include, without limitation, iontophoresis, ultrasound, chemicals including gels, microneedles, sonophoresis, lasers, and electroporatic methods).

In some embodiments, the delivery is effected via a gel, optionally a hydro alcoholic gel containing a combination of enhancers (*e.g.* COMBIGEL (ANTARES PHARMA)).

In various embodiments, the RNA is delivered using needle arrays. Illustrative needle arrays include, but are not limited to AdminPen 600 and those described in U.S. Patent Nos. 7,658,728, 7,785,301, and 8,414,548, the entire disclosure of which are hereby incorporated by reference. Other examples of needles include, for example, the 3M™ Hollow Microstructured Transdermal System and the 3M Solid Microstructured Transdermal Systems (sMTS). *See, e.g.* US Patent Nos. 3,034,507 and 3,675,766; Microneedles for Transdermal Drug Delivery. Advanced Drug Delivery Reviews. 56: 581-587 (2004); Pharm Res. 2011 Jan; 28(1): 31–40, the entire contents of which are hereby incorporated by reference in their entireties.

In some embodiments, microneedles and/or microneedle arrays may be used. In various embodiments, the microneedles and/or microneedle arrays may be, without limitation, solid, RNA-coated, dissolving, biodegradable, and/or hollow. In some embodiments, the delivery is effected via a microneedle system, optionally combined with an electronically controlled micropump that delivers the drug at specific times or upon demand. For example, the MACROFLUX (Alza) system may be used.

Other embodiments are directed to a method for delivering a nucleic acid to a cell *in vivo* comprising applying a nucleic acid to a tissue containing a cell *in vivo*. In one embodiment, the method further comprises applying a transient electric field in the vicinity of the cell. In another embodiment, the method results in the cell *in vivo* internalizing the nucleic acid. In yet another embodiment, the nucleic acid comprises synthetic RNA. In a further embodiment, the method further results in the cell internalizing a therapeutically or cosmetically effective amount of the nucleic acid. In one embodiment, the cell is a skin cell. In another embodiment, the cell is a muscle cell. In yet another embodiment, the cell is a dermal fibroblast. In a further embodiment, the cell is a keratinocyte. In a still further embodiment, the cell is a myoblast. In some embodiments, the nucleic acid comprises a protein of interest. In one embodiment, the protein of interest is a fluorescent protein. In another embodiment, the protein of interest is an extracellular-matrix protein. In yet another embodiment, the protein of interest is a member of the group: elastin, collagen, laminin, fibronectin, vitronectin, lysyl oxidase, elastin binding protein, a growth factor, fibroblast growth factor, transforming growth factor beta, granulocyte colony-stimulating factor, a matrix metalloproteinase, an actin, fibrillin, microfibril-associated glycoprotein, a lysyl-oxidase-like protein, platelet-derived growth factor, a lipase, an uncoupling protein, thermogenin, filaggrin, a fibroblast growth factor, an antibody, and a protein involved with pigment production. In some embodiments, the method further comprises delivering the nucleic acid to the epidermis. In other embodiments, the method further comprises delivering the nucleic acid to the dermis. In still other embodiments, the method further comprises delivering the nucleic acid below the dermis. In one embodiment, the delivering is by injection. In another embodiment, the delivering is by injection using a micro-needle array. In yet another embodiment, the delivering is by topical administration. In a further embodiment, the delivering comprises disruption or removal of a part of the tissue. In a still further embodiment, the delivering comprises disruption or removal of the stratum corneum. In some embodiments, the

nucleic acid is present in solution. In one embodiment, the solution comprises a growth factor. In another embodiment, the growth factor is a member of the group: a fibroblast growth factor and a transforming growth factor. In yet another embodiment, the growth factor is a member of the group: basis fibroblast growth factor and transforming growth factor beta. In other embodiments, the solution comprises cholesterol.

In another embodiment, the method further comprises contacting the cell with one or more nucleic acid molecules. In yet another embodiment, at least one of the one or more nucleic acid molecules encodes a protein of interest. In a further embodiment, the method results in the cell expressing the protein of interest. In a still further embodiment, the method results in the cell expressing a therapeutically or cosmetically effective amount of the protein of interest.

In another embodiment, the cell is contacted with a nucleic acid molecule. In yet another embodiment, the method results in the cell internalizing the nucleic acid molecule. In a further embodiment, the method results in the cell internalizing a therapeutically or cosmetically effective amount of the nucleic acid molecule. In one embodiment, the nucleic acid encodes a protein of interest. In one embodiment, the nucleic acid molecule comprises a member of the group: a dsDNA molecule, a ssDNA molecule, a RNA molecule, a dsRNA molecule, a ssRNA molecule, a plasmid, an oligonucleotide, a synthetic RNA molecule, a miRNA molecule, an mRNA molecule, and an siRNA molecule. In various embodiments, the RNA comprises one or more non-canonical nucleotides.

In some embodiments, the present invention relates to one or more administration techniques described in US Patent Nos. 5,711,964; 5,891,468; 6,316,260; 6,413,544; 6,770,291; and 7,390,780, the entire contents of which are hereby incorporated by reference in their entireties.

The invention also provides kits that can simplify the administration of the nucleic acid drugs described herein and/or any additional agent described herein. An illustrative kit of the invention comprises a nucleic acid drug and/or any additional agent described herein in unit dosage form. In one embodiment, the unit dosage form is a container, such as a pre-filled syringe, which can be sterile, containing any agent described herein and a pharmaceutically acceptable carrier, diluent, excipient, or vehicle. The kit can further comprise a label or printed instructions instructing the use of any agent described herein. The kit or one or more components of the kit may be stored at room temperature, about 4°C, about -20°C, about -80°C, or about -196°C. The kit may also include a lid speculum, topical anesthetic, and a cleaning agent for the administration location. The kit can also further comprise one or more additional agent described herein. In one embodiment, the kit comprises a container containing an effective amount of a nucleic acid drug as disclosed herein and an effective amount of another composition, such as an additional agent as described herein. In some embodiments, the unit dosage form is a pre-loaded (a.k.a. pre-dosed or pre-filled) syringe or a pen needle injector (injection pen)). Such unit dosage forms may comprise the effective doses of nucleic acid drug described herein, *e.g.* about 10 ng to about 2000 ng, *e.g.* about 10 ng, or about 20 ng, or about 50 ng, or about 100 ng, or about 200 ng, or about 300 ng, or about 400 ng, or about 500 ng, or about 600 ng, or about 700 ng, or about 800 ng, or about 900 ng, or about 1000 ng,

or about 1100 ng, or about 1200 ng, or about 1300 ng, or about 1400 ng, or about 1500 ng, or about 1600 ng, or about 1700 ng, or about 1800 ng, or about 1900 ng, or about 2000 ng, or about 3000 ng, or about 4000 ng, or about 5000 ng.

Some embodiments are directed to synthetic RNA molecules with low toxicity and high translation efficiency. Other embodiments are directed to a cell-culture medium for high-efficiency *in vivo* transfection, reprogramming, and gene editing of cells. Other embodiments pertain to methods for producing synthetic RNA molecules encoding reprogramming proteins. Still further embodiments pertain to methods for producing synthetic RNA molecules encoding gene-editing proteins.

Some embodiments are directed to methods of gene-editing and/or gene correction. Some embodiments encompass synthetic RNA-based gene-editing and/or gene correction, *e.g.* with RNA comprising non-canonical nucleotides, *e.g.* RNA encoding one or more of a nuclease, a transcription activator-like effector nuclease (TALEN), a zinc-finger nuclease, a meganuclease, a nickase, a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein a DNA-repair protein, a DNA-modification protein, a base-modification protein, a DNA methyltransferase, an protein that causes DNA demethylation, an enzyme for which DNA is a substrate or a natural or engineered variant, family-member, orthologue, fragment or fusion construct thereof. In some embodiments, the efficiency of the gene-editing and/or gene correction is high, for example, higher than DNA-based gene editing and/or gene correction. In some embodiments, the present methods of gene-editing and/or gene correction are efficient enough for in vivo application. In some embodiments, the present methods of gene-editing and/or gene correction are efficient enough to not require cellular selection (*e.g.* selection of cells that have been edited). In various embodiments, the efficiency of gene-editing of the present methods is about 1%, or about 2%, or about 3%, or about 4%, or about 5%, or about 6%, or about 7%, or about 8%, or about 9%, or about 10%, or about 20%, or about 30%, or about 40%, or about 50%, or about 60%, or about 70%, or about 80%, or about 90%, or about 100%. In various embodiments, the efficiency of gene-correction of the present methods is about 1%, or about 2%, or about 3%, or about 4%, or about 5%, or about 6%, or about 7%, or about 8%, or about 9%, or about 10%, or about 20%, or about 30%, or about 40%, or about 50%, or about 60%, or about 70%, or about 80%, or about 90%, or about 100%

Some embodiments are directed to high-efficiency gene-editing proteins comprising engineered nuclease cleavage or DNA-modification domains. Other embodiments are directed to high-fidelity gene-editing proteins comprising engineered nuclease cleavage or DNA-modification domains. Various embodiments are directed to high-efficiency gene-editing proteins comprising engineered DNA-binding domains. Other embodiments are directed to high-fidelity gene-editing proteins comprising engineered DNA-binding domains. Still other embodiments are directed to gene-editing proteins comprising engineered repeat sequences. Some embodiments are directed to gene-editing proteins comprising one or more CRISPR associated family members. Some embodiments are directed to methods for altering the DNA sequence of a cell by transfecting the cell with or inducing the cell to express a gene-editing protein. Other embodiments are directed to methods for altering the

DNA sequence of a cell that is present in an *in vitro* culture. Still further embodiments are directed to methods for altering the DNA sequence of a cell that is present *in vivo*.

Some embodiments are directed to methods of modulating the secretion or subcellular localization of a polypeptide. In such embodiments, the present invention provides an RNA encoding a protein comprising a signal peptide operably linked to a polypeptide having biological functionality. In an embodiment, the signal peptide modulates the secretion of the polypeptide. In another embodiment, the signal peptide modulates the subcellular localization of the polypeptide. For example, BMP7 comprising at least one FGF21 signal peptide may result in increased secretion of BMP7. In another example, BMP7 comprising at least one FGF21 signal peptide in place of the endogenous BMP7 signal peptide may result in increased secretion of BMP7. In various embodiments, any of the proteins listed in **Table 2A** or **Table 2B** comprising at least one signal peptide listed in the table below may result in increased secretion of the proteins.

Protein	Signal Peptide	SEQ ID NO
Gaussia luciferase	MGVKVLFALICIAVAEA	596
Human BMP7	MHVRSLRAAAPHSFVALWAPLFLLRSALA	597
Human chymotrypsinogen B	MAFLWLLSCWALLGTTFG	598
Human chymotrypsinogen C	MLGITVLAALLACASS	599
Human EPO	MGVHECPAWLWLLLSLLSLPLGLPVLG	600
Human FGF19	MRSGCVVVHVWILAGLWLAVAGRP	601
Human FGF21	MDSDETGFEHSGLWVSVLAGLLLGACQA	602
Human FGF23	MLGARLRLWVCALCSVCSMSVLRA	603
Human IL2	MYRMQLLSCIALSLALVTNS	604
Human IL22	MAALQKSVSSFLMGTLATSCLLLLALLVQGGAA	605
Human IL6	MNSFSTSAFGPVAFSLGLLLVLPAAFPAP	606
Human Interferon Alpha-2	MALTFALLVALLVLSCKSSCSVG	607
Human Interferon Beta	MTNKCLLQIALLLCFSTTALS	608
Human Interferon Gamma	MKYTSYILAFQLCIVLGSLGCYC	609
Human Trypsin-1	MNPLLILTFVAAALA	610

Some embodiments are directed to methods of modulating the serum half-life, secretion, bioavailability, and/or activity of a protein comprising administering a RNA encoding the protein and a RNA encoding a receptor for the protein. For example, IL15 may be administered with its receptor, *e.g.*, IL15RA to enhance one or more of the serum half-life, secretion, bioavailability, and activity of IL15.

Many proteins and peptides, when translated from in vitro transcribed RNA, can exhibit reduced activity resulting from incomplete or inadequate post-translational processing. It has now been discovered that the amount of active protein, polypeptide or peptide produced following RNA transfection can be increased by contacting cells with and/or inducing cells to express a second protein that is capable of processing a polypeptide into the protein, peptide or polypeptide. Certain embodiments are therefore directed to a method for inducing a cell to

express an active protein, polypeptide or peptide comprising contacting the cell with a synthetic RNA molecule encoding a first polypeptide and contacting the cell with a second protein that is capable of processing the first polypeptide into an active protein, polypeptide or peptide.

In certain embodiments, the second protein is administered to a patient. In one embodiment, the second protein is a recombinant protein. In another embodiment, the cells are contacted with a synthetic RNA molecule encoding the second protein. In a further embodiment, the cells are contacted with and/or induced to express an inhibitor of a molecule that inhibits the second protein. In one embodiment, the inhibitor is a short interfering RNA molecule.

In certain embodiments, the second protein is a member of the PCSK family. In other embodiments, the second protein is a proprotein convertase. In still other embodiments, the second protein is a prohormone convertase. In still other embodiments, the second protein is a carboxypeptidase. In one embodiment, the second protein is PCSK3 (Furin/PACE). In another embodiment, the second protein is primarily secreted. In yet another embodiment, the second protein is primarily intracellular. In a further embodiment, the first polypeptide, protein, polypeptide or peptide is selected from the group: a product of proopiomelanocortin, renin, a product of enkephalin, a product of prodynorphin, somatostatin, insulin, agouti-related peptide, glucagon, parathyroid hormone, a member of the transforming growth factor beta superfamily, albumin, beta-secretase 1, nerve growth factor, caldesmon, the alpha-integrins, factor IX, α-melanocyte-stimulating hormone, adrenocorticotropic hormone, β-endorphin, and met-enkefalin.

Glycation and glycosylation are processes by which one or more sugar molecules are bound to a protein. It has now been discovered that altering the number or location of glycation and glycosylation sites can increase or decrease the stability of a protein. Certain embodiments are therefore directed to a protein with one or more glycation or glycosylation sites. In one embodiment, the protein is engineered to have more glycation or glycosylation sites than a natural variant of the protein. In another embodiment, the protein is engineered to have fewer glycation or glycosylation sites than a natural variant of the protein. In yet another embodiment, the protein has increased stability. In yet another embodiment, the protein has decreased stability. In some embodiments, the protein is a circulating protein. In one embodiment, the protein is erythropoietin or a biologically active fragment, variant, analogue, or family-member thereof. In another embodiment, the protein is darbepoetin alfa or a biologically active fragment, variant, analogue, or family-member thereof. In another embodiment, the protein is NOVEPOETIN or a biologically active fragment, variant, analogue, or family-member thereof.

It has been further discovered that in certain situations, including one or more steroids and/or one or more antioxidants in the transfection medium can increase *in vivo* transfection efficiency, *in vivo* reprogramming efficiency, and *in vivo* gene-editing efficiency. Certain embodiments are therefore directed to contacting a cell or patient with a glucocorticoid, such as hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone or betamethasone. Other embodiments are directed to a method for inducing a cell to express a protein of interest by contacting a cell with a medium containing a steroid and contacting the cell with one or

more nucleic acid molecules. In one embodiment, the nucleic acid molecule comprises synthetic RNA. In another embodiment, the steroid is hydrocortisone. In yet another embodiment, the hydrocortisone is present in the medium at a concentration of between about 0.1uM and about 10uM, or about 1uM. Other embodiments are directed to a method for inducing a cell *in vivo* to express a protein of interest by contacting the cell with a medium containing an antioxidant and contacting the cell with one or more nucleic acid molecules. In one embodiment, the antioxidant is ascorbic acid or ascorbic-acid-2-phosphate. In another embodiment, the ascorbic acid or ascorbic-acid-2-phosphate is present in the medium at a concentration of between about 0.5mg/L and about 500mg/L, including about 50mg/L. Still other embodiments are directed to a method for reprogramming and/or gene-editing a cell *in vivo* by contacting the cell with a medium containing a steroid and/or an antioxidant and contacting the cell with one or more nucleic acid molecules, wherein the one or more nucleic acid molecules encodes one or more reprogramming and/or gene-editing proteins. In certain embodiments, the cell is present in an organism, and the steroid and/or antioxidant are delivered to the organism.

Adding transferrin to the complexation medium has been reported to increase the efficiency of plasmid transfection in certain situations. It has now been discovered that adding transferrin to the complexation medium can also increase the efficiency of *in vivo* transfection with synthetic RNA molecules. Certain embodiments are therefore directed to a method for inducing a cell *in vivo* to express a protein of interest by adding one or more synthetic RNA molecules and a transfection reagent to a solution containing transferrin. In one embodiment, the transferrin is present in the solution at a concentration of between about 1mg/L and about 100mg/L, such as about 5mg/L. In another embodiment, the transferrin is recombinant.

In certain situations, including pertaining to culturing, it may be desirable to replace animal-derived components with non-animal-derived and/or recombinant components, in part because non-animal-derived and/or recombinant components can be produced with a higher degree of consistency than animal-derived components, and in part because non-animal-derived and/or recombinant components carry less risk of contamination with toxic and/or pathogenic substances than do animal-derived components. Certain embodiments are therefore directed to a protein that is non-animal-derived and/or recombinant. Other embodiments are directed to a medium, wherein some or all of the components of the medium are non-animal-derived and/or recombinant.

Other embodiments are directed to a method for transfecting a cell *in vivo*. In one embodiment, a cell *in vivo* is transfected with one or more nucleic acids, and the transfection is performed using a transfection reagent, such as a lipid-based transfection reagent. In one embodiment, the one or more nucleic acids includes at least one RNA molecule. In another embodiment, the cell is transfected with one or more nucleic acids, and the one or more nucleic acids encodes at least one of: p53, TERT, an antibody, an extracellular matrix protein, a cytokine, a secreted protein, a membrane-bound protein, an enzyme, a gene-editing protein, a chromatin-modifying protein, a DNA-binding protein, a transcription factor, a histone deacetylase, a pathogen-associated molecular pattern, and a tumor-associated antigen or a biologically active fragment, analogue, variant or family-member thereof. In another embodiment, the cell is transfected repeatedly, such as at least about 2 times during about 10 consecutive days, or at least about 3 times during about 7 consecutive days, or at least about 4 times during

about 6 consecutive days. Some embodiments are directed to a method for increasing expression of telomerase in one of a fibroblast, a hematopoietic stem cell, a mesenchymal stem cells, a cardiac stem cell, a hair follicle stem cell, a neural stem cell, an intestinal stem cell, an endothelial stem cell, an olfactory stem cell, a neural crest stem cell, a testicular cell, and a keratinocyte. Some embodiments are directed to a method for increasing the length of telomeres in one of a fibroblast, a hematopoietic stem cell, a mesenchymal stem cells, a cardiac stem cell, a hair follicle stem cell, a neural stem cell, an intestinal stem cell, an endothelial stem cell, an olfactory stem cell, a neural crest stem cell, a testicular cell, and a keratinocyte. Other embodiments are directed to a method for isolating a cell from a patient, contacting the cell with a nucleic acid drug encoding a component of telomerase (*e.g.*, TERT), and reintroducing the cell to the patient. Various embodiments are directed to a method for increasing the replicative potential of a cell.

Reprogramming can be performed by transfecting cells with one or more nucleic acids encoding one or more reprogramming factors. Examples of reprogramming factors include, but are not limited to: Oct4 protein, Sox2 protein, Klf4 protein, c-Myc protein, l-Myc protein, TERT protein, Nanog protein, Lin28 protein, Utf1 protein, Aicda protein, miR200 micro-RNA, miR302 micro-RNA, miR367 micro-RNA, miR369 micro-RNA and biologically active fragments, analogues, variants and family-members thereof. Certain embodiments are therefore directed to a method for reprogramming a cell *in vivo*. In one embodiment, the cell *in vivo* is reprogrammed by transfecting the cell with one or more nucleic acids encoding one or more reprogramming factors. In one embodiment, the one or more nucleic acids includes an RNA molecule that encodes Oct4 protein. In another embodiment, the one or more nucleic acids also includes one or more RNA molecules that encodes Sox2 protein, Klf4 protein, and c-Myc protein. In yet another embodiment, the one or more nucleic acids also includes an RNA molecule that encodes Lin28 protein. In one embodiment, the cell is a human skin cell, and the human skin cell is reprogrammed to a pluripotent stem cell. In another embodiment, the cell is a human skin cell, and the human skin cell is reprogrammed to a glucose-responsive insulin-producing cell. Examples of other cells that can be reprogrammed and other cells to which a cell can be reprogrammed include, but are not limited to: skin cells, pluripotent stem cells, mesenchymal stem cells, β-cells, retinal pigmented epithelial cells, hematopoietic cells, cardiac cells, airway epithelial cells, neural stem cells, neurons, glial cells, bone cells, blood cells, and dental pulp stem cells. In one embodiment, the cell is contacted with a medium that supports the reprogrammed cell. In one embodiment, the medium also supports the cell.

Importantly, infecting skin cells with viruses encoding Oct4, Sox2, Klf4, and c-Myc, combined with culturing the cells in a medium that supports the growth of cardiomyocytes, has been reported to cause reprogramming of the skin cells to cardiomyocytes, without first reprogramming the skin cells to pluripotent stem cells (*See* Efs *et al* Nat Cell Biol. 2011;13:215-22, the contents of which are hereby incorporated by reference). In certain situations, direct reprogramming (reprogramming one somatic cell to another somatic cell without first reprogramming the somatic cell to a pluripotent stem cell, also known as “transdifferentiation”) may be desirable, in part because culturing pluripotent stem cells can be time-consuming and expensive, the additional handling involved in establishing and characterizing a stable pluripotent stem cell line can carry an increased risk of contamination,

and the additional time in culture associated with first producing pluripotent stem cells can carry an increased risk of genomic instability and the acquisition of mutations, including point mutations, copy-number variations, and karyotypic abnormalities. Certain embodiments are therefore directed to a method for reprogramming a somatic cell *in vivo,* wherein the cell is reprogrammed to a somatic cell, and wherein a characterized pluripotent stem-cell line is not produced.

It has been further discovered that, in certain situations, fewer total transfections may be required to reprogram a cell according to the methods of the present invention than according to other methods. Certain embodiments are therefore directed to a method for reprogramming a cell *in vivo*, wherein between about 1 and about 12 transfections are performed during about 20 consecutive days, or between about 4 and about 10 transfections are performed during about 15 consecutive days, or between about 4 and about 8 transfections are performed during about 10 consecutive days. It is recognized that when a cell is contacted with a medium containing nucleic acid molecules, the cell may likely come into contact with and/or internalize more than one nucleic acid molecule either simultaneously or at different times. A cell can therefore be contacted with a nucleic acid more than once, *e.g.* repeatedly, even when a cell is contacted only once with a medium containing nucleic acids.

Of note, nucleic acids can contain one or more non-canonical or “modified” residues as described herein. For instance, any of the non-canonical nucleotides described herein can be used in the present reprgramming methods. In one embodiment, pseudouridine-5'-triphosphate can be substituted for uridine-5'-triphosphate in an *in vitro*-transcription reaction to yield synthetic RNA, wherein up to 100% of the uridine residues of the synthetic RNA may be replaced with pseudouridine residues. *In vitro*-transcription can yield RNA with residual immunogenicity, even when pseudouridine and 5-methylcytidine are completely substituted for uridine and cytidine, respectively (*see, e.g.,* Angel. Reprogramming Human Somatic Cells to Pluripotency Using RNA [Doctoral Thesis]. Cambridge, MA: MIT; 2011, the contents of which are hereby incorporated by reference). For this reason, it is common to add an immunosuppressant to the transfection medium when transfecting cells with RNA. In certain situations, adding an immunosuppressant to the transfection medium may not be desirable, in part because the recombinant immunosuppressant most commonly used for this purpose, B18R, can be expensive and difficult to manufacture. It has now been discovered that cells *in vivo* can be transfected and/or reprogrammed according to the methods of the present invention, without using B18R or any other immunosuppressant. It has been further discovered that reprogramming cells *in vivo* according to the methods of the present invention without using immunosuppressants can be rapid, efficient, and reliable. Certain embodiments are therefore directed to a method for transfecting a cell *in vivo*, wherein the transfection medium does not contain an immunosuppressant. Other embodiments are directed to a method for reprogramming a cell *in vivo*, wherein the transfection medium does not contain an immunosuppressant. In certain situations, for example when using a high cell density, it may be beneficial to add an immunosuppressant to the transfection medium. Certain embodiments are therefore directed to a method for transfecting a cell *in vivo*, wherein the transfection medium contains an immunosuppressant. Other embodiments are directed to a method for reprogramming a cell *in vivo*, wherein the transfection medium contains an immunosuppressant. In one

embodiment, the immunosuppressant is B18R or a biologically active fragment, analogue, variant or family-member thereof or dexamethasone or a derivative thereof. In one embodiment, the transfection medium does not contain an immunosuppressant, and the nucleic-acid dose is chosen to prevent excessive toxicity. In another embodiment, the nucleic-acid dose is less than about 1mg/cm^2 of tissue or less than about 1mg/100,000 cells or less than about 10mg/kg.

Reprogrammed cells produced according to certain embodiments of the present invention are suitable for therapeutic and/or cosmetic applications as they do not contain undesirable exogenous DNA sequences, and they are not exposed to animal-derived or human-derived products, which may be undefined, and which may contain toxic and/or pathogenic contaminants. Furthermore, the high speed, efficiency, and reliability of certain embodiments of the present invention may reduce the risk of acquisition and accumulation of mutations and other chromosomal abnormalities. Certain embodiments of the present invention can thus be used to generate cells that have a safety profile adequate for use in therapeutic and/or cosmetic applications. For example, reprogramming cells using RNA and the medium of the present invention, wherein the medium does not contain animal or human-derived components, can yield cells that have not been exposed to allogeneic material. Certain embodiments are therefore directed to a reprogrammed cell that has a desirable safety profile. In one embodiment, the reprogrammed cell has a normal karyotype. In another embodiment, the reprogrammed cell has fewer than about 5 copy-number variations (CNVs) relative to the patient genome, such as fewer than about 3 copy-number variations relative to the patient genome, or no copy-number variations relative to the patient genome. In yet another embodiment, the reprogrammed cell has a normal karyotype and fewer than about 100 single nucleotide variants in coding regions relative to the patient genome, or fewer than about 50 single nucleotide variants in coding regions relative to the patient genome, or fewer than about 10 single nucleotide variants in coding regions relative to the patient genome.

Endotoxins and nucleases can co-purify and/or become associated with other proteins, such as serum albumin. Recombinant proteins, in particular, can often have high levels of associated endotoxins and nucleases, due in part to the lysis of cells that can take place during their production. Endotoxins and nucleases can be reduced, removed, replaced or otherwise inactivated by many of the methods of the present invention, including, for example, by acetylation, by addition of a stabilizer such as sodium octanoate, followed by heat treatment, by the addition of nuclease inhibitors to the albumin solution and/or medium, by crystallization, by contacting with one or more ion-exchange resins, by contacting with charcoal, by preparative electrophoresis or by affinity chromatography. It has now been discovered that partially or completely reducing, removing, replacing or otherwise inactivating endotoxins and/or nucleases from a medium and/or from one or more components of a medium can increase the efficiency with which cells can be transfected and reprogrammed. Certain embodiments are therefore directed to a method for transfecting a cell *in vivo* with one or more nucleic acids, wherein the transfection medium is treated to partially or completely reduce, remove, replace or otherwise inactivate one or more endotoxins and/or nucleases. Other embodiments are directed to a medium that causes

minimal degradation of nucleic acids. In one embodiment, the medium contains less than about 1EU/mL, or less than about 0.1EU/mL, or less than about 0.01EU/mL.

In certain situations, protein-based lipid carriers such as serum albumin can be replaced with non-protein-based lipid carriers such as methyl-beta-cyclodextrin. The medium of the present invention can also be used without a lipid carrier, for example, when transfection is performed using a method that may not require or may not benefit from the presence of a lipid carrier, for example, using one or more lipid-based transfection reagents, polymer-based transfection reagents or peptide-based transfection reagents or using electroporation. Many protein-associated molecules, such as metals, can be highly toxic to cells *in vivo*. This toxicity can cause decreased viability, as well as the acquisition of mutations. Certain embodiments thus have the additional benefit of producing cells that are free from toxic molecules.

The associated-molecule component of a protein can be measured by suspending the protein in solution and measuring the conductivity of the solution. Certain embodiments are therefore directed to a medium that contains a protein, wherein about a 10% solution of the protein in water has a conductivity of less than about 500 μmho/cm. In one embodiment, the solution has a conductivity of less than about 50 μmho/cm. In another embodiment, less than about 0.65% of the dry weight of the protein comprises lipids and/or less than about 0.35% of the dry weight of the protein comprises free fatty acids.

The amount of nucleic acid delivered to cells *in vivo* can be increased to increase the desired effect of the nucleic acid. However, increasing the amount of nucleic acid delivered to cells *in vivo* beyond a certain point can cause a decrease in the viability of the cells, due in part to toxicity of the transfection reagent. It has now been discovered that when a nucleic acid is delivered to a population of cells *in vivo* in a fixed volume (for example, cells in a region of tissue), the amount of nucleic acid delivered to each cell can depend on the total amount of nucleic acid delivered to the population of cells and to the density of the cells, with a higher cell density resulting in less nucleic acid being delivered to each cell. In certain embodiments, a cell *in vivo* is transfected with one or more nucleic acids more than once. Under certain conditions, for example when the cells are proliferating, the cell density may change from one transfection to the next. Certain embodiments are therefore directed to a method for transfecting a cell *in vivo* with a nucleic acid, wherein the cell is transfected more than once, and wherein the amount of nucleic acid delivered to the cell is different for two of the transfections. In one embodiment, the cell proliferates between two of the transfections, and the amount of nucleic acid delivered to the cell is greater for the second of the two transfections than for the first of the two transfections. In another embodiment, the cell is transfected more than twice, and the amount of nucleic acid delivered to the cell is greater for the second of three transfections than for the first of the same three transfections, and the amount of nucleic acid delivered to the cells is greater for the third of the same three transfections than for the second of the same three transfections. In yet another embodiment, the cell is transfected more than once, and the maximum amount of nucleic acid delivered to the cell during each transfection is sufficiently low to yield at least about 80% viability for at least two consecutive transfections.

It has now been discovered that modulating the amount of nucleic acid delivered to a population of proliferating cells *in vivo* in a series of transfections can result in both an increased effect of the nucleic acid and increased viability of the cells. It has been further discovered that, in certain situations, when cells *in vivo* are contacted with one or more nucleic acids encoding one or more reprogramming factors in a series of transfections, the efficiency of reprogramming can be increased when the amount of nucleic acid delivered in later transfections is greater than the amount of nucleic acid delivered in earlier transfections, for at least part of the series of transfections. Certain embodiments are therefore directed to a method for reprogramming a cell *in vivo*, wherein one or more nucleic acids is repeatedly delivered to the cell in a series of transfections, and the amount of the nucleic acid delivered to the cell is greater for at least one later transfection than for at least one earlier transfection. In one embodiment, the cell is transfected between about 2 and about 10 times, or between about 3 and about 8 times, or between about 4 and about 6 times. In another embodiment, the one or more nucleic acids includes at least one RNA molecule, the cell is transfected between about 2 and about 10 times, and the amount of nucleic acid delivered to the cell in each transfection is the same as or greater than the amount of nucleic acid delivered to the cell in the most recent previous transfection. In yet another embodiment, the amount of nucleic acid delivered to the cell in the first transfection is between about 20ng/cm^2 and about 250ng/cm^2, or between 100ng/cm^2 and 600ng/cm^2. In yet another embodiment, the cell is transfected about 5 times at intervals of between about 12 and about 48 hours, and the amount of nucleic acid delivered to the cell is about 25ng/cm^2 for the first transfection, about 50ng/cm^2 for the second transfection, about 100ng/cm^2 for the third transfection, about 200ng/cm^2 for the fourth transfection, and about 400ng/cm^2 for the fifth transfection. In yet another embodiment, the cell is further transfected at least once after the fifth transfection, and the amount of nucleic acid delivered to the cell is about 400ng/cm^2.

Certain embodiments are directed to a method for transfecting a cell *in vivo* with a nucleic acid, wherein the amount of nucleic acid is determined by measuring the cell density, and choosing the amount of nucleic acid to transfect based on the measurement of cell density. In one embodiment, the cell density is measured by optical means. In another embodiment, the cell is transfected repeatedly, the cell density increases between two transfections, and the amount of nucleic acid transfected is greater for the second of the two transfections than for the first of the two transfections.

It has now been discovered that, in certain situations, the amount of a circulating protein that is produced in a patient can be increased by administering to a patient a nucleic acid at a plurality of administration sites. In certain embodiments, the amount of a circulating protein is increased relative to the amount of the circulating protein that is produced in a patient by administering to the patient the nucleic acid at a single injection site. In one embodiment, the administering is by injection. In another embodiment, the injection is intradermal injection. In still another embodiment, the injection is subcutaneous or intramuscular injection. In some embodiments, the plurality of administration sites comprise administration sites in the skin. In other embodiments, the plurality of administration sites are at least about 1 or at least about 2 or at least about 5 or at least about 10 or at least about 20 or at least about 50 or at least about 100 administration sites. In one embodiment, the administering is

performed within at least about 5 minutes or at least about 10 minutes or at least about 30 minutes or at least about 1 hour or at least about 2 hours or at least about 5 hours or at least about 12 hours or at least about 1 day. In certain embodiments, the amount of a circulating protein is increased by at least about 10 percent or at least about 20 percent or at least about 50 percent or at least about 100 percent or at least about 3-fold or at least about 5-fold or at least about 10-fold or at least about 20-fold or at least about 50-fold or at least about 100-fold or at least about 500-fold or at least about 1000-fold or greater than 1000-fold.

It has now been discovered that, in certain situations, the *in vivo* transfection efficiency and viability of cells contacted with the medium of the present invention can be improved by conditioning the medium. Certain embodiments are therefore directed to a method for conditioning a medium. Other embodiments are directed to a medium that is conditioned. In one embodiment, the feeders are fibroblasts, and the medium is conditioned for approximately 24 hours. Other embodiments are directed to a method for transfecting a cell *in vivo*, wherein the transfection medium is conditioned. Other embodiments are directed to a method for reprogramming and/or gene-editing a cell *in vivo*, wherein the medium is conditioned. In one embodiment, the feeders are mitotically inactivated, for example, by exposure to a chemical such as mitomycin-C or by exposure to gamma radiation. In certain embodiments, it may be beneficial to use only autologous materials, in part to, for example and not wishing to be bound by theory, avoid the risk of disease transmission from the feeders to the cell or the patient. Certain embodiments are therefore directed to a method for transfecting a cell *in vivo*, wherein the transfection medium is conditioned, and wherein the feeders are derived from the same individual as the cell being transfected. Other embodiments are directed to a method for reprogramming and/or gene-editing a cell *in vivo*, wherein the medium is conditioned, and wherein the feeders are derived from the same individual as the cell being reprogrammed and/or gene-edited.

Several molecules can be added to media by conditioning. Certain embodiments are therefore directed to a medium that is supplemented with one or more molecules that are present in a conditioned medium. In one embodiment, the medium is supplemented with Wnt1, Wnt2, Wnt3, Wnt3a or a biologically active fragment, analogue, variant, agonist, or family-member thereof. In another embodiment, the medium is supplemented with TGF-β or a biologically active fragment, analogue, variant, agonist, or family-member thereof. In yet another embodiment, a cell *in vivo* is reprogrammed according to the method of the present invention, wherein the medium is not supplemented with TGF-β for between about 1 and about 5 days, and is then supplemented with TGF-β for at least about 2 days. In yet another embodiment, the medium is supplemented with IL-6, IL-6R or a biologically active fragment, analogue, variant, agonist, or family-member thereof. In yet another embodiment, the medium is supplemented with a sphingolipid or a fatty acid. In still another embodiment, the sphingolipid is lysophosphatidic acid, lysosphingomyelin, sphingosine-1-phosphate or a biologically active analogue, variant or derivative thereof.

In addition to mitotically inactivating cells, under certain conditions, irradiation can change the gene expression of cells, causing cells to produce less of certain proteins and more of certain other proteins that non-irradiated cells, for example, members of the Wnt family of proteins. In addition, certain members of the Wnt family of proteins

can promote the growth and transformation of cells. It has now been discovered that, in certain situations, the efficiency of reprogramming can be greatly increased by contacting a cell *in vivo* with a medium that is conditioned using irradiated feeders instead of mitomycin-c-treated feeders. It has been further discovered that the increase in reprogramming efficiency observed when using irradiated feeders is caused in part by Wnt proteins that are secreted by the feeders. Certain embodiments are therefore directed to a method for reprogramming a cell *in vivo*, wherein the cell is contacted with Wnt1, Wnt2, Wnt3, Wnt3a or a biologically active fragment, analogue, variant, family-member or agonist thereof, including agonists of downstream targets of Wnt proteins, and/or agents that mimic one or more of the biological effects of Wnt proteins, for example, 2-amino-4-[3,4-(methylenedioxy)benzylamino]-6-(3-methoxyphenyl)pyrimidine.

Because of the low efficiency of many DNA-based reprogramming methods, these methods may be difficult or impossible to use with cells derived from patient samples, which may contain only a small number of cells. In contrast, the high efficiency of certain embodiments of the present invention can allow reliable reprogramming of a small number of cells, including single cells. Certain embodiments are directed to a method for reprogramming a small number of cells. Other embodiments are directed to a method for reprogramming a single cell. In one embodiment, the cell is contacted with one or more enzymes. In another embodiment, the enzyme is collagenase. In yet another embodiment, the collagenase is animal-component free. In one embodiment, the collagenase is present at a concentration of between about 0.1mg/mL and about 10mg/mL, or between about 0.5mg/mL and about 5mg/mL. In another embodiment, the cell is a blood cell. In yet another embodiment, the cell is contacted with a medium containing one or more proteins that is derived from the patient's blood. In still another embodiment, the cell is contacted with a medium comprising: DMEM/F12 + 2mM L-alanyl-L-glutamine + between about 5% and about 25% patient-derived serum, or between about 10% and about 20% patient-derived serum, or about 20% patient-derived serum.

It has now been discovered that, in certain situations, transfecting cells *in vivo* with a mixture of RNA encoding Oct4, Sox2, Klf4, and c-Myc using the medium of the present invention can cause the rate of proliferation of the cells to increase. When the amount of RNA delivered to the cells is too low to ensure that all of the cells are transfected, only a fraction of the cells may show an increased proliferation rate. In certain situations, such as when generating a personalized therapeutic, increasing the proliferation rate of cells may be desirable, in part because doing so can reduce the time necessary to generate the therapeutic, and therefore can reduce the cost of the therapeutic. Certain embodiments are therefore directed to a method for transfecting a cell *in vivo* with a mixture of RNA encoding Oct4, Sox2, Klf4, and c-Myc. In one embodiment, the cell exhibits an increased proliferation rate. In another embodiment, the cell is reprogrammed.

Many diseases are associated with one or more mutations. Mutations can be corrected by contacting a cell with a nucleic acid that encodes a protein that, either alone or in combination with other molecules, corrects the mutation (an example of gene-editing). Examples of such proteins include: a nuclease, a transcription activator-like effector nuclease (TALEN), a zinc-finger nuclease, a meganuclease, a nickase, a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein a DNA-repair protein, a DNA-modification

protein, a base-modification protein, a DNA methyltransferase, an protein that causes DNA demethylation, an enzyme for which DNA is a substrate or a natural or engineered variant, family-member, orthologue, fragment or fusion construct thereof. Certain embodiments are therefore directed to a method for transfecting a cell *in vivo* with a nucleic acid, wherein the nucleic acid encodes a protein that, either alone or in combination with other molecules, creates a single-strand or double-strand break in a DNA molecule. In a one embodiment, the protein is a zinc finger nuclease or a TALEN. In another embodiment, the nucleic acid is an RNA molecule. In yet another embodiment, the single-strand or double-strand break is within about 5,000,000 bases of the transcription start site of a gene selected from the group: SERPINA1, CCR5, CXCR4, GAD1, GAD2, CFTR, HBA1, HBA2, HBB, HBD, FANCA, XPA, XPB, XPC, ERCC2, POLH, HTT, DMD, SOD1, APOE, PRNP, BRCA1, and BRCA2 or an analogue, variant or family-member thereof. In one embodiment, the present invention relates to gene-editing of the MYC protein (*e.g.* correcting one or more muations that may be linked to cancer), optionally with a TALEN. In yet another embodiment, the cell is transfected with a nucleic acid that acts as a repair template by either causing the insertion of a DNA sequence in the region of the single-strand or double-strand break or by causing the DNA sequence in the region of the single-strand or double-strand break to otherwise change. In yet another embodiment, the gene-editing protein contains a DNA modification domain. In yet another embodiment, the gene-editing protein corrects a mutation without creating a single-strand break. In yet another embodiment, the gene-editing protein corrects a mutation without creating a double-strand break. In yet another embodiment, the gene-editing protein corrects a mutation by causing the replacement of one base with another base. In one embodiment, adenine is replaced by cytosine. In another embodiment, adenine is replaced by guanine. In yet another embodiment, adenine is replaced by thymine. In yet another embodiment, cytosine is replaced by adenine. In yet another embodiment, cytosine is replaced by guanine. In yet another embodiment, cytosine is replaced by thymine. In yet another embodiment, guanine is replaced by adenine. In yet another embodiment, guanine is replaced by cytosine. In yet another embodiment, guanine is replaced by thymine. In yet another embodiment, thymine is replaced by adenine. In yet another embodiment, thymine is replaced by cytosine. In yet another embodiment, thymine is replaced by guanine. In one embodiment, the replacement of one base with another base is a one-step process. In another embodiment, the replacement of one base with another base is a multi-step process. In some embodiments, one base is replaced by more than one base, for example, by two bases. In other embodiments, more than one base is replaced by one base. In still other embodiments, more than one base is replaced by more than one base. In some embodiments, the gene-editing protein contains a deaminase domain. In one embodiment the deaminase domain comprises a cytidine deaminase domain. In another embodiment, the deaminase domain comprises an adenosine deaminase domain. In yet another embodiment, the deaminase domain comprises a guanosine deaminase domain. In yet another embodiment, the gene-editing protein comprises a sequence that is at least about 50% or at least about 60% or at least about 70% or at least about 80% or at least about 90% or at least about 95% or at least about 99% homologous to one or more of: SEQ ID NOs: 587, 588, 589, 590, 591, 592, and 593. In yet another embodiment, the gene-editing protein comprises a linker. In one embodiment, the linker is a flexible linker. In another embodiment, the linker positions the deaminase domain in proximity to a target base. In yet another

embodiment, the gene-editing protein deaminates the target base. In yet another embodiment, the gene-editing protein comprises a glycosylase-inhibitor domain. In yet another embodiment, the gene-editing protein comprises glycosylase-inhibitor activity. In one embodiment, the glycosylase inhibitor is a uracil glycosylase inhibitor. In another embodiment, the glycosylase inhibitor is a N-methylpurine DNA glycosylase inhibitor. In yet another embodiment, the cell is reprogrammed, and subsequently, the cell is gene-edited. In yet another embodiment, the cell is gene-edited, and subsequently, the cell is reprogrammed. In yet another embodiment, the gene-editing and reprogramming are performed within about 7 days of each other. In yet another embodiment, the gene-editing and reprogramming occur simultaneously or on the same day. In yet another embodiment, the cell is a skin cell, the skin cell is gene-edited to disrupt the CCR5 gene, the skin cell is reprogrammed to a hematopoietic stem cell, thus producing a therapeutic for HIV/AIDS, and the therapeutic is used to treat a patient with HIV/AIDS. In yet another embodiment, the skin cell is derived from the same patient whom the therapeutic is used to treat.

Certain embodiments are directed to methods and compositions for the treatment of rare diseases. In some embodiments, the rare disease is one or more of: a rare metabolic disease, a rare cardiovascular disease, a rare dermatologic disease, a rare neurologic disease, a rare developmental disease, a rare genetic disease, a rare pulmonary disease, a rare liver disease, a rare kidney disease, a rare psychiatric disease, a rare reproductive disease, a rare musculoskeletal disease, a rare orthopedic disease, an inborn error of metabolism, a lysosomal storage disease, and a rare ophthalmologic disease. In one embodiment, the disease is alpha-1-antitrypsin deficiency. Some embodiments are directed to a treatment comprising a nucleic acid encoding a gene-editing protein that is capable of causing a deletion in a gene that is associated with one or more of: a gain-of-function mutation, a loss-of-function mutation, a recessive mutation, a dominant mutation or a dominant negative mutation. Other embodiments are directed to a treatment comprising a nucleic acid encoding a gene-editing protein that is capable of correcting one or more of: a gain-of-function mutation, a loss-of-function mutation, a recessive mutation, a dominant mutation or a dominant negative mutation. In one embodiment, the treatment ameliorates one or more of the symptoms in a subject. In another embodiment, the subject is a human subject. In yet another embodiment, the subject is a veterinary subject. Some embodiments are directed to a treatment for alpha-1-antitrypsin deficiency comprising administering to a subject a nucleic acid comprising a gene-editing protein that is capable of causing a deletion in or near the SERPINA1 gene. Other embodiments are directed to a treatment for alpha-1-antitrypsin deficiency comprising administering to a subject a nucleic acid encoding a gene-editing protein that is capable of correcting a mutation in or near the SERPINA1 gene. In one embodiment the mutation is the Z mutation. In one embodiment, the deletion or correction reduces the accumulation of polymerized alpha-1-antitrypsin protein in the subject's cells and/or increases the secretion of alpha-1-antitrypsin from the subject's cells. In another embodiment, the treated cells regenerate a diseased organ. In yet another embodiment, the diseased organ is the liver. In yet another embodiment, the diseased organ is the lung. In yet another embodiment, the treatment delays or eliminates the subject's need for a liver and/or lung transplant. Other embodiments are directed to a treatment for epidermolysis bullosa. In one embodiment the epidermolysis

bullosa is dystrophic epidermolysis bullosa. In another embodiment, the epidermolysis bullosa is epidermolysis bullosa simplex. In yet another embodiment, the dystrophic epidermolysis bullosa is recessive dystrophic epidermolysis bullosa. In some embodiments, the treatment comprises administering to a subject a nucleic acid encoding a gene-editing protein that is capable of correcting a mutation in or near the COL7A1 gene. In one embodiment, the correction increases the amount of functional collagen VII produced by the subject's cells. In another embodiment, the treatment reduces the size, severity, and/or frequency of recurrence of skin lesions and/or blisters. Still other embodiments are directed to a treatment for primary hyperoxaluria. In one embodiment the primary hyperoxaluria is type I primary hyperoxaluria. In another embodiment, the treatment comprises administering to a subject a nucleic acid encoding a gene-editing protein that is capable of correcting a mutation in or near the AGXT gene. In yet another embodiment, the treatment delays or eliminates the subject's need for a kidney and/or liver transplant.

Genes that can be edited according to the methods of the present invention to produce therapeutics of the present invention include genes that can be edited to restore normal function, as well as genes that can be edited to reduce or eliminate function. Such genes include, but are not limited to alpha-1-antitrypsin (SERPINA1), mutations in which can cause alpha-1-antitrypsin deficiency, beta globin (HBB), mutations in which can cause sickle cell disease (SCD) and β-thalassemia, breast cancer 1, early onset (BRCA1) and breast cancer 2, early onset (BRCA2), mutations in which can increase susceptibility to breast cancer, C-C chemokine receptor type 5 (CCR5) and C-X-C chemokine receptor type 4 (CXCR4), mutations in which can confer resistance to HIV infection, cystic fibrosis transmembrane conductance regulator (CFTR), mutations in which can cause cystic fibrosis, dystrophin (DMD), mutations in which can cause muscular dystrophy, including Duchenne muscular dystrophy and Becker's muscular dystrophy, glutamate decarboxylase 1 and glutamate decarboxylase 2 (GAD1, GAD2), mutations in which can prevent autoimmune destruction of β-cells, hemoglobin alpha 1, hemoglobin alpha 2, and hemoglobin delta (HBA1, HBA2, and HBD), mutations in which can cause thalassemia, desmoplakin, keratin 5, keratin 14, plectin, integrin alpha-6, integrin beta-4, laminin subunit alpha-3, laminin subunit beta-3, laminin subunit gamma-2, collagen type VII alpha 1, collagen type XVII alpha 1, and matrix metalloproteinase-1 (DSP, KRT5, KRT14, PLEC1, ITGA6, ITGB4, LAMA3, LAMB3, LAMC2, COL7A1, COL17A1, and MMP1), mutations in which can cause epidermolysis bullosa, Huntington (HTT), mutations in which can cause Huntington's disease, superoxide dismutase 1 (SOD1), mutations in which can cause amyotrophic lateral sclerosis (ALS), XPA, XPB, XPC, XPD (ERCC6) and polymerase (DNA directed), eta (POLH), mutations in which can cause xeroderma pigmentosum, leucine-rich repeat kinase 2 (LRRK2), mutations in which can cause Parkinson's disease, and Fanconi anemia, complementation groups A, B, C, D1, D2, E, F, G, I, J, L, M, N, P (FANCA, FANCB, FANCC, FANCD1, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCJ, FANCL, FANCM, FANCN, FANCP), and RAD51 homolog C (S. cerevisiae) (RAD51C), mutations in which can cause Fanconi anemia.

In a specific embodiment, the present invention relates to method of modulating Growth-Factor-Differentiation-Factor-15 (GDF15). In a specific embodiment, there is provided a method of treatment in which an RNA as

described herein is administered to modulate GDF15 levels. In some embodiments, the RNA encodes GDF15. In a specific embodiment, the gene that is edited is Growth-Factor-Differentiation-Factor-15 (GDF15). In various embodiments, the present invention relates to targeting and/or expressing GDF15 to treat or prevent a disease or disorder such as a metabolic disease or disorder (*e.g.*, diabetes (type I and II), insulin resistance, obesity, dyslipidemia, hypercholesterolemia, hyperglycemia, hyperinsulinemia, hypertension, hepatosteaotosis such as non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty acid liver disease (NAFLD), cancer, a disease or disorder associated with impaired lipid metabolism, a disease or disorder associated with impaired renal function (*e.g.*, chronic kidney diseases, nephropathy such as diabetic nephropathy, kidney failure), a disease or disorder associated with impaired hepatic function, a disease or disorder associated with impaired lung function, a vascular or cardiovascular disease or disorder (*e.g.*, coronary artery disease, cardiomyopathy, hypertension, atrial fibrillation, preeclampsia, peripheral artery disease, atherosclerosis, heart failure, acute myocardial infarction, acute coronary syndrome, muscle wasting, hypertensive ventricular hypertrophy, hypertensive cardiomyopathy, ischemic heart disease, myocardial infarction, abdominal aortic aneurysm, a blood clot, deep vein thrombosis, venous stasis disease, phlebitis, varicose veins *etc.*), muscle wasting, inflammation, and a respiratory disease. In a specific embodiment, targeting of GDF15 improves lipid metabolism by mobilizing lipid deposits from the liver and/or other tissues into circulation for use in metabolism.

In certain disorders, the body may increase GDF15 levels in an attempt to counteract one or more negative aspects of the disease state. Certain embodiments are therefore directed to increasing GDF15 levels. In one embodiment, the serum level of GDF15 is increased. In another embodiment, the level of GDF15 in a tissue and/or organ is increased. In yet another embodiment, ALT levels are reduced. In yet another embodiment, AST levels are reduced. In still another embodiment, glucose levels are reduced. In still another embodiment, serum cholesterol levels are increased. In still another embodiment, serum triglyceride levels are increased. In yet another embodiment, food intake is reduced. In yet another embodiment, bodyweight is reduced. In a further embodiment, treatment improves adherence to a diet and/or exercise regimen.

In a specific embodiment, expressing GDF15 improves lipid metabolism by mobilizing lipid deposits from the liver and/or other tissues into circulation for use in metabolism. In a specific embodiment, expressing and/or targeting of GDF15 reduces liver inflammation. In a specific embodiment, expressing and/or targeting of GDF15 treats or prevents one or more of fatty liver, NAFLD, NASH, inflammation, hepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. In a specific embodiment, expressing and/or targeting of GDF15 treats or prevents one or more of chronic kidney disease, acute kidney injury, nephropathy, diabetic nephropathy, kidney failure, and kidney fibrosis. In a specific embodiment, expressing and/or targeting GDF15 in combination with expressing and/or targeting another member of the TGF-β superfamily improves lipid metabolism by mobilizing lipid deposits from the liver and/or other tissues into circulation for use in metabolism, reduces liver inflammatioin, and/or treats or prevents one or more of fatty liver, NAFLD, NASH, inflammation, hepatitis, fibrosis, cirrhosis, hepatocellular carcinoma, chronic kidney disease, acute kidney injury, nephropathy, diabetic nephropathy, kidney failure, and kidney fibrosis.Certain embodiments are directed to a therapeutic comprising a nucleic acid. In one embodiment,

the nucleic acid encodes one or more gene-editing proteins. Other embodiments are directed to a therapeutic comprising one or more cells that are transfected, reprogrammed, and/or gene-edited *in vivo* according to the methods of the present invention. In one embodiment, a cell is transfected, reprogrammed, and/or gene-edited, and the transfected, reprogrammed, and/or gene-edited cell is introduced into a patient. In another embodiment, the cell is harvested from the same patient into whom the transfected, reprogrammed and/or gene-edited cell is introduced. Examples of diseases that can be treated with therapeutics of the present invention include, but are not limited to Alzheimer's disease, spinal cord injury, amyotrophic lateral sclerosis, cystic fibrosis, heart disease, including ischemic and dilated cardiomyopathy, macular degeneration, Parkinson's disease, Huntington's disease, diabetes, sickle-cell anemia, thalassemia, Fanconi anemia, xeroderma pigmentosum, muscular dystrophy, severe combined immunodeficiency, hereditary sensory neuropathy, cancer, and HIV/AIDS. In certain embodiments, the therapeutic comprises a cosmetic. In one embodiment, a cell is harvested from a patient, the cell is reprogrammed and expanded to a large number of adipose cells to produce a cosmetic, and the cosmetic is introduced into the patient. In still another embodiment, the cosmetic is used for tissue reconstruction.

While detailed examples are provided herein for the production of specific types of cells and for the production of therapeutics comprising specific types of cells, it is recognized that the methods of the present invention can be used to produce many other types of cells, and to produce therapeutics comprising one or more of many other types of cells, for example, by reprogramming a cell according to the methods of the present invention, and culturing the cell under conditions that mimic one or more aspects of development by providing conditions that resemble the conditions present in the cellular microenvironment during development.

Certain embodiments are directed to a library of cells with a variety of human leukocyte antigen (HLA) types ("HLA-matched libraries"). An HLA-matched library may be beneficial in part because it can provide for the rapid production and/or distribution of therapeutics without the patient having to wait for a therapeutic to be produced from the patient's cells. Such a library may be particularly beneficial for the production of cosmetics and for the treatment of heart disease and diseases of the blood and/or immune system for which patients may benefit from the immediate availability of a therapeutic or cosmetic.

The DNA sequence of a cell can be altered by contacting the cell with a gene-editing protein or by inducing the cell to express a gene-editing protein. However, previously disclosed gene-editing proteins suffer from low binding efficiency and excessive off-target activity, which can introduce undesired mutations in the DNA of the cell, severely limiting their use *in vivo*, for example in therapeutic and cosmetic applications, in which the introduction of undesired mutations in a patient's cells could lead to the development of cancer. It has now been discovered that gene-editing proteins that comprise the StsI endonuclease cleavage domain (SEQ ID NO: 1) can exhibit substantially lower off-target activity *in vivo* than previously disclosed gene-editing proteins, while maintaining a high level of on-target activity *in vivo*. Other novel engineered proteins have also been discovered that can exhibit high on-target activity *in vivo*, low off-target activity *in vivo*, small size, solubility, and other desirable characteristics when they are used as the nuclease domain of a gene-editing protein: StsI-HA (SEQ ID NO: 2), StsI-HA2 (SEQ ID NO: 3), StsI-UHA (SEQ ID NO: 4), StsI-UHA2 (SEQ ID NO: 5), StsI-HF (SEQ ID NO:

6), and StsI-UHF (SEQ ID NO: 7). StsI-HA, StsI-HA2 (high activity), StsI-UHA, and StsI-UHA2 (ultra-high activity) can exhibit higher on-target activity *in vivo* than both wild-type StsI and wild-type FokI, due in part to specific amino-acid substitutions within the N-terminal region at the 34 and 61 positions, while StsI-HF (high fidelity) and StsI-UHF (ultra-high fidelity) can exhibit lower off-target activity *in vivo* than both wild-type StsI and wild-type FokI, due in part to specific amino-acid substitutions within the C-terminal region at the 141 and 152 positions.

Certain embodiments are therefore directed to a protein. In some embodiments, the protein is present *in vivo*. In other embodiments, the protein comprises a nuclease domain. In one embodiment, the nuclease domain comprises one or more of: the cleavage domain of FokI endonuclease (SEQ ID NO: 53), the cleavage domain of StsI endonuclease (SEQ ID NO: 1), StsI-HA (SEQ ID NO: 2), StsI-HA2 (SEQ ID NO: 3), StsI-UHA (SEQ ID NO: 4), StsI-UHA2 (SEQ ID NO: 5), StsI-HF (SEQ ID NO: 6), and StsI-UHF (SEQ ID NO: 7) or a biologically active fragment or variant thereof.

It has also been discovered that engineered gene-editing proteins that comprise DNA-binding domains comprising certain novel repeat sequences can exhibit lower off-target activity *in vivo* than previously disclosed gene-editing proteins, while maintaining a high level of on-target activity *in vivo*. Certain of these engineered gene-editing proteins can provide several advantages over previously disclosed gene-editing proteins, including, for example, increased flexibility of the linker region connecting repeat sequences, which can result in increased binding efficiency. Certain embodiments are therefore directed to a protein comprising a plurality of repeat sequences. In one embodiment, at least one of the repeat sequences contains the amino-acid sequence: GabG, where “a” and “b” each represent any amino acid. In one embodiment, the protein is a gene-editing protein. In another embodiment, one or more of the repeat sequences are present in a DNA-binding domain. In a further embodiment, “a” and “b” are each independently selected from the group: H and G. In a still further embodiment, “a” and “b” are H and G, respectively. In one embodiment, the amino-acid sequence is present within about 5 amino acids of the C-terminus of the repeat sequence. In another embodiment, the amino-acid sequence is present at the C-terminus of the repeat sequence. In some embodiments, one or more G in the amino-acid sequence GabG is replaced with one or more amino acids other than G, for example A, H or GG. In one embodiment, the repeat sequence has a length of between about 32 and about 40 amino acids or between about 33 and about 39 amino acids or between about 34 and 38 amino acids or between about 35 and about 37 amino acids or about 36 amino acids or greater than about 32 amino acids or greater than about 33 amino acids or greater than about 34 amino acids or greater than about 35 amino acids. Other embodiments are directed to a protein comprising one or more transcription activator-like effector domains. In one embodiment, at least one of the transcription activator-like effector domains comprises a repeat sequence. Other embodiments are directed to a protein comprising a plurality of repeat sequences generated by inserting one or more amino acids between at least two of the repeat sequences of a transcription activator-like effector domain. In one embodiment, one or more amino acids is inserted about 1 or about 2 or about 3 or about 4 or about 5 amino acids from the C-terminus of at least one repeat sequence. Still other embodiments are directed to a protein comprising a plurality of repeat sequences, wherein about every other repeat sequence has a different length than the repeat

sequence immediately preceding or following the repeat sequence. In one embodiment, every other repeat sequence is about 36 amino acids long. In another embodiment, every other repeat sequence is 36 amino acids long. Still other embodiments are directed to a protein comprising a plurality of repeat sequences, wherein the plurality of repeat sequences comprises at least two repeat sequences that are each at least 36 amino acids long, and wherein at least two of the repeat sequences that are at least 36 amino acids long are separated by at least one repeat sequence that is less than 36 amino acids long. Some embodiments are directed to a protein that comprises one or more sequences selected from, for example, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, and SEQ ID NO: 60.

Other embodiments are directed to a protein that comprises a DNA-binding domain. In some embodiments, the DNA-binding domain comprises a plurality of repeat sequences. In one embodiment, the plurality of repeat sequences enables high-specificity recognition of a binding site in a target DNA molecule. In another embodiment, at least two of the repeat sequences have at least about 50%, or about 60%, or about 70%, or about 80%, or about 90%, or about 95%, or about 98%, or about 99% homology to each other. In a further embodiment, at least one of the repeat sequences comprises one or more regions capable of binding to a binding site in a target DNA molecule. In a still further embodiment, the binding site comprises a defined sequence of between about 1 to about 5 bases in length. In one embodiment, the DNA-binding domain comprises a zinc finger. In another embodiment, the DNA-binding domain comprises a transcription activator-like effector (TALE). In a further embodiment, the plurality of repeat sequences includes at least one repeat sequence having at least about 50% or about 60% or about 70% or about 80% or about 90% or about 95% or about 98%, or about 99% homology to a TALE. In a still further embodiment, the gene-editing protein comprises a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein. In one embodiment, the gene-editing protein comprises a nuclear-localization sequence. In another embodiment, the nuclear-localization sequence comprises the amino-acid sequence: PKKKRKV (SEQ ID NO: 471). In one embodiment, the gene-editing protein comprises a mitochondrial-localization sequence. In another embodiment, the mitochondrial-localization sequence comprises the amino-acid sequence: LGRVIPRKIASRASLM (SEQ ID NO: 472). In one embodiment, the gene-editing protein comprises a linker. In another embodiment, the linker connects a DNA-binding domain to a nuclease domain. In a further embodiment, the linker is between about 1 and about 10 amino acids long. In some embodiments, the linker is about 1, about 2, or about 3, or about 4, or about 5, or about 6, or about 7, or about 8, or about 9, or about 10 amino acids long. In one embodiment, the gene-editing protein is capable of generating a nick or a double-strand break in a target DNA molecule.

Certain embodiments are directed to a method for modifying the genome of a cell *in vivo*, the method comprising introducing into a cell *in vivo* a nucleic acid molecule encoding a non-naturally occurring fusion protein comprising an artificial transcription activator-like (TAL) effector repeat domain comprising one or more repeat units 36 amino acids in length and an endonuclease domain, wherein the repeat domain is engineered for recognition of a predetermined nucleotide sequence, and wherein the fusion protein recognizes the predetermined nucleotide sequence. In one embodiment, the cell is a eukaryotic cell. In another embodiment, the

cell is an animal cell. In a further embodiment, the cell is a mammalian cell. In a still further embodiment, the cell is a human cell. In one embodiment, the cell is a plant cell. In another embodiment, the cell is a prokaryotic cell. In some embodiments, the fusion protein introduces an endonucleolytic cleavage in a nucleic acid of the cell, whereby the genome of the cell is modified.

Certain embodiments are directed to a composition for altering the DNA sequence of a cell *in vivo* comprising a nucleic acid, wherein the nucleic acid encodes a gene-editing protein. Other embodiments are directed to a composition for altering the DNA sequence of a cell *in vivo* comprising a nucleic-acid mixture, wherein the nucleic-acid mixture comprises: a first nucleic acid that encodes a first gene-editing protein, and a second nucleic acid that encodes a second gene-editing protein. In one embodiment, the binding site of the first gene-editing protein and the binding site of the second gene-editing protein are present in the same target DNA molecule. In another embodiment, the binding site of the first gene-editing protein and the binding site of the second gene-editing protein are separated by less than about 50 bases, or less than about 40 bases, or less than about 30 bases or less than about 20 bases, or less than about 10 bases, or between about 10 bases and about 25 bases or about 15 bases. In one embodiment, the nuclease domain of the first gene-editing protein and the nuclease domain of the second gene-editing protein are capable of forming a dimer. In another embodiment, the dimer is capable of generating a nick or double-strand break in a target DNA molecule.

Certain embodiments are directed to a therapeutic composition. Other embodiments are directed to a cosmetic composition. In some embodiments, the composition comprises a repair template. In a further embodiment, the repair template is a single-stranded DNA molecule or a double-stranded DNA molecule.

Other embodiments are directed to an article of manufacture for synthesizing a protein or a nucleic acid encoding a protein. In one embodiment, the article is a nucleic acid. In another embodiment, the protein comprises a DNA-binding domain. In a further embodiment, the nucleic acid comprises a nucleotide sequence encoding a DNA-binding domain. In one embodiment, the protein comprises a nuclease domain. In another embodiment, the nucleic acid comprises a nucleotide sequence encoding a nuclease domain. In one embodiment, the protein comprises a plurality of repeat sequences. In another embodiment, the nucleic acid encodes a plurality of repeat sequences. In a further embodiment, the nuclease domain is selected from: FokI, StsI, StsI-HA, StsI-HA2, StsI-UHA, StsI-UHA2, StsI-HF, and StsI-UHF or a natural or engineered variant or biologically active fragment thereof. In one embodiment, the nucleic acid comprises an RNA-polymerase promoter. In another embodiment, the RNA-polymerase promoter is a T7 promoter or a SP6 promoter. In a further embodiment, the nucleic acid comprises a viral promoter. In one embodiment, the nucleic acid comprises an untranslated region. In another embodiment, the nucleic acid is an *in vitro*-transcription template.

Certain embodiments are directed to a method for inducing a cell to express a protein *in vivo*. Other embodiments are directed to a method for altering the DNA sequence of a cell *in vivo* comprising transfecting the cell *in vivo* with a gene-editing protein or inducing the cell to express a gene-editing protein *in vivo*. Still other embodiments are directed to a method for reducing the expression of a protein of interest in a cell *in vivo*. In one

embodiment, the cell is induced to express a gene-editing protein, wherein the gene-editing protein is capable of creating a nick or a double-strand break in a target DNA molecule. In another embodiment, the nick or double-strand break results in inactivation of a gene. Still other embodiments are directed to a method for generating an inactive, reduced-activity or dominant-negative form of a protein *in vivo*. In one embodiment, the protein is survivin. Still other embodiments are directed to a method for repairing one or more mutations in a cell *in vivo*. In one embodiment, the cell is contacted with a repair template. In another embodiment, the repair template is a DNA molecule. In a further embodiment, the repair template does not contain a binding site of the gene-editing protein. In a still further embodiment, the repair template encodes an amino-acid sequence that is encoded by a DNA sequence that comprises a binding site of the gene-editing protein.

In various embodiments, the repair template is about 20 nucleotides, or about 30 nucleotides, or about 40 nucleotides, or about 50 nucleotides, or about 60 nucleotides, or about 70 nucleotides, or about 80 nucleotides, or about 90 nucleotides, or about 100 nucleotides, or about 150 nucleotides, or about 200 nucleotides, or about 300 nucleotides, or about 400 nucleotides, or about 500 nucleotides, or about 750 nucleotides, or about 1000 nucleotides. In various embodiments, the repair template is about 20-1000 nucleotides, or about 20-500 nucleotides, or about 20-400 nucleotides, or about 20-200 nucleotides, or about 20-100 nucleotides, or about 80-100 nucleotides, or about 50-100 nucleotides.

In various embodiments, the mass ratio of RNA (*e.g.* synthetic RNA encoding gene-editing protein) to repair template is about 1:10, or about 1:9, or about 1:8, or about 1:7, or about 1:6, or about 1:5, or about 1:4, or about 1:3, or about 1:2, or about 1:1, or about 2:1, or about 3:1, or about 4:1, or about 5:1, or about 6:1, or about 7:1, or about 8:1, or about 9:1, or about 10:1.

In various embodiments, the molar ratio of RNA (*e.g.* synthetic RNA encoding gene-editing protein) to repair template is about 1:10, or about 1:9, or about 1:8, or about 1:7, or about 1:6, or about 1:5, or about 1:4, or about 1:3, or about 1:2, or about 1:1, or about 2:1, or about 3:1, or about 4:1, or about 5:1, or about 6:1, or about 7:1, or about 8:1, or about 9:1, or about 10:1.

In various embodiments, the repair template has a dual function, causing a repair to a gene-edited target sequence and preventing further binding of a gene-editing protein, thereby reducing or eliminating further gene-editing (*e.g.* via the repair template causing a repair that renders what was the gene-editing protein binding site no longer suitable for gene-editing protein binding). Accordingly, in some embodiments, the present gene-editing methods are tunable to ensure a single gene-edit per target site.

Other embodiments are directed to a method for treating a patient comprising administering to the patient a therapeutically or cosmetically effective amount of a protein or a nucleic acid encoding a protein. In one embodiment, the treatment results in one or more of the patient's symptoms being ameliorated. Certain embodiments are directed to a method for treating a patient comprising: a. inducing a cell to express a protein of interest by transfecting the cell *in vivo* with a nucleic acid encoding the protein of interest and/or b. reprogramming the cell *in vivo*. In one embodiment, the cell is reprogrammed to a less differentiated state. In

another embodiment, the cell is reprogrammed by transfecting the cell with one or more synthetic RNA molecules encoding one or more reprogramming proteins. In a further embodiment, the cell is differentiated. In a still further embodiment, the cell is differentiated into one of: a skin cell, a glucose-responsive insulin-producing cell, a hematopoietic cell, a cardiac cell, a retinal cell, a renal cell, a neural cell, a stromal cell, a fat cell, a bone cell, a muscle cell, an oocyte, and a sperm cell. Other embodiments are directed to a method for treating a patient comprising: a. inducing a cell to express a gene-editing protein by transfecting the cell *in vivo* with a nucleic acid encoding a gene-editing protein and/or b. reprogramming the cell *in vivo*.

Other embodiments are directed to a complexation medium. In one embodiment, the complexation medium has a pH greater than about 7, or greater than about 7.2, or greater than about 7.4, or greater than about 7.6, or greater than about 7.8, or greater than about 8.0, or greater than about 8.2, or greater than about 8.4, or greater than about 8.6, or greater than about 8.8, or greater than about 9.0. In another embodiment, the complexation medium comprises transferrin. In a further embodiment, the complexation medium comprises DMEM. In a still further embodiment, the complexation medium comprises DMEM/F12. Still other embodiments are directed to a method for forming nucleic-acid-transfection-reagent complexes. In one embodiment, the transfection reagent is incubated with a complexation medium. In another embodiment, the incubation occurs before a mixing step. In a further embodiment, the incubation step is between about 5 seconds and about 5 minutes or between about 10 seconds and about 2 minutes or between about 15 seconds and about 1 minute or between about 30 seconds and about 45 seconds. In one embodiment, the transfection reagent is selected from **Table 1**. In another embodiment, the transfection reagent is a lipid or lipidoid. In a further embodiment, the transfection reagent comprises a cation. In a still further embodiment, the cation is a multivalent cation. In a still further embodiment, the transfection reagent is N1-[2-((1S)-1-[(3-aminopropyl)amino]-4-[di(3-amino-propyl)amino]butylcarboxamido)ethyl]-3,4-di[oleyloxy]-benzamide (a.k.a. MVL5) or a derivative thereof.

Certain embodiments are directed to a method for inducing a cell to express a protein by contacting the cell with a nucleic acid *in vivo*. In one embodiment, the cell is a mammalian cell. In another embodiment, the cell is a human cell or a rodent cell. Other embodiments are directed to a cell produced using one or more of the methods of the present invention. In one embodiment, the cell is present in a patient. In another embodiment, the cell is isolated from a patient. Other embodiments are directed to a screening library comprising a cell produced using one or more of the methods of the present invention. In one embodiment, the screening library is used for at least one of: toxicity screening, including: cardiotoxicity screening, neurotoxicity screening, and hepatotoxicity screening, efficacy screening, high-throughput screening, high-content screening, and other screening.

Other embodiments are directed to a kit containing a nucleic acid. In one embodiment, the kit contains a delivery reagent (a.k.a. “transfection reagent”). In another embodiment, the kit is a reprogramming kit. In a further embodiment, the kit is a gene-editing kit. Other embodiments are directed to a kit for producing nucleic acids. In one embodiment, the kit contains at least two of: pseudouridine-triphosphate, 5-methyluridine triphosphate, 5-methylcytidine triphosphate, 5-hydroxymethylcytidine triphosphate, N4-methylcytidine triphosphate, N4-acetylcytidine triphosphate, and 7-deazaguanosine triphosphate or one or more derivatives thereof. Other

embodiments are directed to a therapeutic or cosmetic comprising a nucleic acid. In one embodiment, the therapeutic or cosmetic is a pharmaceutical composition. In another embodiment, the pharmaceutical composition is formulated. In a further embodiment, the formulation comprises an aqueous suspension of liposomes. Example liposome components are set forth in **Table 1**, and are given by way of example, and not by way of limitation. In one embodiment, the liposomes include one or more polyethylene glycol (PEG) chains. In another embodiment, the PEG is PEG2000. In a further embodiment, the liposomes include 1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE) or a derivative thereof. In one embodiment, the therapeutic comprises one or more ligands. In another embodiment, the therapeutic comprises at least one of: androgen, CD30 (TNFRSF8), a cell-penetrating peptide, CXCR, estrogen, epidermal growth factor, EGFR, HER2, folate, insulin, insulin-like growth factor-I, interleukin-13, integrin, progesterone, stromal-derived-factor-1, thrombin, vitamin D, and transferrin or a biologically active fragment or variant thereof. Still other embodiments are directed to a therapeutic or cosmetic comprising a cell generated using one or more of the methods of the present invention. In one embodiment, the therapeutic is administered to a patient for the treatment of any of the diseases or disorders described herein, including by way of non-limitation, type 1 diabetes, heart disease, including ischemic and dilated cardiomyopathy, macular degeneration, Parkinson's disease, cystic fibrosis, sickle-cell anemia, thalassemia, Fanconi anemia, severe combined immunodeficiency, hereditary sensory neuropathy, xeroderma pigmentosum, Huntington's disease, muscular dystrophy, amyotrophic lateral sclerosis, Alzheimer's disease, cancer, and infectious diseases including: hepatitis and HIV/AIDS.

Other embodiments are directed to a method for reprogramming a cell *in vivo*. In one embodiment, the cell is reprogrammed by contacting the cell with one or more nucleic acids. In one embodiment, the cell is contacted with a plurality of nucleic acids encoding at least one of: Oct4 protein, Sox2 protein, Klf4 protein, c-Myc protein, Lin28 protein or a biologically active fragment, variant or derivative thereof. In another embodiment, the cell is contacted with a plurality of nucleic acids encoding a plurality of proteins including: Oct4 protein, Sox2 protein, Klf4 protein, and c-Myc protein or one or more biologically active fragments, variants or derivatives thereof. Still other embodiments are directed to a method for gene editing a cell *in vivo*. In one embodiment, the cell is gene-edited by contacting the cell with one or more nucleic acids.

Certain embodiments are directed to a method for inducing a cell *in vivo* to express a protein of interest comprising contacting a cell *in vivo* with a solution comprising albumin that is treated with an ion-exchange resin or charcoal and one or more nucleic acid molecules, wherein at least one of the one or more nucleic acid molecules encodes a protein of interest. In one embodiment, the method results in the cell expressing the protein of interest. In another embodiment, the one or more nucleic acid molecules comprise a synthetic RNA molecule. In one embodiment, the cell is a skin cell. In another embodiment, the cell is a muscle cell. In yet another embodiment, the cell is a dermal fibroblast. In yet another embodiment, the cell is a myoblast. In one embodiment, the protein of interest is an extracellular matrix protein. In another embodiment, the protein of interest is selected from: elastin, collagen, laminin, fibronectin, vitronectin, lysyl oxidase, elastin binding protein, a growth factor, fibroblast growth factor, transforming growth factor beta, granulocyte colony-stimulating factor, a

matrix metalloproteinase, an actin, fibrillin, microfibril-associated glycoprotein, a lysyl-oxidase-like protein, and platelet-derived growth factor. In one embodiment, the solution is delivered to the dermis. In another embodiment, the delivering is by injection. In yet another embodiment, the delivering is by injection using a microneedle array. In one embodiment, the solution further comprises a growth factor. In another embodiment, the growth factor is selected from: fibroblast growth factor and transforming growth factor beta. In yet another embodiment, the solution further comprises cholesterol.Other embodiments are directed a method for inducing a cell *in vivo* to express a protein of interest comprising contacting a cell *in vivo* with a solution comprising cholesterol and one or more nucleic acid molecules, wherein at least one of the one or more nucleic acid molecules encodes a protein of interest. In one embodiment, the method results in the cell expressing the protein of interest. Still other embodiments are directed to a method for transfecting a cell *in vivo* with a nucleic acid molecule comprising contacting a cell *in vivo* with a solution comprising albumin that is treated with an ion-exchange resin or charcoal and a nucleic acid molecule. In one embodiment, the method results in the cell being transfected with the nucleic acid molecule. In another embodiment, the nucleic acid molecule is one of: a dsDNA molecule, a ssDNA molecule, a dsRNA molecule, a ssRNA molecule, a plasmid, an oligonucleotide, a synthetic RNA molecule, a miRNA molecule, an mRNA molecule, an siRNA molecule. Still other embodiments are directed to a method for treating a patient comprising delivering to a patient a composition comprising albumin that is treated with an ion-exchange resin or charcoal and one or more nucleic acid molecules, wherein at least one of the one or more nucleic acid molecules encodes a protein of interest. In one embodiment, the method results in the expression of the protein of interest in the patient. In another embodiment, the method results in the expression of the protein of interest in the dermis of the patient.

Certain embodiments are directed to a cosmetic composition comprising albumin that is treated with an ion-exchange resin or charcoal and a nucleic acid molecule. Other embodiments are directed to a cosmetic treatment article. In one embodiment, the cosmetic treatment article comprises a device configured to deliver a composition to a patient. In another embodiment, the nucleic acid molecule encodes elastin protein or collagen protein. Still other embodiments are directed to a solution for transfecting a cell *in vivo* comprising cholesterol or a cholesterol analog and one or more nucleic acid molecules. In one embodiment, the cholesterol or cholesterol analog is covalently bound to at least one of the one or more nucleic acid molecules. In another embodiment, the cholesterol analog is an oxysterol. In yet another embodiment, the cholesterol analog includes one or more of: an A-ring substitution, a B-ring substitution, a D-ring substitution, a side-chain substitution, a cholestanoic acid, a cholestenoic acid, a polyunsaturated moiety, a deuterated moiety, a fluorinated moiety, a sulfonated moiety, a phosphorylated moiety, and a fluorescent moiety. In yet another embodiment, the method comprises treating the patient with one or more of: a dermal filler, a neurotoxin (by way of illustration sodium channel inhibitors (*e.g.*, tetrodotoxin), potassium channel inhibitors (*e.g.*, tetraethylammonium), chloride channel inhibitors (*e.g.*, chlorotoxin and curare), calcium channel inhibitors (*e.g.*, conotoxin), synaptic vesicle release inhibitors (*e.g.*, botulinum toxin and tetanus toxin) and blood brain barrier inhibitor (*e.g.*, aluminum and mercury)) and a repair-inducing treatment.

Despite the tendency of transfection reagent nucleic acid complexes to precipitate, form clumps or otherwise degrade when stored for more than a few minutes, the present inventors have surprisingly discovered that transfection reagent nucleic acid complexes produced according to some embodiments of the present invention can be frozen and/or can be stored at various temperatures, including room temperature, about 4°C, about -20°C, about -80°C, and about -196°C for an extended period of time, for example, for several hours, about 1 day, about 1 week, about 1 month, about 1 year, and longer than about 1 year. Some embodiments are therefore directed to a pharmaceutical formulation comprising synthetic RNA and a transfection reagent, wherein the pharmaceutical formulation is provided in solid form. Other embodiments are directed to a pharmaceutical formulation comprising synthetic RNA transfection reagent complexes, wherein the synthetic RNA transfection reagent complexes are provided in solid form. In various embodiments, the synthetic RNA transfection reagent complexes are provided in frozen form. Various embodiments are directed to a method for stabilizing nucleic acid transfection reagent complexes comprising forming nucleic acid transfection reagent complexes and contacting the nucleic acid transfection reagent complexes or vessel in which such are contained with a cryogenic liquid to produce stabilized nucleic acid transfection reagent complexes. In one embodiment, the nucleic acid transfection reagent complexes are stabilized for shipment or storage.

Illustrative subjects or patients refers to any vertebrate including, without limitation, humans and other primates (*e.g.*, chimpanzees and other apes and monkey species), farm animals (*e.g.*, cattle, sheep, pigs, goats, and horses), domestic mammals (*e.g.*, dogs and cats), laboratory animals (*e.g.*, rodents such as mice, rats, and guinea pigs), and birds (*e.g.*, domestic, wild and game birds such as chickens, turkeys and other gallinaceous birds, ducks, geese, and the like). In some embodiments, the subject is a mammal. In some embodiments, the subject is a human.

Definitions

By “molecule” is meant a molecular entity (molecule, ion, complex, *etc.*).

By “RNA molecule” is meant a molecule that comprises RNA.

By “synthetic RNA molecule” is meant an RNA molecule that is produced outside of a cell or that is produced inside of a cell using bioengineering, by way of non-limiting example, an RNA molecule that is produced in an *in vitro*-transcription reaction, an RNA molecule that is produced by direct chemical synthesis or an RNA molecule that is produced in a genetically-engineered *E.coli* cell.

By “transfection” is meant contacting a cell with a molecule, wherein the molecule is internalized by the cell.

By “upon transfection” is meant during or after transfection.

By “transfection reagent” is meant a substance or mixture of substances that associates with a molecule and facilitates the delivery of the molecule to and/or internalization of the molecule by a cell, by way of non-limiting example, a cationic lipid, a charged polymer or a cell-penetrating peptide.

By “reagent-based transfection” is meant transfection using a transfection reagent.

By “medium” is meant a solvent or a solution comprising a solvent and a solute, by way of non-limiting example, Dulbecco’s Modified Eagle’s Medium (DMEM), DMEM + 10% fetal bovine serum (FBS), saline or water.

By “complexation medium” is meant a medium to which a transfection reagent and a molecule to be transfected are added and in which the transfection reagent associates with the molecule to be transfected.

By “transfection medium” is meant a medium that can be used for transfection, by way of non-limiting example, Dulbecco’s Modified Eagle’s Medium (DMEM), DMEM/F12, saline or water.

By “recombinant protein” is meant a protein or peptide that is not produced in animals or humans. Non-limiting examples include human transferrin that is produced in bacteria, human fibronectin that is produced in an *in vitro* culture of mouse cells, and human serum albumin that is produced in a rice plant.

By “Oct4 protein” is meant a protein that is encoded by the POU5F1 gene, or a natural or engineered variant, family-member, orthologue, fragment or fusion construct thereof, by way of non-limiting example, human Oct4 protein (SEQ ID NO: 8), mouse Oct4 protein, Oct1 protein, a protein encoded by POU5F1 pseudogene 2, a DNA-binding domain of Oct4 protein or an Oct4-GFP fusion protein. In some embodiments the Oct4 protein comprises an amino acid sequence that has at least 70% identity with SEQ ID NO: 8, or in other embodiments, at least 75%, 80%, 85%, 90%, or 95% identity with SEQ ID NO: 8. In some embodiments, the Oct4 protein comprises an amino acid sequence having from 1 to 20 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 8. Or in other embodiments, the Oct4 protein comprises an amino acid sequence having from 1 to 15 or from 1 to 10 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 8.

By “Sox2 protein” is meant a protein that is encoded by the SOX2 gene, or a natural or engineered variant, family-member, orthologue, fragment or fusion construct thereof, by way of non-limiting example, human Sox2 protein (SEQ ID NO: 9), mouse Sox2 protein, a DNA-binding domain of Sox2 protein or a Sox2-GFP fusion protein. In some embodiments the Sox2 protein comprises an amino acid sequence that has at least 70% identity with SEQ ID NO: 9, or in other embodiments, at least 75%, 80%, 85%, 90%, or 95% identity with SEQ ID NO: 9. In some embodiments, the Sox2 protein comprises an amino acid sequence having from 1 to 20 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 9. Or in other embodiments, the Sox2 protein comprises an amino acid sequence having from 1 to 15 or from 1 to 10 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 9.

By “Klf4 protein” is meant a protein that is encoded by the KLF4 gene, or a natural or engineered variant, family-member, orthologue, fragment or fusion construct thereof, by way of non-limiting example, human Klf4 protein (SEQ ID NO: 10), mouse Klf4 protein, a DNA-binding domain of Klf4 protein or a Klf4-GFP fusion protein. In some embodiments the Klf4 protein comprises an amino acid sequence that has at least 70% identity with SEQ ID NO: 10, or in other embodiments, at least 75%, 80%, 85%, 90%, or 95% identity with SEQ ID NO: 10. In some embodiments, the Klf4 protein comprises an amino acid sequence having from 1 to 20 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 10. Or in other embodiments, the Klf4 protein

comprises an amino acid sequence having from 1 to 15 or from 1 to 10 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 10.

By “c-Myc protein” is meant a protein that is encoded by the MYC gene, or a natural or engineered variant, family-member, orthologue, fragment or fusion construct thereof, by way of non-limiting example, human c-Myc protein (SEQ ID NO: 11), mouse c-Myc protein, l-Myc protein, c-Myc (T58A) protein, a DNA-binding domain of c-Myc protein or a c-Myc-GFP fusion protein. In some embodiments the c-Myc protein comprises an amino acid sequence that has at least 70% identity with SEQ ID NO: 11, or in other embodiments, at least 75%, 80%, 85%, 90%, or 95% identity with SEQ ID NO: 11. In some embodiments, the c-Myc protein comprises an amino acid having from 1 to 20 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 11. Or in other embodiments, the c-Myc protein comprises an amino acid sequence having from 1 to 15 or from 1 to 10 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 11.

By “erythropoietin” or “erythropoietin protein” is meant a protein that is encoded by the EPO gene, or a natural or engineered variant, family-member, orthologue, fragment or fusion construct thereof, by way of non-limiting example, human erythropoietin (SEQ ID NO: 164), mouse erythropoietin, darbepoetin, darbepoetin alfa, NOVEPOETIN, a binding domain of erythropoietin or an erythropoietin-GFP fusion protein. In some embodiments the erythropoietin comprises an amino acid sequence that has at least 70% identity with SEQ ID NO: 164, or in other embodiments, at least 75%, 80%, 85%, 90%, or 95% identity with SEQ ID NO: 164. In some embodiments, the erythropoietin comprises an amino acid sequence having from 1 to 20 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 164. Or in other embodiments, the erythropoietin comprises an amino acid sequence having from 1 to 15 or from 1 to 10 amino acid insertions, deletions, or substitutions (collectively) with respect to SEQ ID NO: 164.

By “reprogramming” is meant causing a change in the phenotype of a cell, by way of non-limiting example, causing a β-cell progenitor to differentiate into a mature β-cell, causing a fibroblast to dedifferentiate into a pluripotent stem cell, causing a keratinocyte to transdifferentiate into a cardiac stem cell, causing the telomeres of a cell to lengthen or causing the axon of a neuron to grow.

By “reprogramming factor” is meant a molecule that, when a cell is contacted with the molecule and/or the cell expresses the molecule, can, either alone or in combination with other molecules, cause reprogramming, by way of non-limiting example, Oct4 protein, Tert protein or erythropoietin.

By “germ cell” is meant a sperm cell or an egg cell.

By “pluripotent stem cell” is meant a cell that can differentiate into cells of all three germ layers (endoderm, mesoderm, and ectoderm) *in vivo*.

By “somatic cell” is meant a cell that is not a pluripotent stem cell or a germ cell, by way of non-limiting example, a skin cell.

By “hematopoietic cell” is meant a blood cell or a cell that can differentiate into a blood cell, by way of non-limiting example, a hematopoietic stem cell or a white blood cell.

By “cardiac cell” is meant a heart cell or a cell that can differentiate into a heart cell, by way of non-limiting example, a cardiac stem cell or a cardiomyocyte.

By “retinal cell” is meant a cell of the retina or a cell that can differentiate into a cell of the retina, by way of non-limiting example, a retinal pigmented epithelial cell.

By “skin cell” is meant a cell that is normally found in the skin, by way of non-limiting example, a fibroblast, a keratinocyte, a melanocyte, an adipocyte, a mesenchymal stem cell, an adipose stem cell or a blood cell.

By “immunosuppressant” is meant a substance that can suppress one or more aspects of an immune system, and that is not normally present in a mammal, by way of non-limiting example, B18R or dexamethasone.

By “single-strand break” is meant a region of single-stranded or double-stranded DNA in which one or more of the covalent bonds linking the nucleotides has been broken in one of the one or two strands.

By “double-strand break” is meant a region of double-stranded DNA in which one or more of the covalent bonds linking the nucleotides has been broken in each of the two strands.

By “nucleotide” is meant a nucleotide or a fragment or derivative thereof, by way of non-limiting example, a nucleobase, a nucleoside, a nucleotide-triphosphate, *etc.*

By “nucleoside” is meant a nucleotide or a fragment or derivative thereof, by way of non-limiting example, a nucleobase, a nucleoside, a nucleotide-triphosphate, *etc.*

By “gene editing” is meant altering the DNA sequence of a cell, by way of non-limiting example, by transfecting the cell with a protein that causes a mutation in the DNA of the cell or by transfecting the cell with a protein that causes a chemical change in the DNA of the cell.

By “gene-editing protein” is meant a protein that can, either alone or in combination with one or more other molecules, alter the DNA sequence of a cell, by way of non-limiting example, a nuclease, a transcription activator-like effector nuclease (TALEN), a zinc-finger nuclease, a meganuclease, a nickase, a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a DNA-repair protein, a DNA-modification protein, a base-modification protein, a DNA methyltransferase, an protein that causes DNA demethylation, an enzyme for which DNA is a substrate or a natural or engineered variant, family-member, orthologue, domain, fragment or fusion construct thereof.

By “repair template” is meant a nucleic acid containing a region of at least about 70% homology with a sequence that is within 10kb of a target site of a gene-editing protein.

By “repeat sequence” is meant an amino-acid sequence that is present in more than one copy in a protein, to within at least about 10% homology, by way of non-limiting example, a monomer repeat of a transcription activator-like effector.

By “DNA-binding domain” is meant a region of a molecule that is capable of binding to a DNA molecule, by way of non-limiting example, a protein domain comprising one or more zinc fingers, a protein domain comprising one or more transcription activator-like (TAL) effector repeat sequences or a binding pocket of a small molecule that is capable of binding to a DNA molecule.

By “binding site” is meant a nucleic-acid sequence that is capable of being recognized by a gene-editing protein, DNA-binding protein, DNA-binding domain or a biologically active fragment or variant thereof or a nucleic-acid sequence for which a gene-editing protein, DNA-binding protein, DNA-binding domain or a biologically active fragment or variant thereof has high affinity, by way of non-limiting example, an about 20-base-pair sequence of DNA in exon 1 of the human BIRC5 gene.

By “target” is meant a nucleic acid that contains a binding site.

Other definitions are set forth in US Application No. 13/465,490, US Provisional Application No. 61/664,494, US Provisional Application No. 61/721,302, International Application No. PCT/US12/67966, US Provisional Application No. 61/785,404, US Provisional Application No. 61/842,874, International Application No. PCT/US13/68118, US Provisional Application No. 61/934,397, US Application No. 14/296,220, US Provisional Application No. 62/038,608, US Provisional Application No. 62/069,667, and International Application No. PCT/US2015/013949, the contents of which are hereby incorporated by reference in their entireties.

Selected Sequences

SEQ ID NO	Description
1	Stsl
2	Stsl-HA
3	Stsl-HA2
4	Stsl-UHA
5	Stsl-UHA2
6	Stsl-HF
7	Stsl-UHF
8	Oct4
9	Sox2
10	Klf4
11	c-Myc
12	BIRC5_exon1
13	BIRC5_exon2
14	BIRC5_exon3
15	BIRC5_exon4
16	BIRC5-1.1-L
17	BIRC5-1.1-R
18	BIRC5-1.2-L
19	BIRC5-1.2-R
20	BIRC5-1.3-L
21	BIRC5-1.3-R

22	BIRC5-2.1-L
23	BIRC5-2.1-R
24	BIRC5-2.2-L
25	BIRC5-2.2-R
26	BIRC5-3.1-L
27	BIRC5-3.1-R
28	CDK1
29	CDK2
30	CDK3
31	CDK4
32	CDK5
33	CDK6
34	BIRC5
35	HIF1A
36	RRM2
37	KRAS
38	EGFR
39	MYC
40	PKN3
41	KIF11
42	APC
43	BRCA1
44	BRCA2
45	TP53
46	APP
47	HTT
48	IAPP
49	MAPT
50	PRNP
51	SNCA
52	SOD1
53	FokI
54	Repeat1
55	Repeat2
56	Repeat3
57	EO-GHGG-FokI ("GHGG" disclosed as SEQ ID NO: 547)
58	GHGG-FokI ("GHGG" disclosed as SEQ ID NO: 547)
59	EO-GHGG-StsI ("GHGG" disclosed as SEQ ID NO: 547)
60	GHGG-StsI ("GHGG" disclosed as SEQ ID NO: 547)
61	collagen alpha-1(I) chain preproprotein
62	collagen alpha-2(I) chain precursor
63	collagen alpha-1(II) chain isoform 1 precursor
64	collagen alpha-1(II) chain isoform 2 precursor
65	collagen alpha-1(III) chain preproprotein
66	collagen alpha-1(IV) chain preproprotein

67	collagen alpha-2(IV) chain preproprotein
68	collagen alpha-3(IV) chain precursor
69	collagen alpha-4(IV) chain precursor
70	collagen alpha-5(IV) chain isoform 1 precursor
71	collagen alpha-6(IV) chain isoform A precursor
72	collagen alpha-1(V) chain isoform 1 preproprotein
73	collagen alpha-2(V) chain preproprotein
74	collagen alpha-3(V) chain preproprotein
75	collagen alpha-1(VI) chain precursor
76	collagen alpha-2(VI) chain isoform 2C2 precursor
77	collagen alpha-3(VI) chain isoform 1 precursor
78	collagen alpha-1(VII) chain precursor
79	elastin isoform a precursor
80	elastin isoform b precursor
81	elastin isoform c precursor
82	elastin isoform d precursor
83	elastin isoform e precursor
84	elastin isoform f precursor
85	elastin isoform g precursor
86	elastin isoform h precursor
87	elastin isoform i precursor
88	elastin isoform j precursor
89	elastin isoform k precursor
90	elastin isoform l precursor
91	elastin isoform m precursor
92	protein-lysine 6-oxidase isoform 1 preproprotein
93	protein-lysine 6-oxidase isoform 2
94	telomerase reverse transcriptase isoform 1
95	telomerase reverse transcriptase isoform 2
96	fibronectin isoform 1 preproprotein
97	fibronectin isoform 3 preproprotein
98	fibronectin isoform 4 preproprotein
99	fibronectin isoform 5 preproprotein
100	fibronectin isoform 6 preproprotein
101	fibronectin isoform 7 preproprotein
102	vitronectin precursor
103	nidogen-1 precursor
104	laminin subunit alpha-1 precursor
105	insulin-like growth factor I isoform 1 preproprotein
106	fibroblast growth factor 1 isoform 1 precursor
107	fibroblast growth factor 2
108	transforming growth factor beta-1 precursor
109	transforming growth factor beta-2 isoform 1 precursor
110	transforming growth factor beta-2 isoform 2 precursor
111	actin, alpha skeletal muscle

112	actin, aortic smooth muscle
113	actin, cytoplasmic 1
114	actin, alpha cardiac muscle 1 proprotein
115	actin, cytoplasmic 2
116	actin, gamma-enteric smooth muscle isoform 1 precursor
117	actin, gamma-enteric smooth muscle isoform 2 precursor
118	granulocyte colony-stimulating factor isoform a precursor
119	granulocyte colony-stimulating factor isoform b precursor
120	granulocyte colony-stimulating factor isoform c precursor
121	granulocyte colony-stimulating factor isoform d precursor
122	platelet-derived growth factor subunit A isoform 1 preproprotein
123	platelet-derived growth factor subunit A isoform 2 preproprotein
124	platelet-derived growth factor subunit B isoform 1 preproprotein
125	platelet-derived growth factor subunit B isoform 2 preproprotein
126	platelet-derived growth factor C precursor
127	platelet-derived growth factor D isoform 1 precursor
128	platelet-derived growth factor D isoform 2 precursor
129	interstitial collagenase isoform 1 preproprotein
130	interstitial collagenase isoform 2
131	neutrophil collagenase preproprotein
132	stromelysin-2 preproprotein
133	macrophage metalloelastase preproprotein
134	fibrillin-1 precursor
135	fibrillin-2 precursor
136	lysyl oxidase homolog 1 preproprotein
137	lysyl oxidase homolog 2 precursor
138	lysyl oxidase homolog 3 isoform 1 precursor
139	lysyl oxidase homolog 3 isoform 2 precursor
140	lysyl oxidase homolog 3 isoform 3
141	lysyl oxidase homolog 4 precursor
142	microfibrillar-associated protein 2 isoform a precursor
143	microfibrillar-associated protein 2 isoform b precursor
144	microfibrillar-associated protein 5 precursor
145	disintegrin and metalloproteinase domain-containing protein 17 preprotein
146	desmoglein-2 preproprotein
147	DNA polymerase eta isoform 1
148	DNA polymerase eta isoform 2
149	DNA polymerase eta isoform 3
150	ferrochelatase, mitochondrial isoform a precursor
151	ferrochelatase, mitochondrial isoform b precursor
152	filaggrin
153	hyaluronan synthase 1 isoform 1
154	hyaluronan synthase 1 isoform 2
155	hyaluronan synthase 2
156	hyaluronan synthase 3 isoform a

157	hyaluronan synthase 3 isoform b
158	proopiomelanocortin
159	plakophilin-1 isoform 1a
160	plakophilin-1 isoform 1b
161	retinol dehydrogenase 10
162	mitochondrial brown fat uncoupling protein 1
163	tyrosinase precursor
164	erythropoietin
165	epoetin alfa
166	darbepoetin alfa
167	NOVEPOETIN
168	NOVECRIT

This invention is further illustrated by the following non-limiting examples.

EXAMPLES

Example 1 RNA Synthesis

RNA encoding green fluorescent protein ("GFP"), NOVEPOETIN ("EPO"), elastin ("ELN"), tyrosinase ("TYR"), melanocortin-1-receptor ("MC1R"), HAS1, HAS2, HAS3, COL3A1, COL7A1, COL1A1, COL1A2, hTERT, Holly GFP, Fresno RFP, Blitzen Blue, RIBOSLICE gene-editing proteins, TALENs, Cas9, Oct4, Sox2, Klf4, c-Myc-2 (T58A), Lin28, IL2, IL6, IL15, IL22, BMP2, BMP7, BDNF, LIF, BMP6, IL15RA, FGF21, LIF, PTH, KRT5, KRT5-GFP, KRT14, KRT14-GFP, GDF15 and ESM1, and comprising various combinations of canonical and non-canonical nucleotides, was synthesized from DNA templates using the T7 High Yield RNA Synthesis Kit and the Vaccinia Capping System kit with mRNA Cap 2'-O-Methyltransferase (all from New England Biolabs, Inc.), according to the manufacturer's instructions and the present inventors' previously disclosed inventions (US Application No. 13/465,490 (now US Patent No. 8,497,124), International Application No. PCT/US12/67966, US Application No. 13/931,251, International Application No. PCT/US13/68118, and International Application No. PCT/US2015/013949, the contents of all of which are hereby incorporated by reference in their entirety) (**Table 4**). The RNA was then diluted with nuclease-free water to between 100ng/μL and 2000ng/μL. For certain experiments, an RNase inhibitor (Superase·In, Life Technologies Corporation) was added at a concentration of 1μL/100μg of RNA. RNA solutions were stored at room temperature, 4°C, -20°C or -80°C. For reprogramming experiments, RNA encoding Oct4, Sox2, Klf4, c-Myc-2 (T58A), and Lin28 was mixed at a molar ratio of 3:1:1:1.

Table 4. *RNA Synthesis*

Template	Nucleotides	Reaction Volume/μL	ivT Yield/μg
ELN	A, 0.5 7dG, 0.4 5mU, 5mC	20	34.1
ELN	A, 0.5 7dG, 0.4 5mU, 5mC	20	67.6
GFP	A, 0.5 7dG, 0.4 5mU, 5mC	10	60.5
GFP	A, 0.5 7dG, 0.4 5mU, 5hmC	10	25.5

GFP	A, G, U, 5hmC	10	58.3
GFP	A, 0.5 7dG, U, 5hmC	10	47.3
GFP	A, 0.5 7dG, 0.4 5mU, 5cC	10	33.8
GFP	A, G, U, 5hmC	15	30.3
GFP	A, G, U, 5hmC	15	44.6
GFP	A, G, U, 5hmC	15	24.7
TYR	A, G, U, 5hmC	15	45.4
MC1R	A, G, U, 5hmC	15	47.5
TYR	A, G, U, C	20	67.0
TYR	A, G, psU, C	20	93.7
TYR	A, G, 0.4 5mU, C	20	85.7
TYR	A, G, U, 5mC	20	73.4
TYR	A, G, U, 5hmC	20	72.7
TYR	A, 0.5 7dG, U, C	20	62.7
TYR	A, G, psU, 5mC	20	116.3
TYR	A, G, psU, 5hmC	20	102.4
TYR	A, 0.5 7dG, psU, C	20	87.3
TYR	A, G, 0.4 5mU, 5mC	20	106.5
TYR	A, G, 0.4 5mU, 5hmC	20	85.0
TYR	A, 0.5 7dG, 0.4 5mU, C	20	70.9
TYR	A, 0.5 7dG, U, 5mC	20	88.5
TYR	A, 0.5 7dG, U, 5hmC	20	59.1
TYR	A, 0.5 7dG, psU, 5mC	20	7.8
TYR	A, 0.5 7dG, psU, 5hmC	20	98.0
TYR	A, 0.5 7dG, 0.4 5mU, 5mC	20	106.5
TYR	A, 0.5 7dG, 0.4 5mU, 5hmC	20	82.3
HAS1	A, G, U, 5hmC	20	178.4
HAS2	A, G, U, 5hmC	20	59.3
HAS3	A, G, U, 5hmC	20	102.6
TYR	A, G, 0.4 5mU, 5hmC	100	377.3
COL3A1	A, G, 0.4 5mU, 5hmC	20	108.3
COL7A1	A, G, 0.4 5mU, 5hmC	20	94.6
COL1A1 (20 µL)	A, G, 0.4 5mU, 5hmC	20	114.0
COL1A2 (10 µL)	A, G, 0.4 5mU, 5hmC	10	31.3
TYR	A, G, 0.4 5mU, 5hmC	100	249.9
GFP	A, G, 0.4 5mU, 5hmC	100	264.0
hTERT	A, G, 0.4 5mU, 5hmC	100	349.2
GFP	A, G, U, 5hC	20	81.7
GFP	A, G, U, 0.5 5hC	20	65.4
GFP	A, sG, U, C	20	34.7
GFP	A, 0.5 sG, U, C	20	47.5
GFP	A, G, 5hmU, C	20	22.1
GFP	A, G, 0.5 5hmU, C	20	28.4
GFP	A, G, 5cU, C	20	24.4

GFP	A, G, 0.5 5cU, C	20	28.4
GFP	A, G, 5moU, C	20	39.2
GFP	A, G, 0.5 5moU, C	20	34.2
GFP	A, G, U, C	20	42.0
GFP	A, G, 5moU, C	20	53.8
GFP	A, G, 5moU, 5hmC	20	101.5
GFP	A, G, 0.4 5mU, 0.6 5moU, C	20	98.6
GFP	A, G, 0.4 5mU, C	20	99.6
GFP	A, G, U, 5mC	20	106.1
GFP	A, G, U, C	20	85.7
GFP	A, G, 5moU, C	100	398.4
hTERT	A, G, 5moU, C	20	82.6
COL7A1	A, G, 5moU, C	20	34.9
COL7A1	A, G, 5moU, C	100	342.0
Holly GFP	A, G, 5moU, C	20	36.7
Fresno RFP	A, G, 5moU, C	20	72.0
Blitzen Blue	A, G, 5moU, C	20	30.3
hTERT	A, G, 5moU, C	20	49.6
Cas9	A, G, 5moU, C	20	31.6
EPO	A, G, U, C	20	101.0
EPO	A, G, 5moU, C	20	52.9
EPO	A, G, psU, C	20	106.0
COL7A1	A, G, 5moU, C	20	80.2
Oct4 (SEQ ID NO: 8)	A, G, 5moU, C	300	1925.5
Sox2 (SEQ ID NO: 9)	A, G, 5moU, C	100	641.8
Klf4 (SEQ ID NO: 10)	A, G, 5moU, C	100	739.0
c-Myc-2 (T58A)	A, G, 5moU, C	100	574.0
Lin28	A, G, 5moU, C	100	556.0
IL2	A, G, 5moU, C	20	62.4
IL6	A, G, 5moU, C	20	22.2
IL15	A, G, 5moU, C	20	50.4
IL22	A, G, 5moU, C	20	63.6
BMP2	A, G, 5moU, C	20	83.2
BDNF	A, G, 5moU, C	20	45.0
LIF	A, G, 5moU, C	20	54.0
BMP6	A, G, 5moU, C	20	92.2
IL15RA	A, G, 5moU, C	20	91.4
FGF21	A, G, 5moU, C	20	79.2
GFP	A, G, 5moU, C	40	181.0
IL2	A, G, 5moU, C	30	99.4
IL6	A, G, 5moU, C	30	31.2
IL15	A, G, 5moU, C	30	89.8
IL22	A, G, 5moU, C	30	104.0
BDNF	A, G, 5moU, C	30	95.9

BMP2	A, G, 5moU, C	30	112.0
LIF	A, G, 5moU, C	30	116.0
PTH	A, G, 5moU, C	30	88.4
EPO	A, G, 5moU, C	30	83.3
KRT5	A, G, 5moU, C	15	66.6
KRT5-GFP	A, G, 5moU, C	15	81.1
KRT14	A, G, 5moU, C	15	75.1
KRT14-GFP	A, G, 5moU, C	15	90.4
GDF15	A, G, 5moU, C	15	71.1
A1AT TALEN L	A, G, 5moU, C	15	56.4
A1AT TALEN R	A, G, 5moU, C	15	57.3
A1AT RIBOSLICE L_A	A, G, 5moU, C	15	74.3
A1AT RIBOSLICE L_B	A, G, 5moU, C	15	56.4
A1AT RIBOSLICE R_A	A, G, 5moU, C	15	60.3
A1AT RIBOSLICE R_B	A, G, 5moU, C	15	35.7
COL7A1 exon 73 TALEN L	A, G, 5moU, C	15	86.48
COL7A1 exon 73 TALEN R	A, G, 5moU, C	15	83.66
COL7A1 exon 73 rs3L 50A	A, G, 5moU, C	15	103.4
COL7A1 exon 73 rs3L 50B	A, G, 5moU, C	15	112.8
COL7A1 exon 73 rs3R 50A	A, G, 5moU, C	15	81.404
COL7A1 exon 73 rs3R 50B	A, G, 5moU, C	15	78.02
COL7A1 exon 73 TALEN L EA	A, G, 5moU, C	15	88.924
COL7A1 exon 73 TALEN L Het	A, G, 5moU, C	15	75.2
COL7A1 exon 73 TALEN R EA	A, G, 5moU, C	15	86.48
COL7A1 exon 73 TALEN R Het	A, G, 5moU, C	15	62.98
COL7A1 exon 73 TALEN L EA/Het	A, G, 5moU, C	15	82.7
COL7A1 exon 73 TALEN R EA/Het	A, G, 5moU, C	15	69.7
HBB exon 1 TALEN L	A, G, 5moU, C	15	112.8
HBB exon 1 TALEN R	A, G, 5moU, C	15	108.1
PD-1 exon 1 TALEN L	A, G, 5moU, C	15	95.88
PD-1 exon 1 TALEN R	A, G, 5moU, C	15	101.52
ESM1 - transcript variant 1	A,G,5moU,C	15	61
ESM1 - transcript variant 2	A,G,5moU,C	15	66

“A” refers to adenosine-5'-triphosphate, “G” refers to guanosine-5'-triphosphate, “U” refers to uridine-5'-triphosphate, “C” refers to cytidine-5'-triphosphate, “7dG” refers to 7-deazaguanosine-5'-triphosphate, “sG” refers to thienoguanosine-5'-triphosphate, “5mC” refers to 5-methylcytidine-5'-triphosphate, “5hmC” refers to 5-

hydroxymethylcytidine-5'-triphosphate, "5cC" refers to 5-carboxycytidine-5'-triphosphate, "5fC" refers to 5-formylcytidine-5'-triphosphate, "5hC" refers to 5-hydroxycytidine-5'-triphosphate, "psU" refers to 5-pseudouridine-5'-triphosphate, "5mU" refers to 5-methyluridine-5'-triphosphate, "5hmU" refers to 5-hydroxymethyluridine-5'-triphosphate, "5cU" refers to 5-carboxyuridine-5'-triphosphate, and "5moU" refers to 5-methoxyuridine-5'-triphosphate.

Example 2 Preparation of RNA-Transfection-Reagent Complexes

For each microgram of RNA, 1µg RNA and 1µL transfection reagent (LIPOFECTAMINE 3000, Life Technologies Corporation) were first diluted separately in complexation medium (Opti-MEM, Life Technologies Corporation or DMEM/F12 + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 2µg/mL ethanolamine) to a total volume of between 5µL and 100µL each. Diluted RNA and transfection reagent were then mixed and incubated for 10min at room temperature, according to the transfection reagent-manufacturer's instructions.

Example 3 Transfection of Cells with Synthetic RNA

Complexes were prepared according to Example 2, and were then added directly to cells in culture. For transfection in 6-well plates, between 10µL and 250µL of complexes were added to each well of the 6-well plate, which already contained 2mL of transfection medium per well. Plates were shaken gently to distribute the complexes throughout the well. Cells were incubated with complexes for 4 hours to overnight, before replacing the medium with fresh transfection medium (2mL/well). Alternatively, the medium was not replaced. Volumes were scaled for transfection in 24-well and 96-well plates.

Example 4 Toxicity of and Protein Translation from Synthetic RNA Containing Non-Canonical Nucleotides

Primary human fibroblasts were transfected according to Example 2, using RNA synthesized according to Example 1. Cells were fixed and stained 20-24h after transfection using an antibody against Oct4. The relative toxicity of the RNA was determined by assessing cell density at the time of fixation.

Example 5 Delivery of Synthetic RNA to the Skin

The complexation reaction shown in **Table 5** was prepared using RNA encoding green fluorescent protein (GFP) or collagen, type VII, alphal (COL7), synthesized according to Example 1. The concentration of the RNA stock solution was 500µg/mL.

Table 5. *RNA Complexation Reaction*

RNA solution tube	Volume
GFP or COL7 RNA	8µL
FactorPlex™ complexation buffer	42µL
Transfection reagent solution tube	
LIPOFECTAMINE 3000 (LIFE TECHNOLOGIES)	4µL
FactorPlex™ complexation buffer	46µL

Each tube was mixed by pipetting, and the transfection reagent solution tube was incubated for 30s at room temperature. The transfection reagent solution was then transferred to the RNA solution, and the contents were mixed by rapidly pipetting up and down 10 times. Following a 10min incubation, dilutions were prepared according to

Table 6. *Injection Solutions*

Site	RNA	Complexation Volume	FactorPlex™ Volume	RNA amount
1	GFP	7.5µL	22.5µL	0.3µg
2	GFP	15µL	15µL	0.6µg
3	GFP	30µL	0µL	1.2µg
4	COL7	30µL	0µL	1.2µg

For each injection, the corresponding solution was drawn into a 3cc insulin syringe with an 8mm, 31 gauge needle (Becton, Dickinson and Company, Part Number: 328291) and air bubbles were removed. A clear field was selected on the left forearm of a healthy 33 year-old male human subject, and was disinfected with 70% isopropanol and allowed to dry. The needle was positioned at an angle of approximately 10° to the anterior (palmar) forearm with bevel facing up, and was inserted until the bevel was just covered. 30µL of the RNA solution was injected intradermally over the course of approximately 10sec. A distinct wheal appeared during the injection process. The needle was withdrawn, the wheal remained for approximately 1 minute, and no fluid escaped from the injection site. A total of 4 injections were performed according to **Table 6**, and all of the injections were performed between 11 and 28 minutes following the preparation of the RNA complexation reaction. No swelling, redness, or soreness occurred as a result of the injections. A small amount of bleeding occurred when the needle was removed from sites 2 and 4, resulting in the appearance of a small red spot at these sites.

The injection sites were imaged according to the schedule of **Table 7**, and every 24 hours thereafter for 6 days. Fluorescence images were acquired using an inverted microscope (Nikon Eclipse TS100) equipped with an EXFO X-Cite™ 120 fluorescence illumination system and the filter sets shown in **Table 7**. Fluorescence images were captured using a Sony NEX-7 digital camera (**FIGs. 9-12**).

Table 7. *Measurement Parameters*

Site	Time	Image Type	Exposure Time
All	0h	Brightfield	Automatic
1	0h	FITC	1/10s
2	0h	FITC	1/10s
3	0h	FITC	1/10s
4	0h	FITC	1/10s
1	12h	FITC	1/10s
2	12h	FITC	1/10s
3	12h	FITC	1/10s

4	12h	FITC	1/10s
1	12h	FITC	1/20s
2	12h	FITC	1/20s
3	12h	FITC	1/20s
4	12h	FITC	1/20s
All	24h	Brightfield	Automatic
1	24h	FITC	1/20s
2	24h	FITC	1/20s
3	24h	FITC	1/20s
4	24h	FITC	1/20s
1	24h	Cy3.5	1/5s
2	24h	Cy3.5	1/5s
3	24h	Cy3.5	1/5s
4	24h	Cy3.5	1/5s
1	24h	Cy3	1/5s
2	24h	Cy3	1/5s
3	24h	Cy3	1/5s
4	24h	Cy3	1/5s
1	36h	FITC	1/20s
2	36h	FITC	1/20s
3	36h	FITC	1/20s
4	36h	FITC	1/20s
1	48h	FITC	1/20s
2	48h	FITC	1/20s
3	48h	FITC	1/20s
4	48h	FITC	1/20s

An independent experiment was carried out using the 1.2µg dose of GFP RNA, with similar results (**FIG. 12**).

Table 8. *Filter Sets*

Image Type	Filter Set
Cy3	Chroma SP102V2
Cy3.5	Chroma SP103V2
FITC	Chroma SP101

Example 6 Transfection of Human Keratinocytes with RNA Encoding NOVEPOETIN

RNA encoding NOVEPOETIN was synthesized according to Example 1 with three nucleotide combinations: 1) U, G, U, C, 2) U, G, 5moU, C, and 3) U, G, psU, C. Sub-confluent layers of primary human keratinocytes cultured in EpiLife medium were transfected in wells of a 6 well plate according to Example 3 with 1 µg of RNA per well. 12, 24, 36 and 48h following transfection, 0.5 mL of medium was removed and 0.5 mL of fresh EpiLife medium was added to the plate. After the final medium sampling, the cells were harvested by trypsinization, and total RNA

was isolated using the RNeasy mini kit (Qiagen). Genomic DNA was digested using DNase I and RNA was purified. Expression of interferon-β and GAPDH was measured by RT-PCR (**FIG. 5**).

Example 7 Transfection of Human Cells with RNA Encoding hTERT

RNA encoding human telomerase reverse transcriptase (hTERT) was synthesized according to Example 1 with the following nucleotides: U, G, 5moU, C. A sub-confluent layer of primary human dermal fibroblasts cultured in DMEM+10%FBS were transfected in wells of a 24 well plate according to Example 3 with 0.25 µg of RNA per well. 12h after transfection, cells were fixed and stained using a 1:50 dilution of rabbit anti-hTERT antibody (Millipore, Part Number: MABE14) (**FIG. 16**).

Example 8 High-Efficiency Gene Editing by Repeated Transfection with RIBOSLICE

Primary human fibroblasts were plated in 6-well plates coated with recombinant human fibronectin and recombinant human vitronectin (each diluted in DMEM/F12 to a concentration of 1µg/mL, 1mL/well, and incubated at room temperature for 1h) at a density of 10,000 cells/well in transfection medium. The following day, the cells were transfected as in Example 2 with RNA synthesized according to Example 1. The following day cells in one of the wells were transfected a second time. Two days after the second transfection, the efficiency of gene editing was measured using a mutation-specific nuclease assay.

Example 9 Transfection of Cells with Synthetic RNA Containing Non-Canonical Nucleotides and DNA Encoding a Repair Template

For transfection in 6-well plates, 1µg RNA encoding gene-editing proteins targeting exon 16 of the human APP gene, 1µg single-stranded repair template DNA containing a PstI restriction site that was not present in the target cells, and 6µL transfection reagent (LIPOFECTAMINE RNAiMAX, Life Technologies Corporation) were first diluted separately in complexation medium (Opti-MEM, Life Technologies Corporation) to a total volume of 120µL. Diluted RNA, repair template, and transfection reagent were then mixed and incubated for 15min at room temperature, according to the transfection reagent-manufacturer's instructions. Complexes were added to cells in culture. Approximately 120µL of complexes were added to each well of a 6-well plate, which already contained 2mL of transfection medium per well. Plates were shaken gently to distribute the complexes throughout the well. Cells were incubated with complexes for 4 hours to overnight, before replacing the medium with fresh transfection medium (2mL/well). The next day, the medium was changed to DMEM + 10% FBS. Two days after transfection, genomic DNA was isolated and purified. A region within the APP gene was amplified by PCR, and the amplified product was digested with PstI and analyzed by gel electrophoresis.

Example 10 in vivo RIBOSLICE Safety Study

40 female NCr nu/nu mice were injected subcutaneously with 5 x 10^6 MDA-MB-231 tumor cells in 50% Matrigel (BD Biosciences). Cell injection volume was 0.2mL/mouse. The age of the mice at the start of the study was 8 to 12 weeks. A pair match was conducted, and animals were divided into 4 groups of 10 animals each when the tumors reached an average size of 100-150mm^3, and treatment was begun. Body weight was measured every

day for the first 5 days, and then biweekly to the end of the study. Treatment consisted of RIBOSLICE BIRC5-1.2 complexed with a vehicle (LIPOFECTAMINE 2000, Life Technologies Corporation). To prepare the dosing solution for each group, 308µL of complexation buffer (Opti-MEM, Life Technologies Corporation) was pipetted into each of two sterile, RNase-free 1.5mL tubes. 22µL of RIBOSLICE BIRC5-1.2 (500ng/µL) was added to one of the two tubes, and the contents of the tube were mixed by pipetting. 22µL of vehicle was added to the second tube. The contents of the second tube were mixed, and then transferred to the first tube, and mixed with the contents of the first tube by pipetting to form complexes. Complexes were incubated at room temperature for 10min. During the incubation, syringes were loaded. Animals were injected either intravenously or intratumorally with a total dose of 1µg RNA/animal in 60µL total volume/animal. A total of 5 treatments were given, with injections performed every other day. Doses were not adjusted for body weight. Animals were followed for 17 days. No significant reduction in mean body weight was observed, demonstrating the *in vivo* safety of RIBOSLICE gene-editing RNA.

Example 11 Screening of Reagents for Delivery of Nucleic Acids to Cells

Delivery reagents including polyethyleneimine (PEI), various commercial lipid-based transfection reagents, a peptide-based transfection reagent (N-TER, Sigma-Aldrich Co. LLC.), and several lipid-based and sterol-based delivery reagents were screened for transfection efficiency and toxicity *in vitro*. Delivery reagents were complexed with RIBOSLICE BIRC5-1.2, and complexes were delivered to HeLa cells in culture. Toxicity was assessed by analyzing cell density 24h after transfection. Transfection efficiency was assessed by analyzing morphological changes. The tested reagents exhibited a wide range of toxicities and transfection efficiencies. Reagents containing a higher proportion of ester bonds exhibited lower toxicities than reagents containing a lower proportion of ester bonds or no ester bonds.

Example 12 High-Concentration Liposomal RIBOSLICE

High-Concentration Liposomal RIBOSLICE was prepared by mixing 1µg RNA at 500ng/µL with 3µL of complexation medium (Opti-MEM, Life Technologies Corporation), and 2.5µL of transfection reagent (LIPOFECTAMINE 2000, Life Technologies Corporation) per µg of RNA with 2.5µL of complexation medium. Diluted RNA and transfection reagent were then mixed and incubated for 10min at room temperature to form High-Concentration Liposomal RIBOSLICE. Alternatively, a transfection reagent containing DOSPA or DOSPER is used.

Example 13 In Vivo RIBOSLICE Efficacy Study – Subcutaneous Glioma Model

40 female NCr nu/nu mice were injected subcutaneously with 1 x 10^7 U-251 tumor cells. Cell injection volume was 0.2mL/mouse. The age of the mice at the start of the study was 8 to 12 weeks. A pair match was conducted, and animals were divided into 4 groups of 10 animals each when the tumors reached an average size of 35-50mm^3, and treatment was begun. Body weight was measured every day for the first 5 days, and then biweekly to the end of the study. Caliper measurements were made biweekly, and tumor size was calculated. Treatment consisted of RIBOSLICE BIRC5-2.1 complexed with a vehicle (LIPOFECTAMINE 2000, Life Technologies

Corporation). To prepare the dosing solution, 294µL of complexation buffer (Opti-MEM, Life Technologies Corporation) was pipetted into a tube containing 196µL of RIBOSLICE BIRC5-1.2 (500ng/µL), and the contents of the tube were mixed by pipetting. 245µL of complexation buffer was pipetted into a tube containing 245µL of vehicle. The contents of the second tube were mixed, and then transferred to the first tube, and mixed with the contents of the first tube by pipetting to form complexes. Complexes were incubated at room temperature for 10min. During the incubation, syringes were loaded. Animals were injected intratumorally with a total dose of either 2µg or 5µg RNA/animal in either 20µL or 50µL total volume/animal. A total of 5 treatments were given, with injections performed every other day. Doses were not adjusted for body weight. Animals were followed for 25 days.

Example 14 Liposome Formulation and Nucleic-Acid Encapsulation

Liposomes are prepared using the following formulation: 3.2mg/mL N-(carbonyl-ethoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine (MPEG2000-DSPE), 9.6mg/mL fully hydrogenated phosphatidylcholine, 3.2mg/mL cholesterol, 2mg/mL ammonium sulfate, and histidine as a buffer. pH is controlled using sodium hydroxide and isotonicity is maintained using sucrose. To form liposomes, lipids are mixed in an organic solvent, dried, hydrated with agitation, and sized by extrusion through a polycarbonate filter with a mean pore size of 800nm. Nucleic acids are encapsulated by combining 10µg of the liposome formulation per 1µg of nucleic acid and incubating at room temperature for 5 minutes.

Example 15 Folate-Targeted Liposome Formulation

Liposomes are prepared using the following formulation: 3.2mg/mL N-(carbonyl-ethoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine (MPEG2000-DSPE), 9.6mg/mL fully hydrogenated phosphatidylcholine, 3.2mg/mL cholesterol, 2mg/mL ammonium sulfate, and histidine as a buffer, with 0.27mg/mL 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[folate(polyethylene glycol)-5000] (FA-MPEG5000-DSPE) added to the lipid mixture. pH is controlled using sodium hydroxide and isotonicity is maintained using sucrose. To form liposomes, lipids are mixed in an organic solvent, dried, hydrated with agitation, and sized by extrusion through a polycarbonate filter with a mean pore size of 800nm. Nucleic acids are encapsulated by combining 10µg of the liposome formulation per 1µg of nucleic acid and incubating at room temperature for 5 minutes.

Example 16 Therapy Comprising Liposomal Protein-Encoding RNA

Liposomes encapsulating synthetic RNA encoding a therapeutic protein, synthesized according to Example 1, are prepared according to Example 14 or Example 15. The liposomes are administered by injection or intravenous infusion.

Example 17 Generation of Elastin ivT-RNA template

Total RNA was extracted from neonatal human dermal fibroblasts using the RNeasy mini kit (QIAGEN GmbH), according to the manufacturer's instructions. cDNA encoding human elastin was prepared using MonsterScript™

Reverse Transcriptase (Epicentre Biotechnologies) and the primer: AAAAAAACCGGT TCATTTTCTCTTCCGGCCAC (SEQ ID NO: 483). An *in vitro* transcription (ivT) template was prepared from the cDNA by PCR amplification of the elastin coding sequence (CDS) using the primers: F: AAAAAAGCTAGCATGGCGGGTCTGACG (SEQ ID NO: 484), and R: AAAAAAACCGGTTCATTTTCTCTTCCGGCCAC (SEQ ID NO: 485). The PCR product was then purified using agarose gel electrophoresis and the QIAquick Gel Extraction Kit (QIAGEN GmbH) and was cloned into a vector containing the human beta globin (HBB) 5' and 3' untranslated regions and a strong Kozak sequence. The vector was amplified, purified, and linearized prior to RNA synthesis.

Example 18 Generation of Tyrosinase ivT-RNA Template

Total RNA was extracted from human epidermal melanocytes using the RNeasy mini kit (QIAGEN GmbH), according to the manufacturer's instructions. cDNA encoding human tyrosinase was prepared using MonsterScript™ Reverse Transcriptase (Epicentre Biotechnologies). An *in vitro* transcription (ivT) template was prepared from the cDNA by PCR amplification of the tyrosinase coding sequence (CDS). The PCR product was then purified using agarose gel electrophoresis and the QIAquick Gel Extraction Kit (QIAGEN GmbH) and was cloned into a vector containing the human beta globin (HBB) 5' and 3' untranslated regions and a strong Kozak sequence. The vector was amplified, purified, and linearized prior to RNA synthesis.

Example 19 Synthesis of Tyrosinase RNA

RNA encoding human tyrosinase was synthesized according to Example 1, using the DNA template of Example 18 and the T7 High Yield RNA Synthesis Kit (New England Biolabs, Inc.), according to the manufacturer's instructions (**Table 4**). Samples of the RNA were analyzed by agarose gel electrophoresis to assess the quality of the RNA. The RNA was then diluted to 1µg/µL. The RNA solution was stored at 4C.

Example 20 Increasing Melanin Production in Skin by Transdermal Injection via Syringe of RNA Encoding Tyrosinase

The RNA of Example 19 was loaded into a syringe and delivered by intradermal injection to the ventral forearm of a healthy 33 year-old male patient over the course of approximately 30 seconds.

Example 21 Increasing Melanin Production in Skin by Combined Delivery of RNA Encoding Tyrosinase and Electroporation

The area of skin treated in Example 20 was exposed to electrical pulses of between 10V and 155V and between approximately 10 milliseconds and approximately 1 second using a two-electrode array electrically connected to a capacitor. The patient reported a tingling sensation at all voltages and penetration depths. The treated area became darker after 24-48 hours. The experiment was repeated several times, with similar results.

Example 22 Increasing Melanin Production in Skin by Topical or Intradermal Application of RNA Encoding Tyrosinase

The RNA of Example 19 or the liposomes of Example 16 are applied directly to the skin, with or without disruption of the stratum corneum or injected intradermally or delivered by injection to the epidermis using a dose of one microgram or less per square centimeter. Optionally, an electric field is applied as in Example 21 or using a surface-contact patch to enhance delivery of the RNA.

Example 23 Increasing Elastin Production in Skin by Transdermal Delivery of RNA Encoding Elastin

RNA encoding elastin was prepared according to Example 1. The RNA is delivered as in Example 20, 21, or 22.

Example 24 Increasing Collagen Production in Skin by Transdermal Delivery of RNA Encoding Collagen

RNA encoding collagen was prepared according to Example 1. The RNA is delivered as in Example 20, 21, or 22.

Example 25 Anemia Therapy Comprising Delivery of RNA Encoding NOVEPOETIN

RNA encoding NOVEPOETIN was prepared according to Example 1. The RNA is delivered as in Example 20, 21, or 22.

Example 26 Increasing Production of Actin in Skeletal Muscle by Intramuscular Delivery of RNA Encoding Actin

RNA encoding actin is prepared according to Example 1. The RNA is delivered to the patient via intramuscular injection with or without the use of an electric field as in Example 20, 21, or 22.

Example 27 Wound Healing Treatment

RNA encoding basic fibroblast growth factor or IL22 is prepared according to Example 1. The RNA is delivered as in Example 20, 21, or 22.

Example 28 Anti-Scarring Treatment

RNA encoding collagenase is prepared according to Example 1. The RNA is delivered as in Example 20, 21, or 22.

Example 29 Production of Botulinum Toxin

RNA encoding botulinum toxin is prepared according to Example 1. The RNA is delivered as in Example 20, 21, or 22.

Example 30 Increasing Collagen Production in Skin Cells by Transfection with RNA Encoding Collagen I

RNA comprising the coding sequence of the human COL1A1 gene was synthesized according to Example 1. Primary human dermal fibroblasts were plated in wells of a 24-well plate, and were transfected according to Example 2. Between 24 and 72 hours after transfection, the cells were fixed and stained using an antibody targeting collagen I. Many extracellular deposits of collagen were visible in the transfected wells.

Example 31 Increasing Collagen Production in Skin Cells by Transfection with RNA Encoding Collagen VII

RNA comprising the coding sequence of the human COL7 gene was synthesized according to Example 1. Primary human dermal fibroblasts were plated in wells of a 24-well plate, and were transfected according to Example 2. Between 24 and 72 hours after transfection, the cells were fixed and stained using an antibody targeting collagen VII. Transfected cells exhibited high levels of collagen VII, compared to an un-transfected control.

Example 32 Increasing Collagen Production in Skin by Transdermal Injection via Syringe of RNA Encoding Collagen I or Collagen VII

RNA comprising the coding sequence of the human COL1A1 gene or the human COL7 gene was synthesized according to Example 1. The RNA is loaded into a syringe and delivered to the dermis of a patient over the course of approximately 30 seconds or as in Example 20, 21, or 22.

Example 33 Increasing Collagen Production in Skin by Combined Delivery of RNA Encoding Collagen I or Collagen VII and Electroporation

The area of skin treated in Example 32 is exposed to electrical pulses of between 10V and 155V and between approximately 50 microseconds and approximately 1 second using a multi-electrode array electrically connected to a power source.

Example 34 Storage and Stability of Synthetic RNA Complexes

A complexation reaction using RNA encoding GFP was prepared according to Example 5. Following the 10 min incubation, the complexation reaction was divided into three equal parts, one of which was diluted 1:10 in FactorPlex™ complexation medium, one of which was diluted 1:10 in sterile, nuclease-free water, and one of which was left undiluted. Each of the three parts was then further divided into four equal parts, one of which was applied to primary human dermal fibroblasts according to Example 3, one of which was left at room temperature for six hours before applying to primary human dermal fibroblasts according to Example 3, one of which was placed at 4ºC for six hours before applying to primary human dermal fibroblasts according to Example 3, and one of which was snap frozen in liquid nitrogen and placed at -80°C for six hours before applying to primary human dermal fibroblasts according to Example 3. The cells were imaged using a fluorescence microscope approximately 24 hours after the first transfection (**FIG. 17**). All wells contained GFP-positive cells, demonstrating that the synthetic RNA complexes were stable and maintained activity in all of the storage conditions tested.

Example 35: In Vivo Analysis of NOVECRIT

RNA encoding NOVEPOETIN was synthesized according to Example 1 with the nucleotide combination A, G, 5moU, C. In this Example, NOVECRIT was formulated with a lipid delivery vehicle, specifically LIPOFECTAMINE 3000. In this Example, NOVECRIT encoded NOVEPOETIN, a novel, high-stability erythropoiesis-stimulating agent.

A 15-day maximum tolerated dose (MTD) study was performed to evaluate safety (rat, n=62). *In vivo* toxicology and biodistribution, as well as pharmacodynamics and dose response and therapeutic effect, specifically on

erythropoiesis, were evaluated. Furthermore, the immune response was monitored by analysis of cytokines in treated animals.

Sixty-nine, naïve, 8 week old male Sprague-Dawley rats (*Rattus norvegicus*) weighing 253 to 274 grams at receipt were used (HARLAN LABORATORIES). Animals were acclimated to the study room for at least seven days prior to dosing. On Day -2 all animals were shaved in the dorsal lumbar area and four intradermal sites (upper left, upper right, lower right and lower left) were designated on the dorsal back using a permanent marker. Sixty-four animals were randomly assigned to four treatment groups, with the remaining five animals serving as spares. Two animals were dropped from the study because of incomplete dosing.

The following study design was used (total dose volumes (µL) were constant):

Group	Dose Level (µg)	Dose Route	Conc. (µg/mL)	Dose Vol. (µL)	Number of Males
1	0	Intradermal	0	50	$4^a + 2^b + 2^h$
2	0.25	Intradermal	5.0	50	$4^a + 2^b + 2^c + 2^d + 2^e + 2^f + 2^g + 2^h$
3	1.0	Intradermal	20	50	$4^a + 2^b + 2^c + 2^d + 2^e + 2^f + 2^g + 2^h$
4	4 X 1.0 µg (4.0 µg total)	Intradermal	20	50	$4^a + 2^b + 3^c + 3^d + 2^e + 2^f + 2^g + 2^h$

ID: [a] Toxicology animals necropsy on Day 15, TK animals with terminal tissue collections on Days 6 ([b]) and 24 ([c]) hours postdose, and on Days 3 ([d]), 4 ([e]), 6 ([f]), 8 ([g]), and 15 ([h])

Blood was collected from the vena cava from anesthetized animals prior to necropsy or terminal tissue collection. Whenever possible, blood was collected via a single draw and then divided appropriately. Blood specimens for toxicokinetic analysis were collected from two animals per time point for Group 1 at 6 hours postdose and on Day 15. For Groups 2-4, blood specimens were collected at 6 and 24 hours postdose, and on Days 3, 4, 6, 8, and 15.

Blood specimens for hematology assessment were collected from all toxicology animals on Day 15 following an overnight fast, and all TK animals scheduled for terminal tissue collections at 6 and 24 hours postdose and on Days 8 and 15. Whole blood (1.3 mL) was deposited into K2EDTA tubes and analyzed using an Advia 120 automated analyzer.

Blood specimens for coagulation assessment were collected from all toxicology animals on Day 15 following an overnight fast. Coagulation specimens (1.8 mL) were collected into 3.2% sodium citrate tubes, processed according to standard procedures and analyzed using a STA Compact automated analyzer.

Blood specimens for serum chemistry assessments were collected from all toxicology animals on Day 15 following an overnight fast. Serum chemistry specimens (1 mL) were collected into serum separator tubes, processed according to standard procedures and analyzed using an AU680 analyzer.

Blood specimens for cytokine analysis were collected from animals scheduled for terminal tissue collection at 5 and 24 hours postdose and Day 8. Cytokine specimens (1 mL) were collected into K2EDTA tubes and processed to plasma according to standard procedures. TNFα, IL-6, and IFNα cytokine levels in plasma samples were studied. The study measured the production of TNFα, IL-6, and IFNα cytokines in plasma samples following dosing with the test article on Day 1 (6 hours post-dose), Day 2 (24 hours post-dose) and Day 8.

Study Outline for Cytokine Analysis Samples:

Group	NOVECRIT Dose Level (µg)	Dose Concentration (µg/mL)	Dose Volume (µL)	Number of Rats (Males)	Endpoints
1	0	0	50	2[b]	Plasma TNFα, IL-6, and IFNα cytokine analysis
2	0.25	5.0	50	2[b] + 2[c] +2[g]	
3	1.0	20	50	2[b] + 2[c] +2[g]	
4	4 x 1.0 µg (4.0 µg total)	20	50	2[b] + 2[c] +2[g]	

b = plasma samples collected 6 hours post-dose, c = plasma samples collected 24 hours post-dose, g = plasma samples collected 8 days post-dose.

For TNFα analysis, plasma samples were analyzed using a commercially-available assay kit from R&D SYSTEMS (cat. no. RTA00). The rat TNFα ELISA is a solid phase enzyme-linked immunosorbent assay. The ELISA kit employs a TNFα-specific anti-rat monoclonal antibody for solid phase immobilization (pre-coated on the microtiter plate), and HRP conjugated to an anti-rat TNFα polyclonal antibody for detection. The reference standard provided with the kit is a recombinant rat TNFα. For each assay, plasma samples and standards were diluted with the diluent provided in each respective kit. For the TNFα ELISA, plasma samples were diluted 1:2. The standard curve consisted of six (6) serial 2-fold concentrations ranging from 800 to 12.5 pg/mL. Controls were reconstituted with diluent, and blanks contained diluent only.

Following sample, standard, control, or diluent addition (50 µL per well, each in duplicate), plates were incubated for 2 hours at room temperature. Following a wash step to remove unbound substances, HRP conjugate was added to each well (100 µL/well), and plates were incubated for 2 hours at room temperature. Following a second wash step, 100 µL/well TMB substrate was added to the plate. The plate was incubated for 30 minutes at room temperature, protected from light, to allow the color reaction to develop. The reaction was stopped following the addition of HCl Stop Solution (100 µL/well). The optical density was read on a SpectraMax 340 (MOLECULAR DEVICES) plate reader at 450 nm, within 30 minutes following addition of Stop Solution. The intensity of the color measured was in proportion to the amount of rat TNFα bound in the initial step. A standard curve was generated for each assay plate, and test sample TNFα concentrations were determined by interpolation of absorbance A_{450} values from the standard curve and dilution factor. The assay range for the

TNFα kit is 12.5 - 800 pg/mL, with a minimum detectable concentration of less than 10 pg/mL (with the 1:2 minimum required dilution for plasma samples).

For IL-6 analysis, plasma IL-6 samples were analyzed using a commercially-available assay kit from R&D SYSTEMS (cat. no. R6000B – IL-6). The rat IL-6 ELISA is a solid phase enzyme-linked immunosorbent assay. The ELISA kit employs anti-rat IL-6 monoclonal antibody for solid phase immobilization (pre-coated on the microtiter plate), and HRP conjugated to IL-6-specific anti-rat polyclonal antibody for detection. The reference standard provided with the kit is a recombinant rat IL-6. Plasma samples were used undiluted (as provided), and standards were diluted with the diluent provided in the kit. The standard curve consisted of six (6) serial 2-fold concentrations ranging from 4,000 to 62.5 pg/mL. Controls were reconstituted with diluent, and blanks contained diluent only. Following sample, standard, control, or diluent addition (50 µL per well, each in duplicate), plates were incubated for 2 hours at room temperature. Following a wash step to remove unbound substances, HRP conjugate was added to each well (100 µL/well), and plates were incubated for 2 hours at room temperature. Following a second wash step, 100 µL/well TMB substrate was added to the plate. The plate was incubated for 30 minutes at room temperature, protected from light, to allow the color reaction to develop. The reaction was stopped following the addition of HCl Stop Solution (100 µL/well). The optical density was read on a SpectraMax 340 (MOLECULAR DEVICES) plate reader at 450 nm, within 30 minutes following addition of Stop Solution. The intensity of the color measured was in proportion to the amount of rat IL-6 bound in the initial step. A standard curve was generated for each assay plate, and test sample IL-6 concentrations were determined by interpolation of absorbance A450 values from the standard curve and dilution factor. The assay range for the IL-6 kit is 62.5 – 4,000 pg/mL, with a minimum detectable concentration of less than 21 pg/mL.

For IFNα analysis, plasma IFNα samples were analyzed using a commercially-available assay kit from NOVATEINBIO (cat. no. BG-RAT11380). The ELISA is a solid phase enzyme-linked immunosorbent assay. The ELISA kit employs anti-rat IFNα monoclonal antibody for solid phase immobilization (pre-coated on the microtiter plate), and HRP conjugated antibody specific for IFNα for detection. Plasma samples were diluted 1:4, and the standards were used as provided in the kit. Standards consisted of six (6) serial 2-fold concentrations ranging from 100 to 3.1 pg/mL. Blanks contained diluent only. Following sample, standard, or diluent addition (50 µL per well, each in duplicate), HRP conjugate was added to each well (100 µL/well), and plates were incubated for 1 hours at 37°C. Following a wash step, 50 µL/well each of Chromogen Solution A and Chromogen Solution B were added to the plate. The plate was incubated for 15 minutes at 37°C, protected from light, to allow the color reaction to develop. The reaction was stopped following the addition of Stop Solution (50 µL/well). The optical density was read on a SpectraMax 340 (MOLECULAR DEVICES) plate reader at 450 nm. The intensity of the color measured was in proportion to the amount of rat IFNα bound in the initial step. A standard curve was generated for each assay plate, and test IFNα concentrations were determined by interpolation of absorbance A450 values from the standard curve and dilution factor. The assay range for the IFNα kit is 3.1 – 100 pg/mL, with a minimum detectable concentration of less than 1 pg/mL (4 pg/mL, with the 1:4 dilution required for plasma samples).

The results of this study were, *inter alia*, that NOVECRIT was not detected at the injection site 24h after dosing (as assayed by RT-PCR). More specifically, NOVECRIT was not detected in any of the following samples (RT-PCR): serum (6h, 24h, 48h and 72h after dosing), liver (6h and 24h after dosing), and kidney (6h and 24h after dosing). Further, positive controls (spiked with NOVECRIT) yielded a robust signal in all tissues (as assayed RT-PCR). **FIG. 18** depicts single administration of NOVECRIT induced a rapid increase and sustained level of NOVEPOIETIN in serum. The Y axis shows concentration of NOVEPOIETIN protein (mU/mL). This suggests, without wishing to be bound by theory, that the studied RNA therapeutic is able to provide therapeutically important pharmacodynamic properties. In fact, this PD behavior is vastly improved relative to wild type EPO (which is known in the art to have a half-life of about 4-12 hours).

Furthermore, serum spiked with NOVECRIT showed near-instant degradation of the RNA (as assayed by RT-PCR). Without wishing to be bound by theory, this data indicates that the present RNA therapeutics are safe and have little chance of toxicity limitations, for example, liver or kidney toxicities.

FIG. 19 depicts a single administration of NOVECRIT stimulated erythropoiesis, yielding elevated hematocrit for at least 14 days. The left panel shows % hematocrit on the Y axis, while the right panel shows % reticulocytes. Accordingly, the studied RNA therapeutic is fully functional.

With respect to cytokines, IL-6 and TNFα cytokine levels were below assay detection thresholds for all animals at each of the timepoints evaluated in this study. Low levels of IFN-α were only detectable in the Day 8 samples from animals in Groups 3 and 4. **FIG. 20** depicts a table summarizing TNFα, IL-6, and IFNα cytokine levels in plasma samples collected from a maximum tolerated dose of NOVECRIT in male Sprague Dawley rats. Without wishing to be bound by theory, this data indicates that the present RNA therapeutics do not stimulate an unfavorable immunogenicity which has limited the therapeutic utility of certain RNA therapeutics.

Example 36: Gene Editing of the COL7A1 Gene

The present RNA-based gene editing approaches were applied to the COL7A1 gene. This gene is of interest because, *inter alia*, it is frequently involved in dystrophic epidermolysis bullosa. **FIG. 21** depicts a SURVEYOR assay using the DNA of primary adult human dermal fibroblasts transfected with RNA TALENs targeting the sequence TGAGCAGAAGTGGCTCAGTG (SEQ ID NO: 467) and TGGCTGTACAGCTACACCCC (SEQ ID NO: 468), located within the COL7A1 gene. The bands present in the +RNA lane indicate editing of a region of the gene that is frequently involved in dystrophic epidermolysis bullosa. **FIG. 22** depicts another SURVEYOR assay using the DNA of primary adult human dermal fibroblasts transfected with RNA TALENs, now targeting the sequence TTCCACTCCTGCAGGGCCCC (SEQ ID NO: 469) and TCGCCCTTCAGCCCGCGTTC (SEQ ID NO: 470), located within the COL7A1 gene. The bands present in the +RNA lane indicate editing of a region of the gene that is frequently involved in dystrophic epidermolysis bullosa. This data points to, among others, a gene editing approach to the treatment of certain genetic disorders such as dystrophic epidermolysis bullosa.

Example 37: Gene-editing of the MYC gene using a Synthetic RNA with Non-Canonical Nucleotides

Experiments were conducted with *in vitro* transcribed synthetic RNA molecules containing non-canonical nucleotides and encoding gene-editing proteins. The immunogenicity and the gene-editing efficiency of *in vitro* transcribed synthetic RNA molecules having (1) only pseudouridine (psU) as a non-canonical nucleotide; (2) only 5-methylcytidine (5mC) as a non-canonical nucleotide; and (3) both of pseudouridine and 5-methylcytidine as non-canonical nucleotides was evaluated (as well as controls).

Specifically, RNA containing the following nucleotide combinations: (i) A,G,U,C, (ii) A,G,psU,C, (iii) A,G,U,5mC, and (iv) A,G,psU,5mC, and encoding TALEN pairs targeting the following DNA sequences, which can be found within the MYC gene: TCGGCCGCCGCCAAGCTCGT (SEQ ID NO: 474) and TGCGCGCAGCCTGGTAGGAG (SEQ ID NO: 475), were synthesized according to the methods described herein. Human dermal fibroblasts (MA001SK) were plated in 6-well and 24-well tissue culture plates in DMEM with 10% FBS at 100,000 and 10,000 cells per well, respectively. The next day, the cells were transfected in the 6-well plate with 2 µg of RNA (1 µg for each component of the TALEN pair) and the cells were transfected in the 24-well plate with 0.2 µg of RNA (0.1 µg for each component of the TALEN pair) according to the methods described herein. 24 hours after transfection, the total RNA from the cells in the 24-well culture plate was isolated using an RNeasy Mini Kit (74106; QIAGEN), including isolating the total RNA from a sample of cells that had not been transfected with RNA (negative control; "Neg." in **FIG. 23**). The genomic DNA was removed by a 15 minute digestion with DNase I (RNase-Free) (M0303L; NEW ENGLAND BIOLABS) and the reaction purified using an RNeasy Mini Kit. 1 µL of total RNA was used to assess gene expression by real-time RT-PCR using TAQMAN gene-expression assays (APPLIED BIOSYSTEMS) designed to detect expression of the immunogenicity markers TLR3, IFIT1, and IFIT2 (**FIG. 23**). The data were normalized to both the positive experimental control sample ("A,G,U,C") and to a loading control (GAPDH).

48 hours after transfection, the genomic DNA was isolated from the cells in the 6-well culture plate using a DNeasy Blood and Tissue Kit (69506; QIAGEN), including from a sample of cells that had not been transfected with RNA (negative control, "Neg." in **FIG. 24**). A 970 bp region of the MYC gene surrounding the predicted TALEN cut location was amplified using a 35 cycle 2-step PCR reaction containing the following primers: TAACTCAAGACTGCCTCCCGCTTT (SEQ ID NO: 476) and AGCCCAAGGTTTCAGAGGTGATGA (SEQ ID NO: 477). 160 ng was hybridized in 5 µL of amplified sequence from RNA-treated cells to 160 ng in 5 µL of amplified sequences from untreated MA001SK cells by mixing the two sequences with 0.5 µL of 1M KCl and 0.5 µL of 25mM $MgCl_2$ and running the following program in a thermocycler: 95ºC for 10 minutes; 95ºC to 85ºC at 0.625C/s; 85ºC to 25ºC at 0.125C/s. The SURVEYOR assay was performed by adding 0.5µL of SURVEYOR nuclease and 0.5µL of Enhancer from the SURVEYOR Mutation Detection Kit (706020I; INTEGRATED DNA TECHNOLOGIES) to the hybridized product, mixing, and incubating at 42ºC for 25 minutes. The protocol above was also used to process the positive control DNA sample provided with the SURVEYOR Mutation Detection Kit as a positive experimental control for the SURVEYOR Assay ("Assay Pos." in **FIG. 24**). Samples were analyzed by agarose gel electrophoresis (**FIG. 24**). For each sample, gene-editing efficiency was calculated as a ratio of the intensity of the digested bands (indicated by "*" in **FIG. 24**) to that of the undigested band.

As shown in **FIG. 23** below, the samples from cells transfected with the positive control RNA (A,G,U,C), and the samples from cells transfected with RNA containing either pseudouridine or 5-methylcytidine exhibited upregulation of all three of the immunogenicity markers TLR3, IFIT1, and IFIT2. The sample from cells transfected with RNA containing both pseudouridine and 5-methylcytidine exhibited negligible upregulation of the immunogenicity markers (less than 0.01-fold of the positive control), demonstrating that *in vitro* transcribed synthetic RNA with both pseudouridine and 5-methylcytidine and encoding a gene-editing protein can evade detection by the innate-immune system of mammalian cells.

Further, as shown in **FIG. 24** below, the sample from cells transfected with RNA containing both pseudouridine and 5-methylcytidine exhibited highly efficient gene editing (41.7%), which was greater than the efficiency exhibited by samples from cells transfected with RNA containing pseudouridine alone (35.2%), demonstrating that *in vitro* transcribed synthetic RNA comprising both pseudouridine and 5-methylcytidine and encoding a gene-editing protein can both (i) gene-edit mammalian cells at high efficiency, and (ii) gene-edit mammalian cells at higher efficiency than *in vitro* transcribed synthetic RNA comprising pseudouridine and not comprising 5-methylcytidine.

Example 38: COL7A1 Gene Editing and Repair in Human Cells

RNA encoding gene editing proteins targeting the following sequences in the COL7A1 gene was synthesized according to Example 1: TGAGCAGAAGTGGCTCAGTG (SEQ ID NO: 473) and TGGCTGTACAGCTACACCCC (SEQ ID NO: 468) (see also table below).

RNA Synthesis

Template	Nucleotides	Reaction Volume/µL	ivT Yield/µg
COL7A1 TALEN 1L	A, G, 5moU, C	20	120.528
COL7A1 TALEN 1R	A, G, 5moU, C	20	120.204
COL7A1 TALEN 1L	A, G, 5moU, C	15	81.94
COL7A1 TALEN 1R	A, G, 5moU, C	15	61.88

50,000 primary human epidermal keratinocytes (HEKn, Gibco) were plated in wells of 6-well plates in EpiLife + Supplement S7. The next day, cells were transfected according to Example 3 with 1 µg of RNA encoding each component of the gene editing pair and 2 µg of a single-stranded DNA repair template having a length of 60, 70, 80, 90 or 100 nucleotides ("nt"). 48 hours after transfection, genomic DNA was purified. A segment of the COL7A1 gene was amplified using the primers GCATCTGCCCTGCGGGAGATC (SEQ ID NO: 478) and CCACGTTCTCCTTTCTCTCCCCGTTC (SEQ ID NO: 479), which produce a 535 bp amplicon. The efficiency of gene editing was assessed using T7 Endonuclease I ("T7E1", New England Biolabs) according to the manufacturer's instructions. Bands of approximately 385 bp and 150 bp indicate successful gene editing. **FIG. 25**

and **FIG. 29** show the result of digestion with T7EI, analyzed by agarose gel electrophoresis. **FIG. 27** and **FIG. 29** show the result of digestion with MluI-HF, analyzed by agarose gel electrophoresis. Because the repair template contains the sequence ACGCGT (SEQ ID NO: 480), digestion of the amplified product with MluI-HF (New England Biolabs) produces bands of approximately 385 bp and 150 bp in the case of successful gene repair.

RNA encoding gene editing proteins targeting the following sequences in the COL7A1 gene was synthesized according to Example 1: TGAGCAGAAGTGGCTCAGTG (SEQ ID NO: 473) and TGGCTGTACAGCTACACCCC (SEQ ID NO: 468). 50,000 primary human epidermal keratinocytes (HEKn, Gibco) were plated in wells of 6-well plates in EpiLife + Supplement S7. The next day, cells were transfected according to Example 3 with 1 µg of RNA encoding each component of the gene editing pair and 1-4 µg of an 80 nucleotide single-stranded DNA repair template. 48 hours after transfection, genomic DNA was purified. A segment of the COL7A1 gene was amplified using the primers GCATCTGCCCTGCGGGAGATC (SEQ ID NO: 481) and CCACGTTCTCCTTTCTCTCCCCGTTC (SEQ ID NO: 482), which produce a 535 bp amplicon. The efficiency of gene editing was assessed using T7 Endonuclease I ("T7E1", New England Biolabs) according to the manufacturer's instructions. Bands of approximately 385 bp and 150 bp indicate successful gene editing. **FIG. 26** show the result of digestion with T7EI, analyzed by agarose gel electrophoresis. **FIG. 28** show the result of digestion with MluI-HF, analyzed by agarose gel electrophoresis. Because the repair template contains the sequence ACGCGT (SEQ ID NO: 480), digestion of the amplified product with MluI-HF (New England Biolabs) produces bands of approximately 385 bp and 150 bp in the case of successful gene repair.

Example 39: Expression of BMP7 Variants in Human Cells

RNA encoding wild type BMP7 and RNA encoding variants of BMP7 was synthesized according to Example 1 (see also table below).

RNA Synthesis

Template	Nucleotides	Reaction Volume/µL	ivT Yield/µg
BMP7 Wild Type	A, G, 5moU, C	15	125.8
BMP7 Variant A	A, G, 5moU, C	15	120.36
BMP7 Variant B	A, G, 5moU, C	15	143.14
BMP7 Variant C	A, G, 5moU, C	15	106.42

50,000 primary human dermal fibroblasts (MA001SK, Factor Bioscience) or 100,000 primary human epidermal keratinocytes (HEKn, Gibco) were plated in DMEM+10% FBS or EpiLife + Supplement S7, respectively. Cells were transfected according to Example 3 with 1 µg of RNA encoding wild type BMP7 or a variant thereof. 24 hours after transfection, the medium was sampled and secreted BMP7 levels were measured with a human BMP7 ELISA kit (ab99985, Abcam) using medium diluted 10-fold according to the manufacturer's instructions.

Secreted BMP7 levels were determined by measuring 450 nm absorbance using a microplate reader (EMax Plus, Molecular Devices). Secreted BMP7 levels are shown in **FIG. 30**.

Example 40: Expression of Parathyroid Hormone (PTH) in Human Cells

RNA encoding PTH was synthesized according to Example 1 (see also table below).

RNA Synthesis

Template	Nucleotides	Reaction Volume/µL	ivT Yield/µg
PTH	A, G, 5moU, C	15	51.68

100,000 human epidermal keratinocytes (HEKn, Gibco) were plated in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 1 µg of RNA encoding PTH. 24 hours after transfection, the medium was sampled and secreted PTH levels were measured using a human PTH ELISA kit (EIA-PTH-1, Ray Biotech) according the manufacturer's instructions. Secreted PTH levels were determined by measuring 450 nm absorbance using a microplate reader (EMax Plus, Molecular Devices). Secreted PTH levels are shown in **FIG. 31**.

Example 41: Intradermal, Subcutaneous, Rectal and Nasal Administration of NOVECRIT for the Treatment of Anemia

A repeat dose toxicity study of Novecrit was conducted for the treatment of anemia. Specifically, 8-10 weeks old male Sprague Dawley rats were administered with Novecrit via intradermal, subcutaneous, rectal, or nasal routes once per day on days 1, 8, and 15. The animals were assigned to groups and treated as indicated in the table below:

Group	**Group Color**	**Test Article**	**Dose Route**	**Dose Level (µg)**	**Dose Concentration (µg/mL)**	**Dose Volume (µL)**	**Number of Animals**
							Males
1	White	Control	Intradermal	0.0	0.0	50	3[a] + 8[b]
2	Yellow	Novecrit	Intradermal	4X (0.25 µg /injection; 1.0 µg total)	5.0	50	3[a] + 8[b]
3	Green	Novecrit	Subcutaneous	4.0	20.0	200	3[a] + 8[b]
4	Blue	Novecrit	Rectal	4.0	20.0	200	3[a] + 8[b]
5	Red	Novecrit	Nasal	4.0	20.0	200	3[a] + 8[b]

Note: Total dose volume (µL/per animal) are constant

[a] Toxicity animals (also called main study animals), necropsy on Day 44

[b]TK animals, euthanized as n = 2/time point on Days 2, 16, 23 and 44

More particularly, Group 1 was dosed via intradermal injection. Each dose was administered in four intradermal injections of 50 µL/injection for a total of 200 uL per animal. Injections were carried out on previously marked sites near the midline of the dorsal lumbar area (upper left, upper right, lower left and lower right quadrants). Group 2 was dosed four intradermal injections at 0.25 µg each (1.0 µg total) into previously marked sites near the midline of the dorsal lumbar area (upper left, upper right, lower left and lower right quadrants). Group 3 was dosed by subcutaneous injections into an area of the back located in the lower dorsal thoracic/lumbar region. Group 4 was dosed by rectal administration. The animal was manually restrained and the abdomen of each rat was manually palpated to remove any fecal matter. If deemed necessary, the rectum was lavaged with up to 2 ml of saline for enema followed by manual palpation of the abdomen to remove the fecal matter, if any. Novecrit was drawn into a syringe and an appropriately sized gavage needle with a rounded tip (ball) was attached to the syringe. A lubricant jelly was applied to the insertion device to aid with insertion; it was advanced approximately 1cm into the lumen of the colon and the Novecrit instilled. The rat was then maintained in a head-down position for approximately 20 - 30 seconds to limit the expulsion of solution. Group 5 was dosed via nasal route. The animal was anesthetized (per SNBL USA SOP). The animal was laid on its back with the head elevated. The dose was dispensed slowly into the nares. Approximately half the dose volume was administered to one nare. The remaining dose volume was administered to another nare. The first dose was administered on Day 1, and the last dose on Day 15.

The rats were clinically monitored including their food consumption and body weight. In addition, blood was collected for hematology, coagulation, and serum chemistry analysis as indicated below:

Toxicity Group Specimen collection frequency

Time Point	Hematology	Coagulation	Serum Chemistry
Day 44	1X (n = 3/Group)	1X (n = 3/Group	1X (n = 3/Group)

x = Number of times procedure performed

Analysis was done on the toxicokinetic group as follows:

In-text Table 3: Toxicokinetic Group Specimen collection frequency

Time Point	Hematology[a]	TK	Cytokines
Acclimation	1X (n = 8/Group)	-	-
Day 2	-	1X (n = 2/Group, 24 hours postdose)	1X (n = 2/Group, 24 hours postdose)
Day 8	Pre-dose (n = 6/Group)	-	-
Day 15	Pre-dose (n = 6/Group)	-	-
Day 16	-	1X (n = 2/Group, 24 hours postdose)	1X (n = 2/Group, 24 hours postdose)
Day 22	1X (n = 4/Group)	-	-
Day 23	-	1X (n = 2/Group)	1X (n = 2/Group)
Day 29	1X (n = 2/Group)	-	-
Day 36	1X (n = 2/Group)	-	-
Day 43	1X (n = 2/Group)	-	-
Day 44	-	1X (n = 2/Group)	1X (n = 2/Group)

x = Number of times procedure performed

TK = toxicokinetics

Terminal necropsy for toxicity animals occurred on Day 44. TK animals were euthanized on Days 2, 16, 23, and 44. Pathological analysis was conducted on the animals.

As shown in **FIG. 32**, administration of NOVECRIT stimulated erythropoiesis resulting in elevated hematocrit for at least 14 days in all four study groups compared to control.

Example 42: Intradermal Administration of RNA Encoding BMP7 Variants for the Treatment of Diabetic Nephropathy

A ZDSD rat model was utilized to study the effects of RNAs encoding BMP7 variants for the prevention and treatment of diabetic nephropathy. Specifically, ZDSD rats were treated with RNAs encoding BMP7 variants administered intradermally. A schematic of the study design is provided in **FIG. 33**. The animals were assigned to groups and treated as indicated in the table below:

Group Number	Treatment	No. of Animals	Dose Level (µg)	Dose Conc. (µg /ml)	Dose Volume (ml/kg)	Frequency	Route of Admin.
1	Vehicle	24	0	0	0.1	2x/wk	I.D.
2	FTB-F1 (wt BMP7)	6	1	5	0.1	2x/wk	I.D.
3	FTB-F2 (BMP7 variant A)	6	1	5	0.1	2x/wk	I.D.
4	FTB-F3 (BMP7 variant B)	6	1	5	0.1	2x/wk	I.D.
5	Lisinopril	6	Standard	Standard	5	Continuous	Diet
6 [a]	Vehicle	20	0	0	0.2/rat	3x/wk	I.D.
7 [a]	FTB-F2 (BMP7 variant A)	10	2	10	0.2/rat	3x/wk	I.D.

[a] Group 1 animals at the end of the "Prevention" arm were randomized into Groups 6 and 7 (n=20 or 10 each, respectively) to define the "Treatment" arm. The remaining 6 animals from Group 1 were euthanized for kidney collection and blood draw at the end of the "Prevention" arm.

To study the effect of the RNAs on prevention of diabetic nephropathy, animals were delivered from the barrier (PCO-5638) to the vivarium (PCO-Rm C) and allowed 3 days for acclimation. All animals were placed on 5SCA diabetogenic diet for 3 weeks (weekly body weight measurements were taken). Animals were then returned to regular 5008 diet for the duration of the study (weekly body weight measurements were taken). After 2 weeks on 5008 diet, body weight measurement, blood draw (500 ul) and a 24 hour baseline urine collection (urinary albumin and creatinine measurements) were performed on all animals. 36 rats were randomized to groups 1, 2 and 3 based on body weight, glucose and urinary albumin. Groups 1, 2, 3 and 4 received either vehicle or test article (i.d.) via intradermal administration (2x/week, Mon and Thur). Group 5 was administered Lisinopril admixed in the 5008 diet (food consumption will begin on this group of animals). Blood draws (500 ul, tail vein) were taken from Groups 2, 3 and 4, 24 hours after each dose for the first 2 weeks and then 1x/week thereafter. After 4 weeks of dosing, blood sample via tail vein (500 ul) was taken from all animals (Groups 1-5). At the end of 8 weeks of dosing, a 24 hour urine collection was performed (urinary albumin and creatinine measurements) together with a tail vein (500 ul) blood sample from Group 1 (n=18 going into the Treatment arm). Results for urine volume, creatinine, and albumin is shown in **FIG. 35**. As shown in **FIG. 35**, treatment with RNA encoding BMP7 Variant A resulted in reduced levels of urine albumin in rats afflicted with diabetic nephropathy compared to the control, indicating superior kidney function in the treated animals compared to the control animals (placebo

group). To terminate the study, all animals were euthanized with CO_2 asphyxiation and a blood draw was performed via cardiac puncture to collect serum for BUN, creatinine and glucose, and plasma for compound exposure and biomarker analysis. Both kidneys were dissected and fixed for histology. **FIG. 34** shows the serum level of BMP7 protein in Groups 1, 2, 3, and 4. Results indicate that the serum levels of BMP7 protein in these groups were as follows: Group 4, Group 3 > Group 2, Group 1.

A study was also conducted to analyze the effect of the RNAs encoding BMP7 variants on treating diabetic nephropathy. Specifically, the vehicle animals from Group 1 (Prevention arm, n=18) were randomized based on body weight, glucose and urine albumin (Groups 6, n=20; 7, n=10;). Animals received either Vehicle or BMP7 variant-encoding RNAs (intradermal, 2x/week, Mon and Thur), groups 6 and 7, respectively. After 4 weeks of treatment, animals were euthanized with CO_2 asphyxiation and a blood draw will be performed via cardiac puncture to collect serum for BUN, creatinine and glucose, and plasma for compound exposure and biomarker analysis. Both kidneys were dissected and fixed for histology. As shown in **FIG. 36**, treatment with RNA encoding BMP7 Variant A significantly decreased urine albumin level in rats afflicted with diabetic nephropathy (p=0.0015), indicating superior kidney function in the treated animals. In addition, the treatment group showed significantly lower kidney weight at termination (p=0.018), and significantly lower serum creatinine at termination (p=0.016). These results suggested that BMP7 variant-encoding RNA effectively treated diabetic nephropathy and promoted superior kidney function compared to the control animals (placebo group).

An illustrative study protocol is provided below:

Week	Day	Procedure
15 weeks old	-7	• Animals arrive in Room C from the barrier
	0	• BW*, Stat Strip, and Place animals on 5SCA for 3 wks
1	7	• BW*, Stat Strip
2	14	• BW*, Stat Strip
3	21	• BW*, Stat Strip, put animals on 5008
4	28	• BW*, Stat Strip
	34	• BW*, Tail vein blood draw and randomize for Prevention arm (Grps 1, 2, 3, 4, 5)
5	35	• Begin 24 hr urine collection
	36	• Collect 24 hr urine
	39	• BW* • Intradermal dosing Grps 1,2, 3 and 4, and put Grp 5 on admixed 5008 diet • Begin food consumption on group 5
	40	• Collect 24 blood sample for exposure (gps 2, 3, & 4)

	42	• Dosing
	43	• Collect 24 blood sample for exposure (gps 2, 3, & 4)
6 (1 P)	46	• BW*, Dosing • Food consumption group 5
	47	• Collect 24 blood sample for exposure (gps 2, 3, & 4)
	49	• Dosing
	50	• Collect 24 blood sample for exposure (gps 2, 3, & 4)
7 (2 P)	53	• BW*, Dosing • Food consumption group 5
	54	• Collect 24 blood sample for exposure (gps 2, 3, & 4)
	56	• Dosing
8 (3 P)	60	• BW*, Dosing • Food consumption group 5
	61	• Collect 24 blood sample for exposure (gps 2, 3, & 4)
	63	• Dosing
9 (4 P)	67	• BW*, Dosing • Food consumption group 5 • Blood draw (tail vein)
	68	• Blood draw (all groups) • Collect 24 blood sample for exposure (gps 2, 3, & 4)
	70	• Dosing
10 (5 P)	74	• BW*, Dosing • Food consumption group 5
	75	• Collect 24 blood sample for exposure (gps 2, 3, & 4)
	77	• Dosing
11 (6 P)	81	• BW*, Dosing • Food consumption group 5
		• Collect 24 blood sample for exposure (gps 2, 3, & 4)
	84	• Dosing
12 (7 P)	88	• BW*, Dosing • Food consumption group 5
	89	• Collect 24 blood sample for exposure (gps 2, 3, & 4)
	91	• Dosing
13 (8 P)	95	• BW*, dosing • Food consumption group 5 • Blood draw (tail vein) (all groups)
	96	• Begin 24 hr urine collection

	97	• Collect 24 hr urine • Terminate Groups 1 (n=6), 2, 3, 4 and 5 cardiac puncture blood draw, and collect kidneys, weigh and fix.
	98	• BW* and randomize (BW*, glucose, albumin) Group 1 (n=18) rats into Groups 6, 7 and 8 • Dose • Food Consumption group 8
	103	• Dose
14 (1 T)	106	• BW*, Dosing • Food Consumption group 8
	110	• Dosing
15 (2 T)	113	• BW*, Dosing • Food Consumption group 8
	117	• Dosing
16 (3 T)	120	• BW*, Dosing • Food Consumption group 8
	124	• Dosing
17 (4T)	127	• BW*, Terminate, cardiac puncture blood draw, and collect kidneys, weigh and fix.

*BW: body weight measurement

In an illustrative study, the protocol was amended from above towards the end of the study as follows:

Week [Treatment Arm]	Day	• BW • Begin 24 hr urine collection
	81	• Collect 24 hr urine
		• BW, Blood draw • Randomize (BW, glucose, albumin) rats into Groups 6 and 7
1 T		• BW, Dose • 12 hr PK sample
		• Dose
		• Dose and Begin 24 hr Urine collection
	89	• Collect 24 hr Urine and Dose
2 T		• BW, Dose • 12 hr PK sample
		• Dose
		• Begin 24 hr Urine collection
	96	• Collect 24 hr Urine and Dose
3 T		• BW, Dose • 12 hr PK sample
		• Dose
		• Begin 24 hr Urine collection
		• Collect 24 hr Urine and Dose (last dose)
4 T		• BW

		• No activity
		• Begin 24 hr urine collection
		• Collect 24 hr urine • BW, Terminate, cardiac puncture blood draw, and collect kidneys, weigh and fix.

During both studies, pathological analysis is conducted as follows:

Specimen to be Collected	Method of Collection	Anti-Coagulant	Specimen to be Analyzed	Clinical Chemistry	Method of Analysis
Urine	24hr Metabolism Cages	NA	Urine	Creatinine/ Albumin	AU480/ ICL Elisa
Whole Blood	Tail Vein	None	Serum	BUN Creatinine Glucose/	AU480/ Sponsor
Whole Blood	Cardiac Puncture (Grps 1, 2, 3, 4 and 5; and 6, 7, 8)	None	Serum	BUN Creatinine Glucose/ Cmpd Exp & Biomarker	AU480/ Sponsor

Altogether, these results suggested that RNAs encoding BMP-7 variants effectively prevented the development of diabetic nephropathy in rats. In addition, these RNAs also effectively treated and restored kidney functions in rats already afflicted with diabetic nephropathy. RNA encoding BMP7 Variant A was particularly effective at preventing and treating diabetic nephropathy in rats.

Example 43: Transfection of Human Keratinocytes with RNA Encoding BDNF, BMP-2, BMP-6, IL-2, IL-6, IL-15, IL-22, LIF or FGF-21

100,000 human epidermal keratinocytes (HEK, Gibco) were plated in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg of RNA encoding BDNF, BMP-2, BMP-6, IL-2, IL-6, IL-15, IL-22, LIF or FGF-21. 24 hours after transfection, the medium was sampled and secreted protein levels were measured using a human ELISA kit (see Table below) according the manufacturer's instructions. Secreted protein levels were determined by measuring 450 nm absorbance using a microplate reader (EMax Plus, Molecular Devices). Secreted protein levels are shown in **FIG. 34**, panels A-I.

Protein	Part Number	Vendor

BDNF	DBNT00	R&D Systems
BMP-2	DBP200	R&D Systems
BMP-6	ab99984	Abcam
IL-2	D2050	R&D Systems
IL-6	D6050	R&D Systems
IL-15	D1500	R&D Systems
IL-22	D2200	R&D Systems
LIF	DLF00	R&D Systems
FGF-21	DF2100	R&D Systems

Example 44: Transfection of Human Keratinocytes with RNA Encoding IL-15 and/or IL-15RA

100,000 human epidermal keratinocytes (HEK, Gibco) were plated in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg of RNA encoding IL-15 or 1 µg each of RNA encoding IL-15 and RNA encoding IL-15RA. 24 hours after transfection, the medium was sampled and secreted IL-15 levels were measured using a human IL-15 ELISA kit (D1500, R&D Systems) according the manufacturer's instructions. Secreted IL-15 levels were determined by measuring 450 nm absorbance using a microplate reader (EMax Plus, Molecular Devices). Secreted IL-15 levels are shown in **FIG. 35**. As demonstrated in **FIG. 35**, co-transfection of IL-15 and IL-15RA significantly increased secreted IL-15 levels compared to transfection with IL-15 alone.

Example 45: Pharmacokinetic Study Via Intradermal Injection in Rats

Studies were conducted to evaluate the responses of Sprague Dawley rats to intradermal administration of various RNAs. Specifically, 8-10 weeks old, female Sprague Dawley rats weighing about 200 g to about 350 g were used for this study. A total of 33 rats were tested, and the animals were assigned to study groups and treated as indicated in the Table below:

Group	Group Color	Test Article	Dose Route	Dose Level (µg)	Dose Concentration (µg/mL)	Dose Volume (µL/per injection)[a]	Number of Animals
							Females
1	White	Control (NOVEP OEITIN)	ID	4.0	20.0	200 (4 x 50)	3[b]
2	Yellow	TA1 (IL2)	ID	4.0	20.0	200 (4 x 50)	3[b]
3	Green	TA2 (IL6)	ID	4.0	20.0	200 (4 x 50)	3[b]
4	Blue	TA3 (IL15)	ID	4.0	10.0	200 (4 x 50)	3[b]
5	Red	TA4 (IL15 + IL15RA)	ID	4.0	20.0 (10.0 each)	200 (4 x 50)	3[b]
6	Dark Grey	TA5 (IL22)	ID	4.0	20.0	200 (4 x 50)	3[b]

7	Purple	TA6 (BMP2)	ID	4.0	20.0	200 (4 x 50)	3[b]
8	Black	TA7 (BDNF)	ID	4.0	20.0	200 (4 x 50)	3[b]
9	White/ Yellow	TA8 (LIF)	ID	4.0	20.0	200 (4 x 50)	3[b]
10	Green/Blue	TA9 (PTH)	ID	4.0	20.0	200 (4 x 50)	3[b]
11	Red/Dark Grey	TA10 (FGF21)	ID	4.0	20.0	200 (4 x 50)	3[b]

[a]Total dose volume (µL/per animal) was constant. Each animal received four intradermal injections of 50 µL/per injection for a total of 200 µL per animal.

[b]Animals, euthanized on Day 3 without examination or necropsy

Intradermal = ID

For the study, the animals were treated with 4 ug of RNA. All groups were dosed via intradermal injection. Each dose was administered in four intradermal injections of 50 µL/injection for a total of 200 uL per animal. Injections occurred into previously marked sites near the midline of the dorsal lumbar area (upper left, upper right, lower left and lower right quadrants). Dose time (after the last injection) was recorded. Additional markings were made as needed to allow for identification of the dose site. Animals were administered with the RNAs on day 1 and euthanized on day 3. Clinical observations were made on the rats twice daily. Food consumption and body weight were also monitored.

During the study, approximately 1 ml of blood samples was collected from the jugular vein for pharmacokinetic analysis as follows:

Time Point	PK[a]
Acclimation	-
Day 1	12 hours postdose
Day 2	24 hours postdose
Day 3	48 hours postdose

[a]Time points for blood collection (n = 3 animals/Group/Time point)
PK = Pharmacokinetics

Results indicate that following administration of RNAs encoding FGF21, IL15, IL15 and IL15R, IL6, IL22, and NOVEPOEITIN, these proteins were readily detected in the blood with protein levels peaking at approximately 12 hours post injection (**FIG. 39**). Of note, the proteins tested in this study can be taken up by cells and tissues and/or can exert an effect near the site of expression without appreciable accumulation in systemic circulation.

Example 46: Wound-Healing Therapy Comprising RNA Encoding IL22

Primary human epidermal keratinocytes (HEKn-APF) were plated in 6-well plates coated with recombinant human Type-1 collagen at a density of 200,000 cells/well in keratinocytes medium (EpiLife + Supplement S7). After 24h, cells were transfected with 2 µg/well RNA encoding IL22 synthesized according to Example 1 and

50mM D-Glucose was added to the wells. The following day, a line was scratched in each well using a plastic 10µL pipette tip. Wells were imaged at 0h and 24h after scratching. The size of the scratch was measured using at both times, and healing was determined by calculating the ration of the size of the scratch at 24h to the size of the scratch at 0h (**FIG. 40**).

Example 47: A1AT Gene Editing and Repair in Human Cells

RNA encoding gene-editing proteins targeting the following sequences in the A1AT gene was synthesized according to Example 1: L1: TAAGGCTGTGCTGACCATCG (SEQ ID NO: 611), R1: TAAAAACATGGCCCCAGCAG (SEQ ID NO: 612), and R2: TCTAAAAACATGGCCCCAGC (SEQ ID NO: 613). Cells were gene edited and gene-editing efficiency was measured according to Example 38 (**FIG 41**). Additionally, cells were co-transfected with gene editing proteins targeting sequences L1 and R1 and a repair template comprising the sequence: cccctccaggccgtgcataaggctgtgctgaccatcgacgtcaaagggactgaagctgctggggccatgtttttagaggcc (SEQ ID NO: 614), and gene-repair efficiency was measured according to Example 38, using the AatII enzyme (**FIG 42**). Another sample of cells was transfected with gene-editing proteins targeting the following sequences in the A1AT gene: L2: TGCCTGGTCCCTGTCTCCCT (SEQ ID NO: 615) and R3: TGTCTTCTGGGCAGCATCTC (SEQ ID NO: 616). Gene-editing efficiency was measured according to Example 38 (**FIG 43**).

Example 48: Alpha-1-Antitrypsin Deficiency Therapy Comprising RNA Encoding Gene-Editing Proteins and a Repair Template

RNA encoding gene-editing proteins targeting the following sequences: L: TAAGGCTGTGCTGACCATCG (SEQ ID NO: 611) and R: TAAAAACATGGCCCCAGCAG (SEQ ID NO: 612) and a repair template comprising the sequence: RT: cccctccaggccgtgcataaggctgtgctgaccatcgacgagaaagggactgaagctgctggggccatgtttttagaggcc (SEQ ID NO: 617) are formulated with a vehicle according to the methods of the present invention and delivered to a subject afflicted with A1AT deficiency by intraportal administration, resulting in correction of the Z mutation in the subject's liver cells, reduction of polymerized Z protein accumulation in the subject's liver cells, increased secretion and serum levels of functional A1AT, and amelioration of one or more of the subject's symptoms.

Example 49: Friedrich's Ataxia Therapy Comprising RNA Encoding Gene-Editing Proteins

RNA encoding one or more gene-editing proteins capable of creating one or more double strand breaks in FXNA (SEQ ID NO: 582) and RNA encoding one or more gene-editing proteins capable of creating one or more double strand breaks in FXNB (SEQ ID NO: 583) are synthesized according to Example 1. RNA is formulated according to the methods of the present invention, and delivered to the heart of a patient with Friedrich's ataxia using a catheter. Target-sequence pairs are selected from: Pair 1: TCCCACACGTGTTATTTGGC (SEQ ID NO: 618) and TGGCAACCAATCCCAAAGTT (SEQ ID NO: 619); Pair 2: TAATAAATAAAAATAAAAAA (SEQ ID NO: 620) and TTGCCTATTTTTCCAGAGAT (SEQ ID NO: 621).

Example 50: Alpha-1-Antitrypsin Deficiency Therapy Comprising RNA Encoding Gene-Editing Proteins

RNA encoding one or more gene-editing proteins capable of creating one or more double strand breaks in A1AT_A (SEQ ID NO: 584) is synthesized according to Example 1. RNA is formulated according to the methods of the present invention, and is delivered to the liver of a patient with A1AT deficiency by intraportal injection.

Example 51: Alpha-1-Antitrypsin Deficiency Therapy Comprising RNA Encoding Gene-Editing Proteins and a Short Repair Template

RNA encoding one or more gene-editing proteins capable of creating one or more double strand breaks in A1AT_B (SEQ ID NO: 585) is synthesized according to Example 1. RNA and a single stranded DNA sequence containing the sequence: A1AT_RT (SEQ ID NO: 586) are formulated according to the methods of the present invention, and are delivered to the liver of a patient with A1AT deficiency by intraportal injection.

Example 52: Gene-Editing Proteins Comprising DNA-Binding and Deaminase Activity

RNA encoding a gene-editing protein comprising two or more repeat sequences, followed by: BASE_EDIT_FRONT (SEQ ID NO: 587), followed by any of: BASE_EDIT_ADA1 (SEQ ID NO: 588), BASE_EDIT_ADA2 (SEQ ID NO: 589), BASE_EDIT_ADA3 (SEQ ID NO: 590), BASE_EDIT_ADA4 (SEQ ID NO: 591), BASE_EDIT_CDA1 (SEQ ID NO: 592) and BASE_EDIT_CDA2 (SEQ ID NO: 593) is synthesized according to Example 1. The gene-editing protein is capable of correcting one or more mutations within 1 to 50 bases downstream of the target sequence.

Example 53: Gene Editing of A1AT,COL7A1, HBB, and PD-1

With reference to Example 1, Table 4, the following templates and targets were used:

Template	Target Sequence	SEQ ID NO:
A1AT TALEN L	TGCCTGGTCCCTGTCTCCCT	615
A1AT TALEN R	TGTCTTCTGGGCAGCATCTC	616
A1AT RIBOSLICE L_A	TGCCTGGTCCCTGTCTCCCT	615
A1AT RIBOSLICE L_B	TGCCTGGTCCCTGTCTCCCT	615
A1AT RIBOSLICE R_A	TGTCTTCTGGGCAGCATCTC	616
A1AT RIBOSLICE R_B	TGTCTTCTGGGCAGCATCTC	616
COL7A1 exon 73 TALEN L	TATTCCCGGGCTCCCAGGCA	622
COL7A1 exon 73 TALEN R	TCTCCTGGCCTTCCTGCCTC	612
COL7A1 exon 73 rs3L 50A	TATTCCCGGGCTCCCAGGCA	622
COL7A1 exon 73 rs3L 50B	TATTCCCGGGCTCCCAGGCA	622
COL7A1 exon 73 rs3R 50A	TCTCCTGGCCTTCCTGCCTC	612
COL7A1 exon 73 rs3R 50B	TCTCCTGGCCTTCCTGCCTC	612
COL7A1 exon 73 TALEN L EA	TATTCCCGGGCTCCCAGGCA	622
COL7A1 exon 73 TALEN L Het	TATTCCCGGGCTCCCAGGCA	622
COL7A1 exon 73 TALEN R EA	TCTCCTGGCCTTCCTGCCTC	612
COL7A1 exon 73 TALEN R Het	TCTCCTGGCCTTCCTGCCTC	612
COL7A1 exon 73 TALEN L EA/Het	TATTCCCGGGCTCCCAGGCA	622
COL7A1 exon 73 TALEN R EA/Het	TCTCCTGGCCTTCCTGCCTC	612

HBB exon 1 TALEN L	TGGTGCATCTGACTCCTGAG	623
HBB exon 1 TALEN R	TCACCTTGCCCCACAGGGCA	624
PD-1 exon 1 TALEN L	TCCAGGCATGCAGATCCCAC	625
PD-1 exon 1 TALEN R	TTGTAGCACCGCCCAGACGA	626
TTR (forward (top) and reverse (bottom)	TGCTGTCCGAGGCAGTCCTG TCAGCAGCCTTTCTGAACAC	639; 640
TTR (forward (top) and reverse (bottom)	TGTCCGAGGCAGTCCTGCCA TCAGCAGCCTTTCTGAACAC	641; 642
TTR (forward (top) and reverse (bottom)	TCCGAGGCAGTCCTGCCATC TCAGCAGCCTTTCTGAACAC	643; 644
TTR (forward (top) and reverse (bottom)	TGTCCGAGGCAGTCCTGCCA TCATCAGCAGCCTTTCTGAA	645; 646
TTR (forward (top) and reverse (bottom)	TCCGAGGCAGTCCTGCCATC TCATCAGCAGCCTTTCTGAA	647; 648
TTR (forward (top) and reverse (bottom)	TCCGAGGCAGTCCTGCCATC TGTCATCAGCAGCCTTTCTG	649; 650

About 100,000 primary human neonatal epidermal keratinocytes were plated in EpiLife + Supplement S7 and transfected according to Example 3 with RNA encoding gene-editing proteins that target the sequences L: TGCCTGGTCCCTGTCTCCCT (SEQ ID NO: 615) and R: TGTCTTCTGGGCAGCATCTC (SEQ ID NO: 616), which were located approximately 75 bp from the Alpha-1-Antitrypsin (A1AT) start codon. Cells were gene edited, and gene-editing efficiency was measured as previously described. Results as shown in **FIG. 46** demonstrate efficient gene-editing by the gene editing proteins.

About 100,000 primary human neonatal epidermal keratinocytes were plated in EpiLife + Supplement S7 and transfected according to Example 3 with RNA encoding gene-editing proteins that target the sequences L: TATTCCCGGGCTCCCAGGCA (SEQ ID NO: 622) and R: TCTCCTGGCCTTCCTGCCTC (SEQ ID NO: 612), which were located near the end of exon 73 of COL7A1. Cells were gene edited, and gene-editing efficiency was measured as previously described. Results as shown in **FIG. 47** demonstrate efficient gene-editing by the gene editing proteins.

About 50,000 primary human neonatal epidermal keratinocytes were plated in EpiLife + Supplement S7 and transfected according to Example 3 with RNA encoding various gene-editing proteins that target the sequences L: TATTCCCGGGCTCCCAGGCA (SEQ ID NO: 622) and R: TCTCCTGGCCTTCCTGCCTC (SEQ ID NO: 612), which were located near the end of exon 73 of COL7A1. In particular, the gene-editing proteins comprised the endonuclease cleavage domain of FokI and variants thereof. The variants included a FokI variant with enhanced activity (S35P, K58E), a FokI heterodimer (*i.e.*, L: Q103E, N113D, I116L; and R: E107K, H154R, I155K), and a combination thereof (*i.e.*, L: S35P, K58E, Q103E, N113D, I116L; and R: S35P, K58E, E107K, H154R, I155K). Cells were gene edited, and gene-editing efficiency was measured as previously described. Results as shown in **FIG. 48** demonstrate efficient gene-editing by the gene editing proteins.

About 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) were plated in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg RNA encoding the HBB exon 1 TALEN

L and HBB exon 1 TALEN R gene-editing proteins (1 µg each). 48 hours after transfection, DNA was harvested and analyzed for gene editing (T7E1 assay; forward primer: gccaaggacaggtacggctgtcatc (SEQ ID NO: 627); reverse primer: cttgccatgagccttcaccttagggttg (SEQ ID NO: 628); product size: 518nt; predicted band sizes: 300nt, 218nt). Results as shown in **FIG. 61** demonstrate efficient gene-editing by the gene editing proteins.

About 100,000 primary human neonatal epidermal keratinocytes (animal-protein free) were plated in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg RNA encoding the PD1 exon 1 TALEN L and PD1 exon 1 TALEN R gene-editing proteins (1 µg each). After 48 hours, DNA was harvested and analyzed for gene editing (T7E1 assay; forward primer: tcctctgtctccctgtctctgtctctctctc (SEQ ID NO: 594); reverse primer: ggacttgggccaggggaggag (SEQ ID NO: 595); product size: 612nt; predicted band sizes: 349nt, 263nt). Results as shown in **FIG. 62** demonstrate efficient gene-editing by the gene editing proteins.

Example 54: Transfection of Primary Human Keratinocytes with RNA Encoding GDF15, IFKB, KRT5, KRT14, SOD3, or hESM1

As shown in **FIG. 49**, 100,000 primary human neonatal epidermal keratinocytes were plated in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg of RNA encoding hGDF15. Following transfection, the culture media was sampled at various time points and analyzed for hGDF15 levels using ELISA (R&D DGD150) according to manufacturer's instructions. **FIG. 49** demonstrates that hGDF15 levels were upregulated in a time-dependent manner following transfection.

As shown in **FIG. 50**, 100,000 primary human neonatal epidermal keratinocytes were plated in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg of RNA encoding IFKB or an IFKB variant (S32A and S36A). Following transfection, the culture media was sampled at various time points and analyzed for IFKB levels using ELISA (Abcam, ab176644) according to manufacturer's instructions. **FIG. 50** demonstrates increased levels IFKB or the IFKB variant following transfection.

As shown in **FIG. 51**, 100,000 primary human neonatal epidermal keratinocytes were plated in 6-well plates in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg of RNA encoding KRT5 or KRT14 (or GFP tagged versions of KRT5 or KRT14). Following transfection, GFP imaging was carried out to determine KRT5 or KRT14 expression. **FIG. 51** demonstrates efficient transfection and increased levels KRT5-GFP or KRT14-GFP following transfection.

As shown in **FIG. 52**, 20,000 primary human neonatal epidermal keratinocytes were plated in 24-well plates in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 0.2 µg of RNA encoding SOD3. Following transfection, cells were fixed and stained for 24 hours with a 1:100 dilution of NBP2-38493 (Novus) rabbit anti human SOD3 primary antibody and a 1:1000 dilution of 488 donkey anti-rabbit secondary antibody. Results demonstrate efficient transfection and robust levels of SOD3 in transfected cells.

As shown in **FIG. 60**, 200,000 primary human neonatal epidermal keratinocytes (animal-protein free) were plated in 6-well plates in EpiLife + Supplement S7. Cells were transfected according to Example 3 with 2 µg RNA

encoding hESM1. 52 hours after transfection, the culture medium was analyzed for ESM1 by ELISA (Abcam ab213776). Results demonstrate efficient transfection and robust levels of hESM1 in transfected cells.

Example 55: In Vivo Targeting of GDF15 (MIC1)

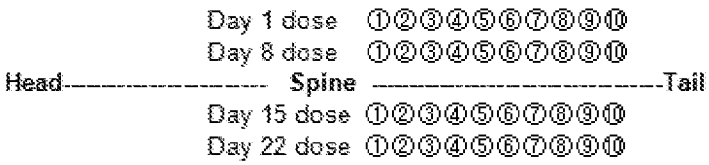
Studies were conducted to evaluate the responses of Zucker-obese (ZDF) rats to administration of RNA encoding hGDF15. The Zucker-obese rats (ZDF) are a well-studied obesity model that mimics many aspects of the human disease. Specifically, 8-10 weeks old male rats were used for this study. A total of 15 ZDF and 15 wildtype control Sprague-Dawley rats were tested, and the animals were assigned to study groups and treated as indicated in the Table below:

Group	Group Color	Rat Species	Test Article	Dose				Number of Males
				Route	Level (µg)	Concentration (µg/mL)	Volume[a] (µL)	
1	White	Sprague-Dawley	Control	Intradermal	0	0	50 per site; 500 total	5
2	Yellow	Sprague-Dawley	FG-02 (*i.e.*, RNA encoding GDF15)		10X (0.5 µg /injection; 5 µg total)	10	50 per site; 500 total	10
3	Green	ZDF	Control		0	0	50 per site; 500 total	5
4	Blue	ZDF	FG-02 (*i.e.*, RNA encoding GDF15)		10X (0.5 µg /injection; 5 µg total)	10	50 per site; 500 total	10

[a] Note: Total dose volume (µL/per animal) was constant

Groups 1 to 4 were dosed by intradermal (ID) injection. Each dose was administered on the back in ten ID injections of 50 µL/injection for a total of 500 uL per animal.

Each dose site was as follows:



RNA or control was administered once weekly (Days 1, 8, and 15), with the first dose being on Day 1, and the last dose on Day 15. Animals were euthanized, without examination on Day 44.

Blood was collected from the rats according to the schedule below and used for serum chemistry and pharmacokinetics analysis:

Time Point (Study Week)	Serum Chemistry	PK

Time Point (Study Week)	Serum Chemistry	PK
Acclimation (Week -2)	-	-
Dosing (Week 1)	2x	Day 1 (1x), 2 (1x), 3 (1x), 4 (1x), and 5 (1x)
Dosing (Week 2)	2x	Day 9[c]
Dosing (Week 3)	2x	Day 16[c]
Dosing (Week 4)	2x	Day 23
Dosing (Week 5)	2x	-
Dosing (Week 6)	2x	-
Dosing (Week 7)	1x	-

– = Not applicable
PK = Pharmacokinetics
x = Number of times procedure performed
[c] Sample collected 24 hours postdose

Serum chemistry analysis was carried out using an AU680 analyzer for the following: Albumin, Alkaline Phosphatase, Alanine Aminotransferase, Aspartate Aminotransferase, Total Bilirubin, Calcium, Total Cholesterol, Creatine Kinase, Creatinine, Glucose, Inorganic Phosphorus, Total Protein, Triglyceride, Sodium, Potassium, Chloride, Globulin, Albumin/Globulin Ratio, and Blood Urea Nitrogen. Results for changes in the serum levels of ALT, AST, total cholesterol, triglycerides, and glucose are provided in **FIGs. 53-58**. As shown in the **FIG. 58**, administration of RNA encoding GDF15 into ZDF rats resulted in reduced ALT, AST, and Glucose levels but elevated total cholesterol and triglyceride levels in the serum. These results suggest that diabetic obese animals treated with RNA encoding GDF15 exhibited improved liver health, as indicated by decreased serum levels of ALT and AST, improved (lower) blood glucose levels, and lipid mobilization, as indicated by increased serum cholesterol and triglyceride levels. These results therefore suggest that RNA encoding GDF15 may be used to treat, *inter alia*, diabetes, obesity, fatty liver, and other diseases that include liver inflammation, elevated blood glucose, and/or abnormal lipid metabolism.

The serum levels of GDF15 in the treated rats were confirmed as shown in **FIG. 59**. As shown, robust GDF15 levels were observed even at day 16 (*i.e.*, day 15+24h) in both ZDF and control Sprague-dawley rats injected with RNA encoding GDF15.

EQUIVALENTS

2017312113 18 Nov 2020

Those skilled in the art will recognize, or be able to ascertain, using no more than routine experimentation, numerous equivalents to the specific embodiments described specifically herein. Such equivalents are intended to be encompassed in the scope of the following claims.

INCORPORATION BY REFERENCE

All patents and publications referenced herein are hereby incorporated by reference in their entireties.

Throughout the specification and claims, unless the context requires otherwise, the word “comprise” or variations such as “comprises” or “comprising”, will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

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The claims defining the invention are as follows:

1. An *in vivo* method to treat cancer in a subject comprising:

administering to a tumor cell in the subject a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-L1, PD-L2, and OX40L, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of the tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell in the subject, resulting in the stimulation or enhancement of an immune response in the subject,

thereby treating cancer in the subject.

2. An *in vivo* method to treat cancer in a subject comprising:

administering to the subject by intratumoral injection a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a cell in the tumor, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell in the tumor of the subject, resulting in the stimulation or enhancement of an immune response in the subject;

thereby treating cancer in the subject.

3. An *in vivo* method for treating cancer in a subject comprising:

administering to a cell in the subject a non-viral, cell-free composition comprising a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

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wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of the cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell in the subject,

resulting in the stimulation or enhancement of an immune response in the subject, thereby treating cancer in the subject.

4. The method of any one of claims 1-3, wherein the synthetic RNA further comprises one or more of the group selected from: 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine, pseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine.

5. The method of claim 4, wherein at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% of the non-canonical nucleotides comprises one or more of 5-hydroxycytidine, 5-methylcytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-methoxycytidine, pseudouridine, 5-hydroxyuridine, 5-methyluridine, 5-hydroxymethyluridine, 5-carboxyuridine, 5-formyluridine, 5-methoxyuridine, 5-hydroxypseudouridine, 5-methylpseudouridine, 5-hydroxymethylpseudouridine, 5-carboxypseudouridine, 5-formylpseudouridine, and 5-methoxypseudouridine.

6. The method of any one of claims 1-5, wherein the synthetic mRNA comprises a 5′ cap structure.

7. The method of any one of claims 1-6, wherein the synthetic mRNA comprises a 5′-UTR comprising a Kozak consensus sequence.

8. The method of any one of claims 1-6, wherein the synthetic mRNA comprises a 5′-UTR comprising a sequence that increases RNA stability *in vivo.*

9. The method of any one of claims 1-6, wherein the synthetic mRNA comprises a 3′-UTR comprising a sequence that increases RNA stability *in vivo.*

10. The method of any one of claims 1-6, wherein the synthetic mRNA comprises a 3′ poly(A) tail.

11. The method of any one of claims 1-10 , wherein the gene-editing protein is a TALEN.

12. The method of claim 8, wherein the 5′-UTR comprises an alpha-globin or beta-globin 5′-UTR sequence.

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13. The method of claim 9, wherein the 3'-UTR comprises an alpha-globin or beta-globin 3'-UTR sequence.

14. Use of a non-viral, cell-free composition in the manufacture of a medicament for an *in vivo* method of treating cancer in a subject, the medicament comprising:

a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-L1, PD-L2, and OX40L, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a tumor cell, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the tumor cell, resulting in the stimulation or enhancement of an immune response in the subject.

15. Use of a non-viral, cell-free composition in the manufacture of a medicament for an *in vivo* method of treating cancer in a subject, the medicament comprising:

a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a cell in the tumor, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell in the tumor of the subject, resulting in the stimulation or enhancement of an immune response in the subject.

16. Use of a non-viral, cell-free composition in the manufacture of a medicament for an *in vivo* method of treating cancer in a subject, the medicament comprising:

a synthetic messenger RNA (mRNA) encoding a gene-editing protein capable of creating a single-strand or double-strand break in an immune checkpoint molecule gene, wherein the immune checkpoint molecule gene is selected from PD-1, PD-L1, PD-L2, CTLA-4, ICOS, LAG3, OX40, OX40L, and TIM3, wherein the synthetic mRNA comprises 5-methoxyuridine,

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wherein the gene-editing protein is selected from a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein, a TALEN, and a zinc finger nuclease, and

causing a single-strand or double-strand break in the DNA of a cell of the subject, the single-strand or double-strand break being localized to an immune checkpoint molecule gene in the cell,

resulting in the stimulation or enhancement of an immune response in the subject.

FIG. 1

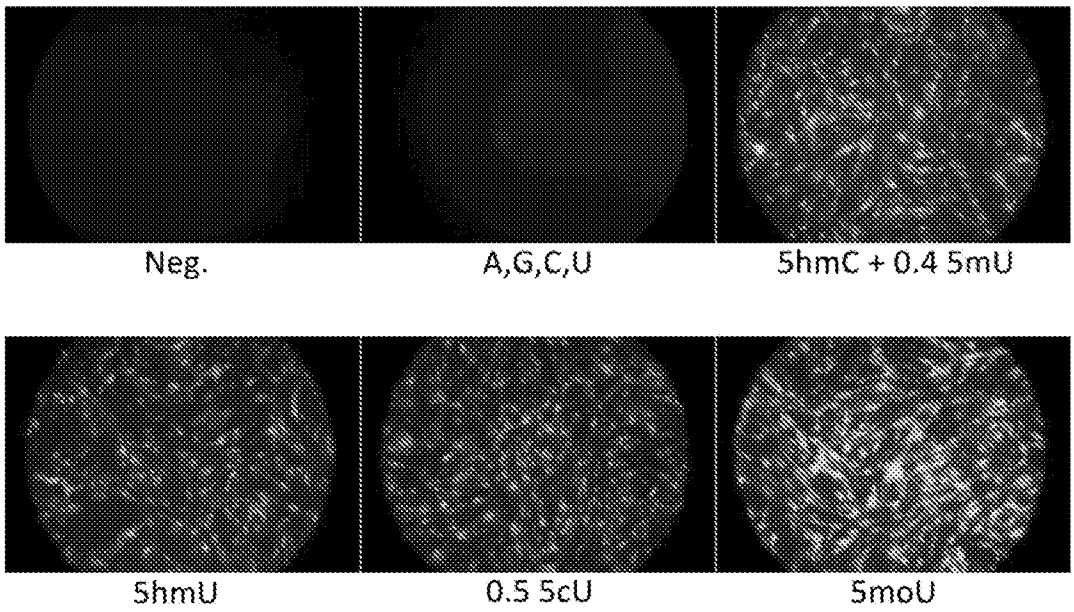

Neg.
A,G,C,U
5hmC + 0.4 5mU
5hmU
0.5 5cU
5moU

FIG. 2

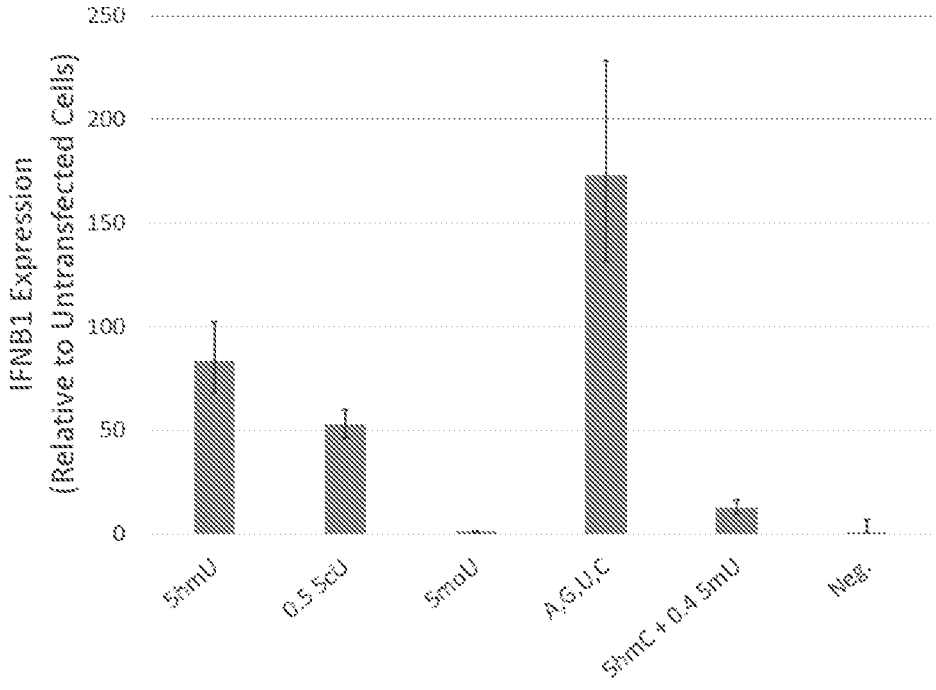

IFNB1 Expression
(Relative to Untransfected Cells)
250
200
150
100
50
0
5hmU
0.5 5cU
5moU
A,G,U,C
5hmC + 0.4 5mU
Neg.

FIG. 3

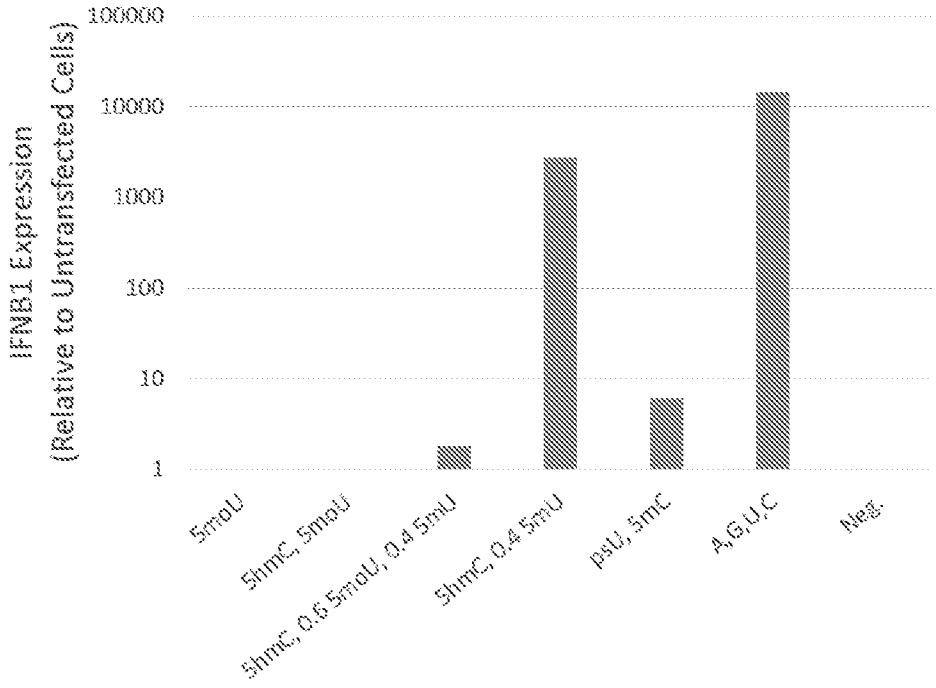

IFNB1 Expression
(Relative to Untransfected Cells)
100000
10000
1000
100
10
1
5moU
5hmC, 5moU
5hmC, 0.6 5moU, 0.4 5mU
5hmC, 0.4 5mU
psU, 5mC
A,G,U,C
Neg.

FIG. 4

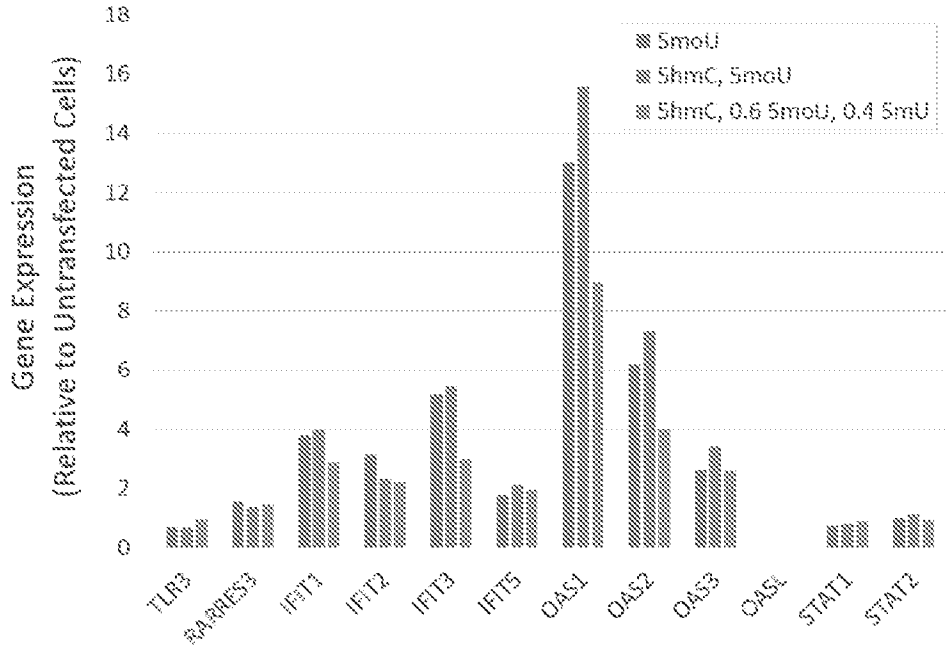

Gene Expression
(Relative to Untransfected Cells)
18
16
14
12
10
8
6
4
2
0
5moU
5hmC, 5moU
5hmC, 0.6 5moU, 0.4 5mU
TLR3
#ARRES3
IFIT1
IFIT2
IFIT3
IFIT5
OAS1
OAS2
OAS3
OASL
STAT1
STAT2

FIG. 5

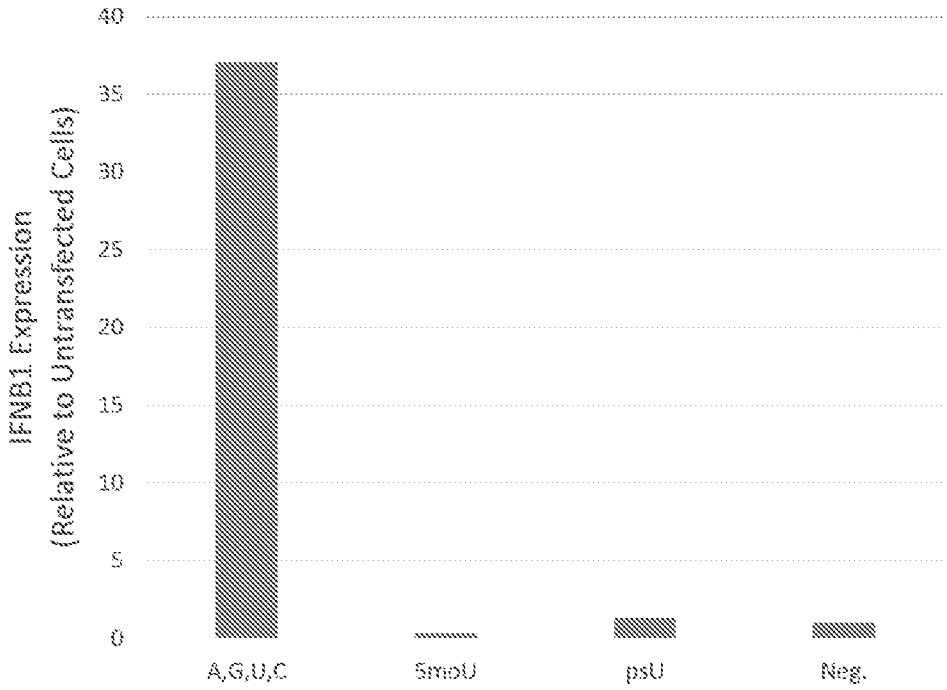

IFNB1 Expression
(Relative to Untransfected Cells)
40
35
30
25
20
15
10
5
0
A,G,U,C
5moU
psU
Neg.

FIG. 6

FIG. 7

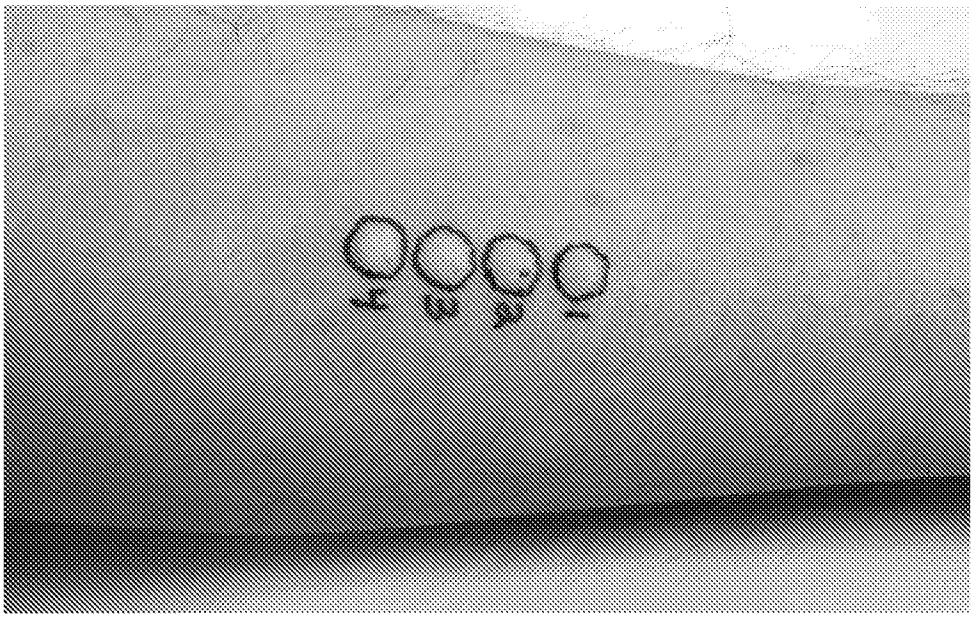


FIG. 8

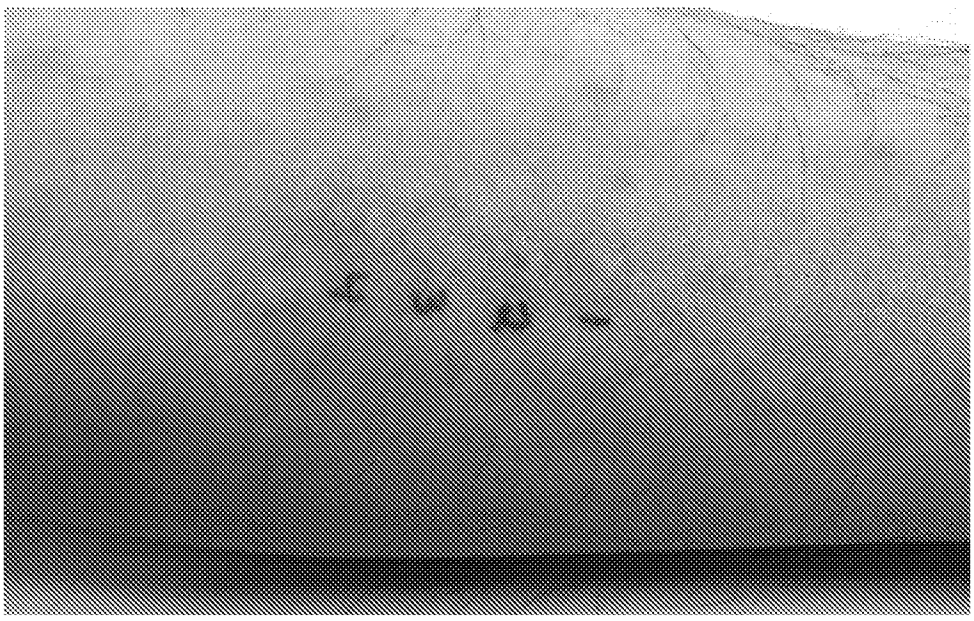


FIG. 9

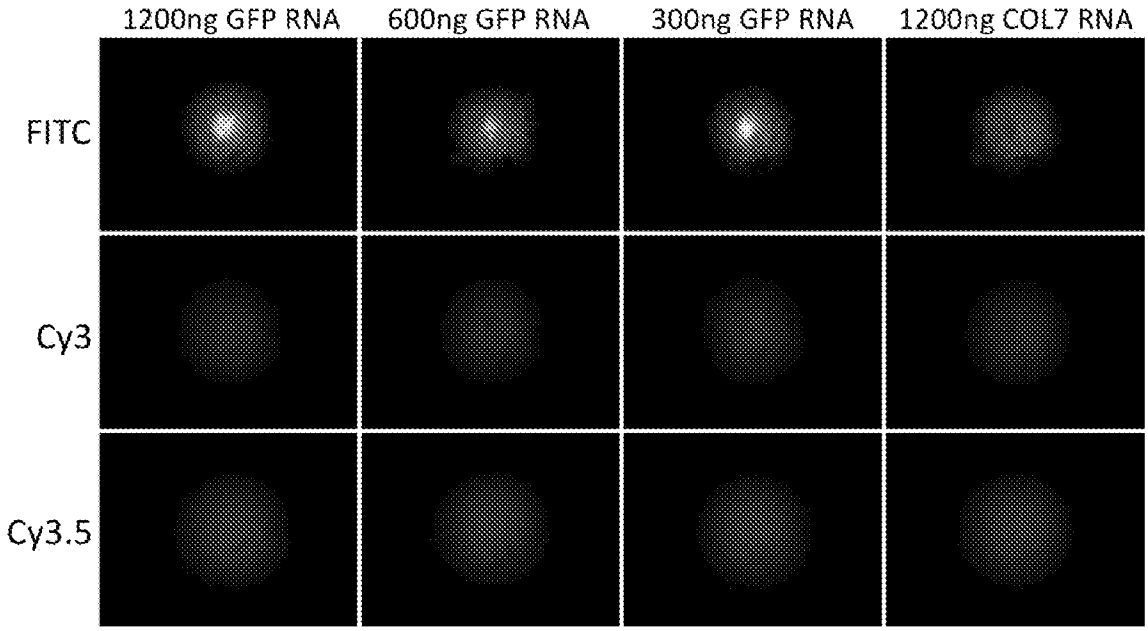

1200ng GFP RNA
600ng GFP RNA
300ng GFP RNA
1200ng COL7 RNA
FITC
Cy3
Cy3.5

FIG. 10

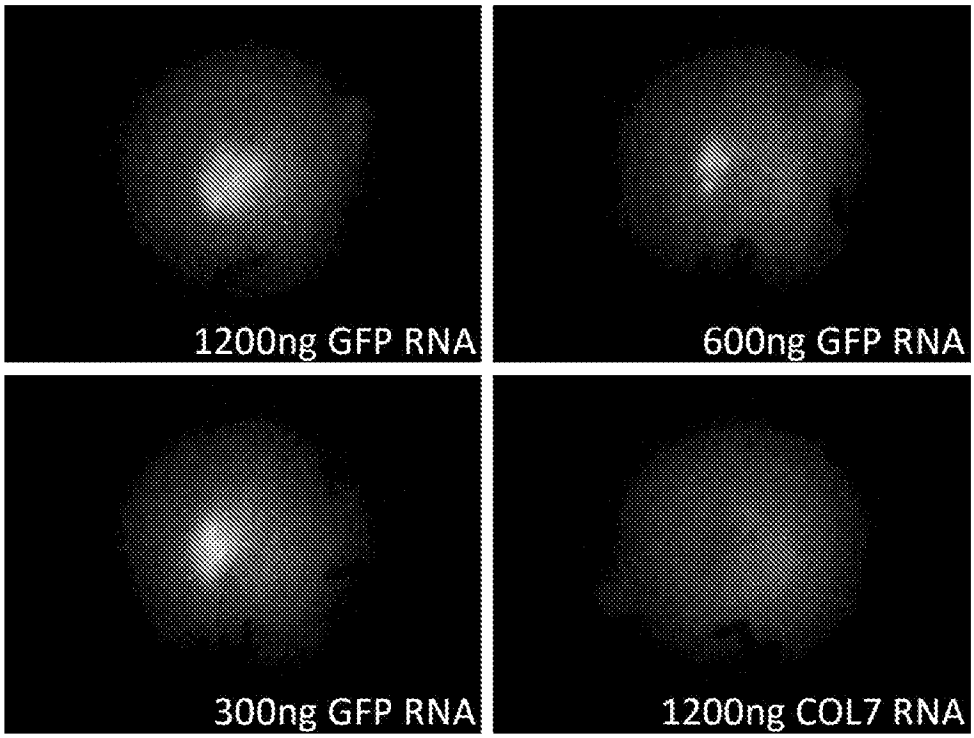

1200ng GFP RNA
600ng GFP RNA
300ng GFP RNA
1200ng COL7 RNA

FIG. 11

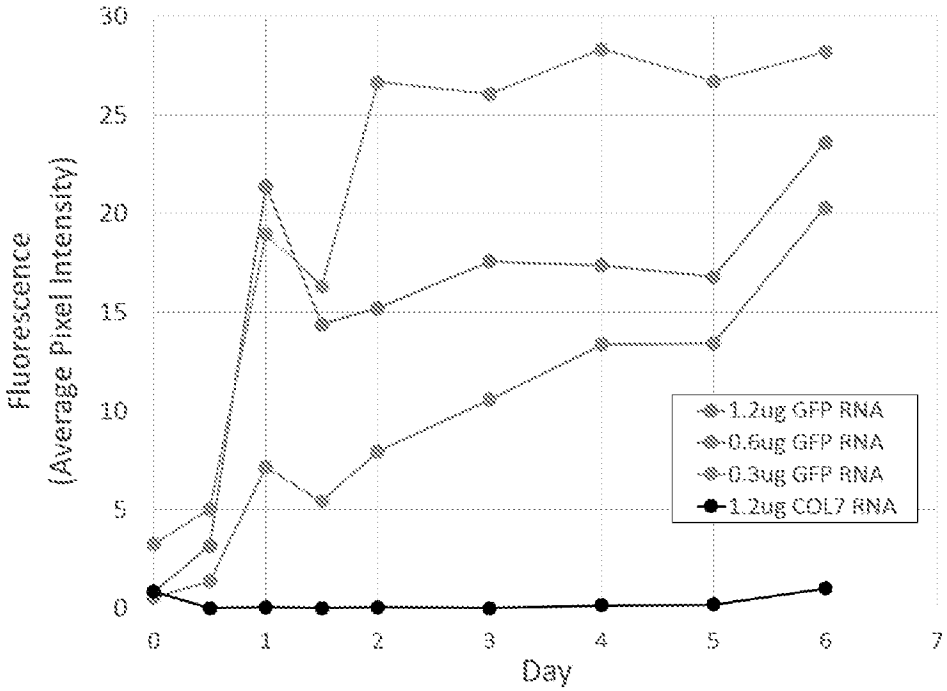

30
25
20
15
10
5
0
Fluorescence
(Average Pixel Intensity)
0
1
2
3
4
5
6
7
Day
1.2ug GFP RNA
0.6ug GFP RNA
0.3ug GFP RNA
1.2ug COL7 RNA

FIG. 12

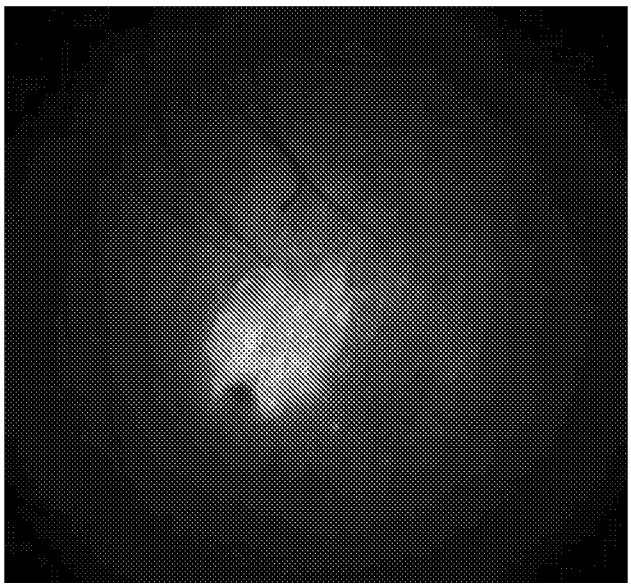
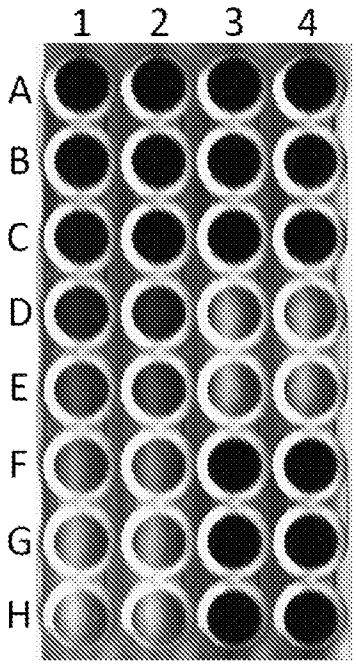
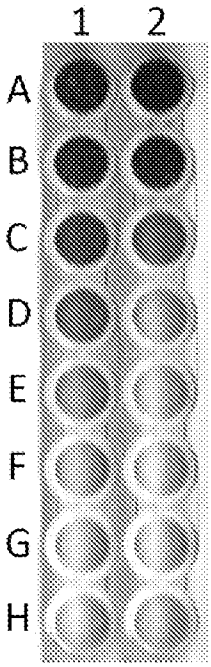


FIG. 13



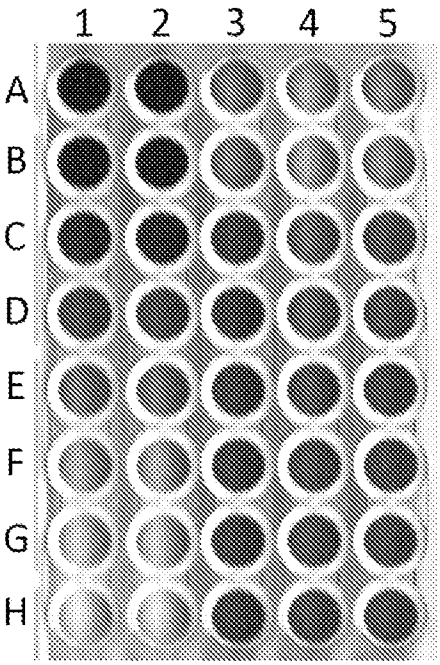
A1, A2	EPO Standard, 100 mU/mL
B1, B2	EPO Standard, 50 mU/mL
C1, C2	EPO Standard, 25 mU/mL
D1, D2	EPO Standard, 12.5 mU/mL
E1, E2	EPO Standard, 6.25 mU/mL
F1, F2	EPO Standard, 3.12 mU/mL
G1, G2	EPO Standard, 1.56 mU/mL
H1, H2	EPO Standard, 0 mU/mL
A3, A4	EPO RNA (A, G, U, C), 24h
B3, B4	EPO RNA (A, G, 5 moU, C), 24h
C3, C4	EPO RNA (A, G, psU, C), 24h
D3, D4	GFP RNA, 24h
E3, E4	untransfected, 24h
F3, F4	1:100 EPO RNA (A, G, U, C), 24h
G3, G4	1:100 EPO RNA (A, G, 5 moU, C), 24h
H3, H4	1:100 EPO RNA (A, G, psU, C), 24h

FIG. 14



A1	EPO Standard, 100 mU/mL
B1	EPO Standard, 50 mU/mL
C1	EPO Standard, 25 mU/mL
D1	EPO Standard, 12.5 mU/mL
E1	EPO Standard, 6.25 mU/mL
F1	EPO Standard, 3.12 mU/mL
G1	EPO Standard, 1.56 mU/mL
H1	EPO Standard, 0 mU/mL
A2	1:100 EPO RNA (A, G, 5 moU, C), 24h
B2	1:500 EPO RNA (A, G, 5 moU, C), 24h
C2	1:2500 EPO RNA (A, G, 5 moU, C), 24h
D2	1:12500 EPO RNA (A, G, 5 moU, C), 24h
E2	1:62500 EPO RNA (A, G, 5 moU, C), 24h
F2	1:312500 EPO RNA (A, G, 5 moU, C), 24h
G2	1:1562500 EPO RNA (A, G, 5 moU, C), 24h
H2	1:7812500 EPO RNA (A, G, 5 moU, C), 24h

FIG. 15



A1, A2	EPO Standard, 100 mU/mL
B1, B2	EPO Standard, 50 mU/mL
C1, C2	EPO Standard, 25 mU/mL
D1, D2	EPO Standard, 12.5 mU/mL
E1, E2	EPO Standard, 6.25 mU/mL
F1, F2	EPO Standard, 3.12 mU/mL
G1, G2	EPO Standard, 1.56 mU/mL
H1, H2	EPO Standard, 0 mU/mL
A3, B3	1:2500 EPO RNA (A, G, U, C), 12h
C3, D3	1:2500 EPO RNA (A, G, U, C), 24h
E3, F3	1:2500 EPO RNA (A, G, U, C), 36h
G3, H3	1:2500 EPO RNA (A, G, U, C), 48h
A4, B4	1:2500 EPO RNA (A, G, 5 moU, C), 12h
C4, D4	1:2500 EPO RNA (A, G, 5 moU, C), 24h
E4, F4	1:2500 EPO RNA (A, G, 5 moU, C), 36h
G4, H4	1:2500 EPO RNA (A, G, 5 moU, C), 48h
A5, B5	1:2500 EPO RNA (A, G, psU, C), 12h
C5, D5	1:2500 EPO RNA (A, G, psU, C), 24h
E5, F5	1:2500 EPO RNA (A, G, psU, C), 36h
G5, H5	1:2500 EPO RNA (A, G, psU, C), 48h

FIG. 16

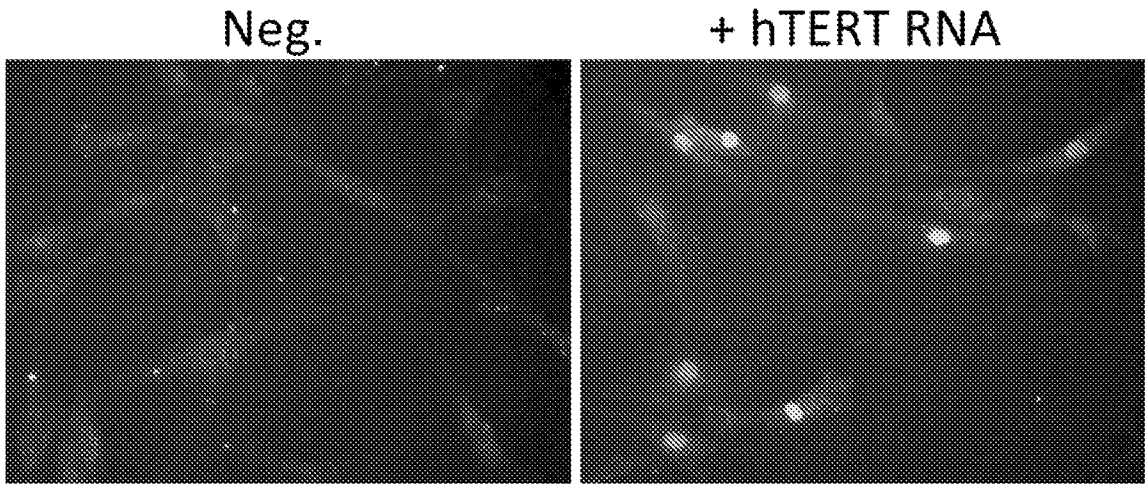

Neg.
+ hTERT RNA

FIG. 17

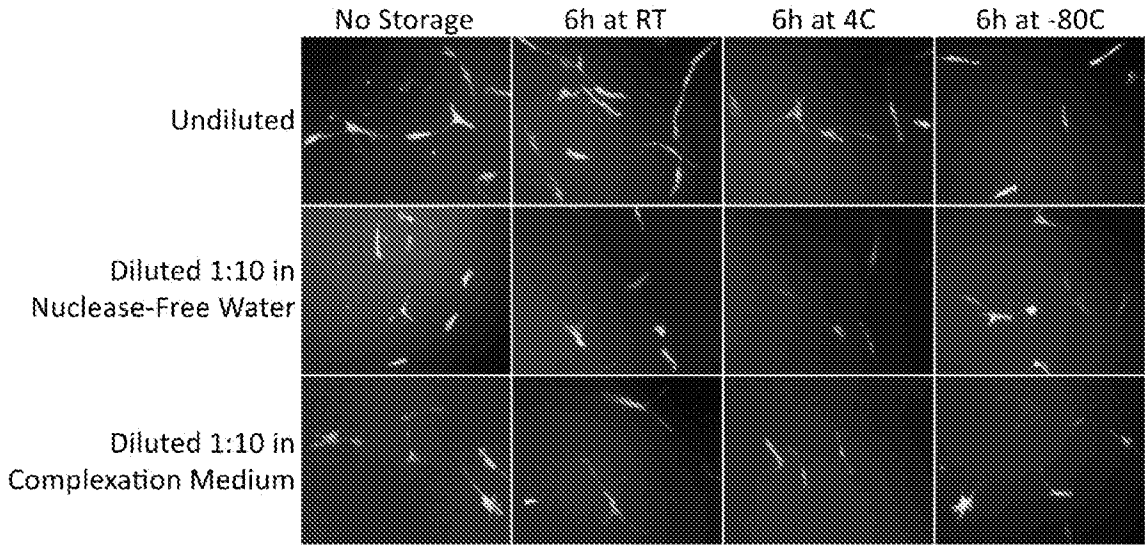

No Storage
6h at RT
6h at 4C
6h at -80C
Undiluted
Diluted 1:10 in Nuclease-Free Water
Diluted 1:10 in Complexation Medium

FIG. 18

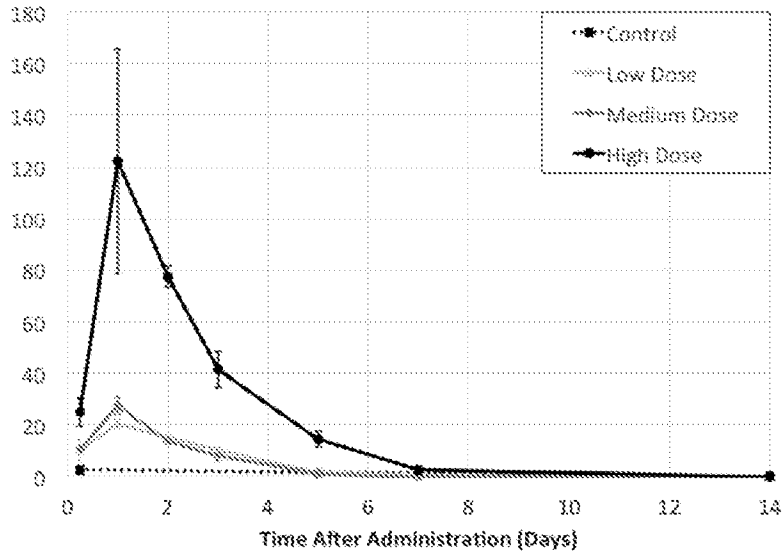

180
160
140
120
100
80
60
40
20
0
0
2
4
6
8
10
12
14
Time After Administration (Days)
Control
Low Dose
Medium Dose
High Dose

FIG. 19

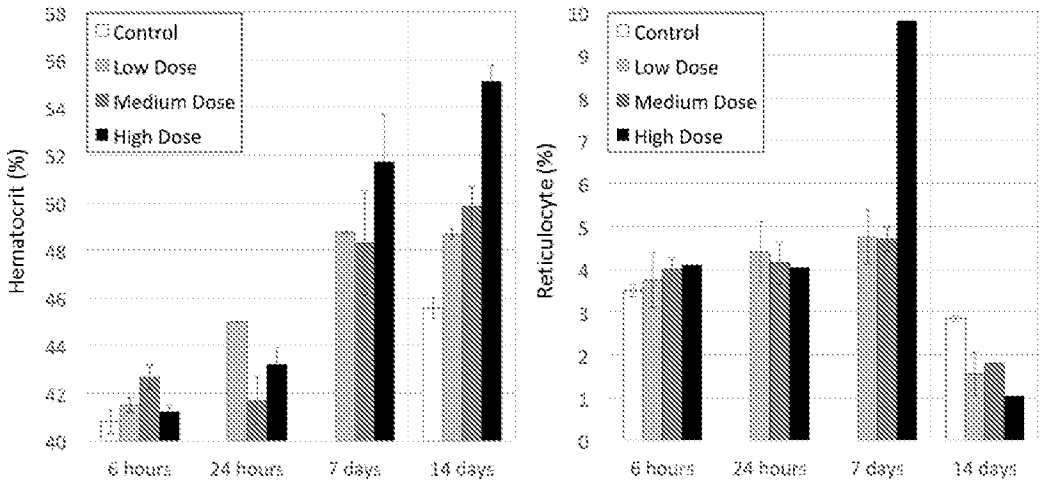

Hematocrit (%)
58
56
54
52
50
48
46
44
42
40
6 hours
24 hours
7 days
14 days
Control
Low Dose
Medium Dose
High Dose
Reticulocyte (%)
10
9
8
7
6
5
4
3
2
1
0
6 hours
24 hours
7 days
14 days
Control
Low Dose
Medium Dose
High Dose

FIG. 20

Animal #	Group	Day	Time Point	Sex	IL-6 (pg/mL)	TNFα (pg/mL)	IFNα (pg/mL)
5	1	D1	6H	M	ND	ND	ND
6	1	D1	6H	M	ND	ND	ND
13	2	D1	6H	M	ND	ND	ND
14	2	D1	6H	M	ND	ND	ND
31	3	D1	6H	M	ND	ND	ND
32	3	D1	6H	M	ND	ND	ND
49	4	D1	6H	M	ND	ND	ND
50	4	D1	6H	M	ND	ND	ND
15	2	D2	24H	M	ND	ND	ND
16	2	D2	24H	M	ND	ND	ND
33	3	D2	24H	M	ND	ND	ND
34	3	D2	24H	M	ND	ND	ND
52	4	D2	24H	M	ND	ND	ND
63	4	D2	24H	M	ND	ND	ND
23	2	D8		M	ND	ND	ND
24	2	D8		M	ND	ND	ND
41	3	D8		M	ND	ND	11.95
42	3	D8		M	ND	ND	9.13
59	4	D8		M	ND	ND	7.66
60	4	D8		M	ND	ND	12.51

ND = Not Detectable (<10 pg/mL for TNF-alpha; < 21 pg/mL for IL-6; <4 pg/mL for IFN-alpha)

FIG. 21

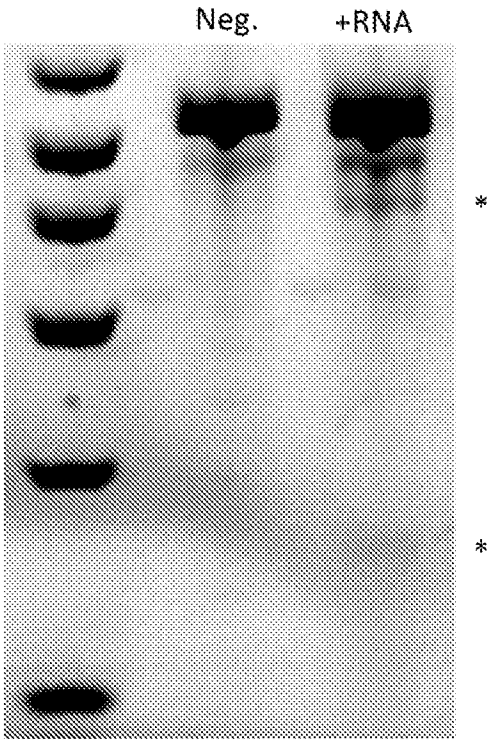


FIG. 22

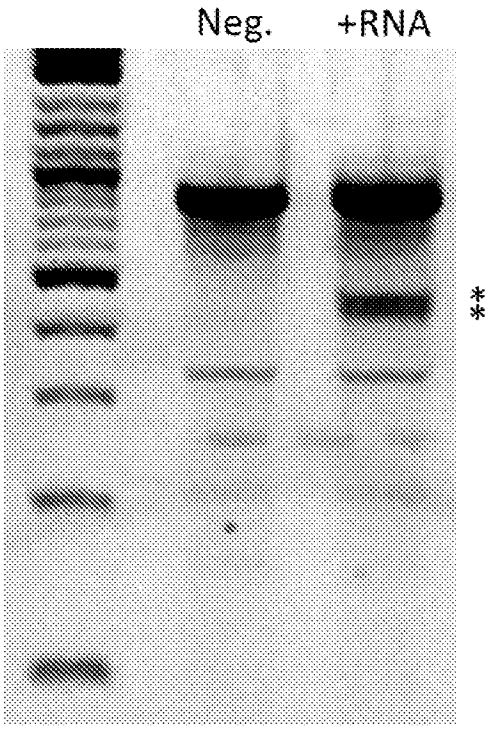


FIG. 23

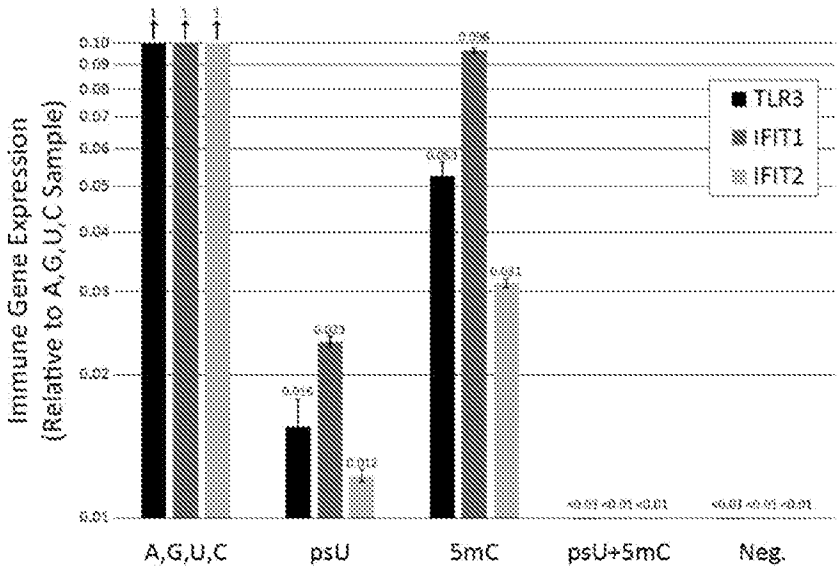

Immune Gene Expression
(Relative to A,G,U,C Sample)
TLR3
IFIT1
IFIT2
A,G,U,C
psU
5mC
psU+5mC
Neg.

FIG. 24

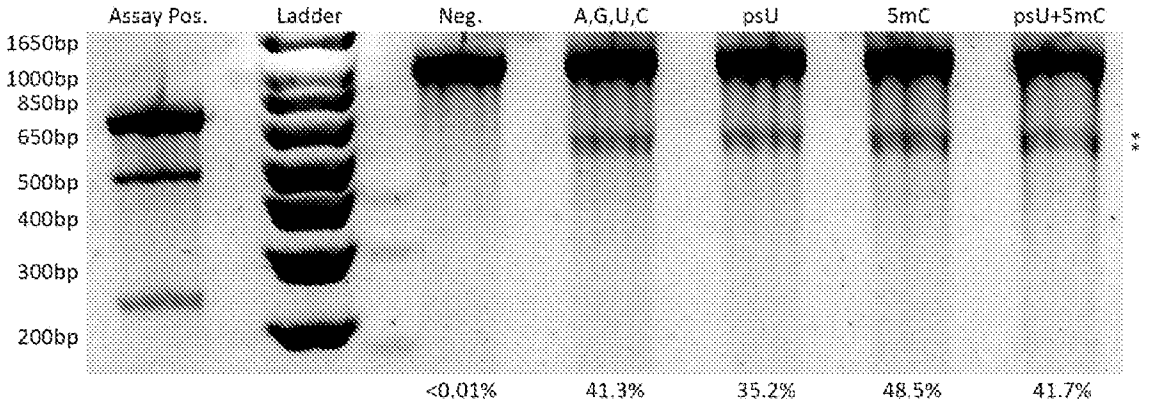

Assay Pos.
Ladder
Neg.
A,G,U,C
psU
5mC
psU+5mC
1650bp
1000bp
850bp
650bp
500bp
400bp
300bp
200bp
**
<0.01%
41.3%
35.2%
48.5%
41.7%

FIG. 25

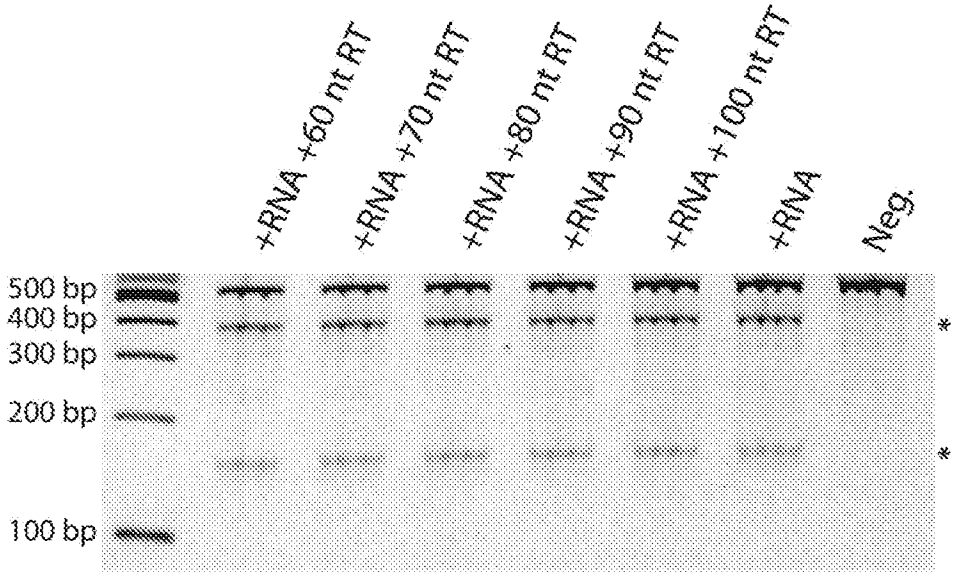

+RNA +60 nt RT
+RNA +70 nt RT
+RNA +80 nt RT
+RNA +90 nt RT
+RNA +100 nt RT
+RNA
Neg.
500 bp
400 bp
300 bp
200 bp
100 bp
*
*

FIG. 26

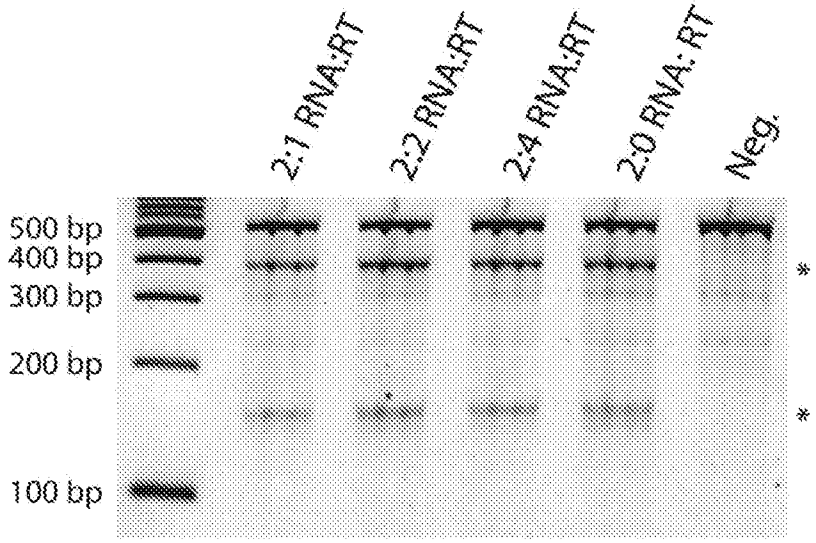

2:1 RNA:RT
2:2 RNA:RT
2:4 RNA:RT
2:0 RNA:RT
Neg.
500 bp
400 bp
300 bp
200 bp
100 bp
*
*

FIG. 27

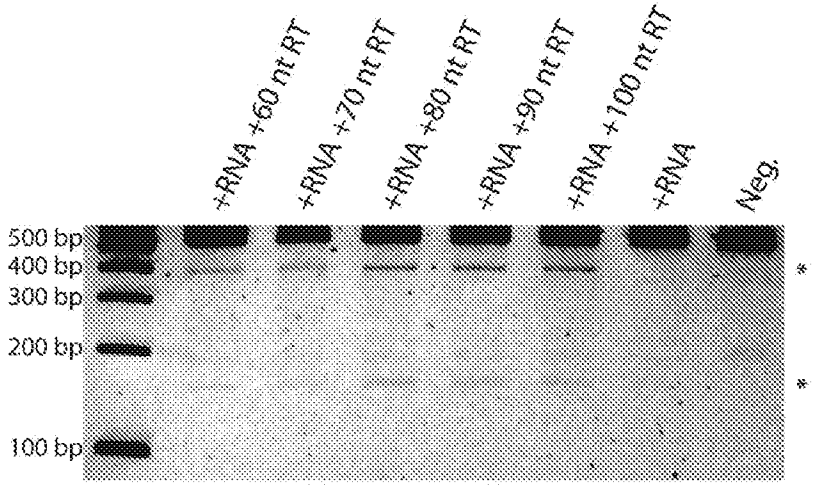

+RNA +60 nt RT
+RNA +70 nt RT
+RNA +80 nt RT
+RNA +90 nt RT
+RNA +100 nt RT
+RNA
Neg.
500 bp
400 bp
300 bp
200 bp
100 bp
*
*

FIG. 28

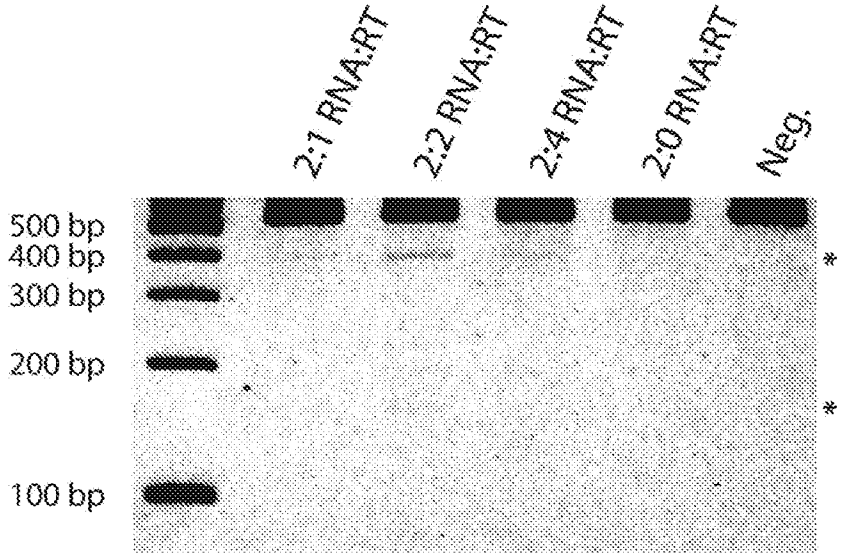

2:1 RNA:RT
2:2 RNA:RT
2:4 RNA:RT
2:0 RNA:RT
Neg.
500 bp
400 bp
300 bp
200 bp
100 bp
*
*

FIG. 29

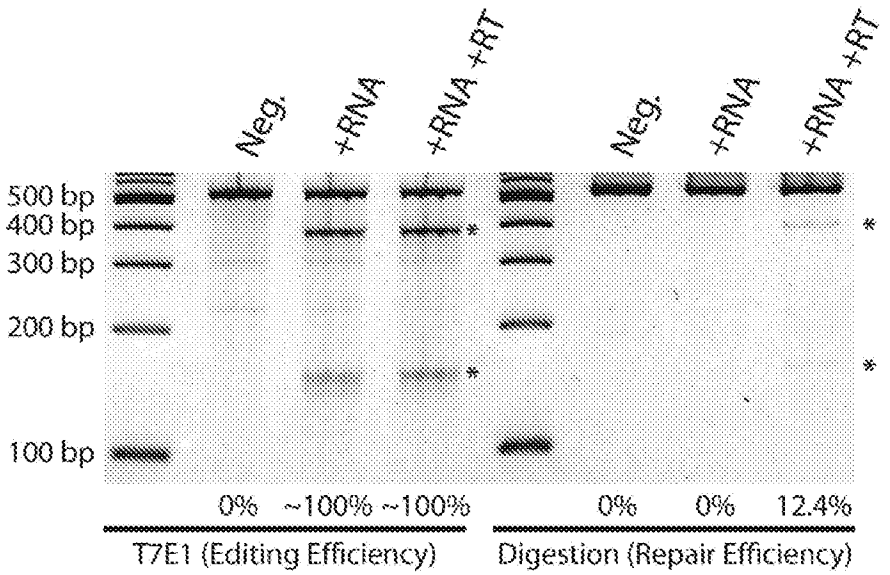

Neg.
+RNA
+RNA +RT
Neg.
+RNA
+RNA +RT
500 bp
400 bp
300 bp
200 bp
100 bp
*
*
*
*
0% ~100% ~100%
0% 0% 12.4%
T7E1 (Editing Efficiency)
Digestion (Repair Efficiency)

FIG. 30

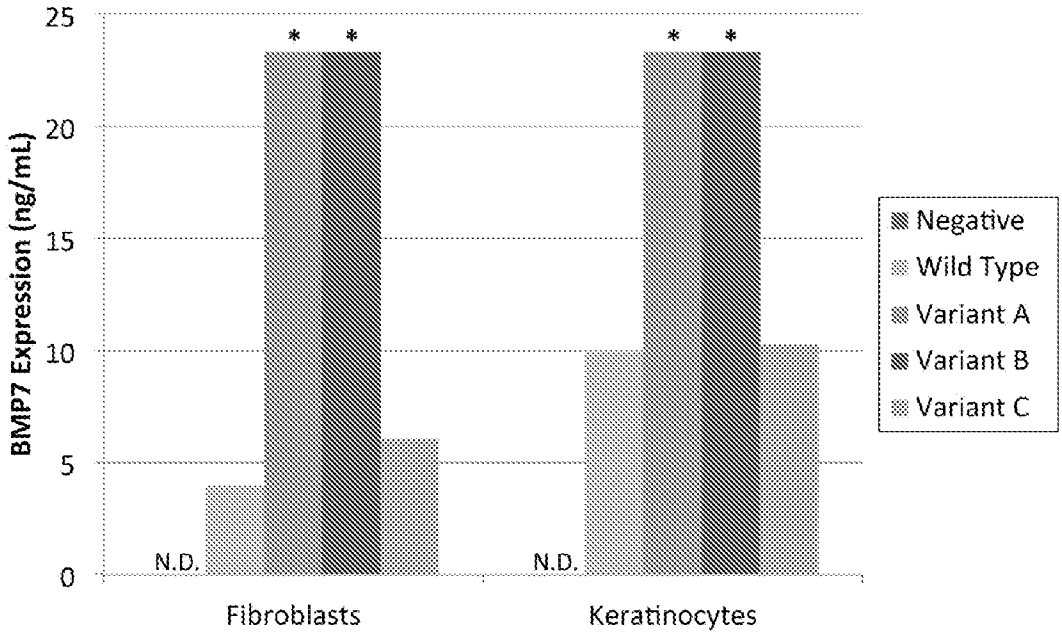

BMP7 Expression (ng/mL)
25
20
15
10
5
0
*
*
*
*
N.D.
N.D.
Fibroblasts
Keratinocytes
Negative
Wild Type
Variant A
Variant B
Variant C

FIG. 31

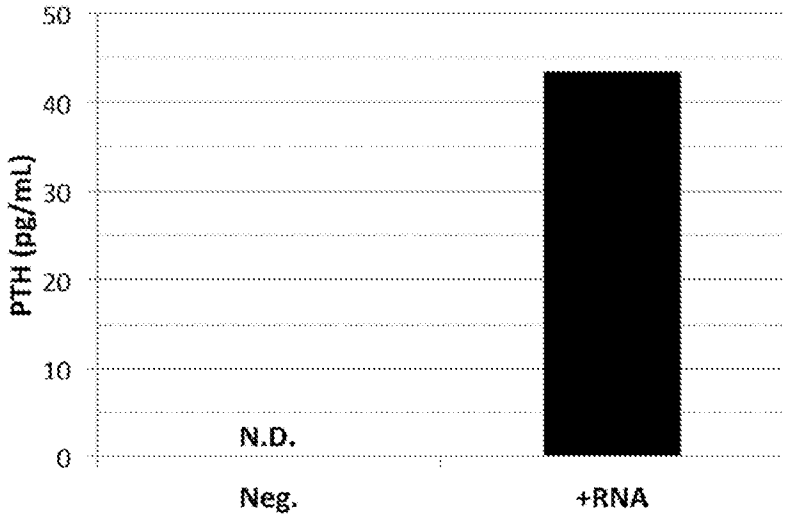
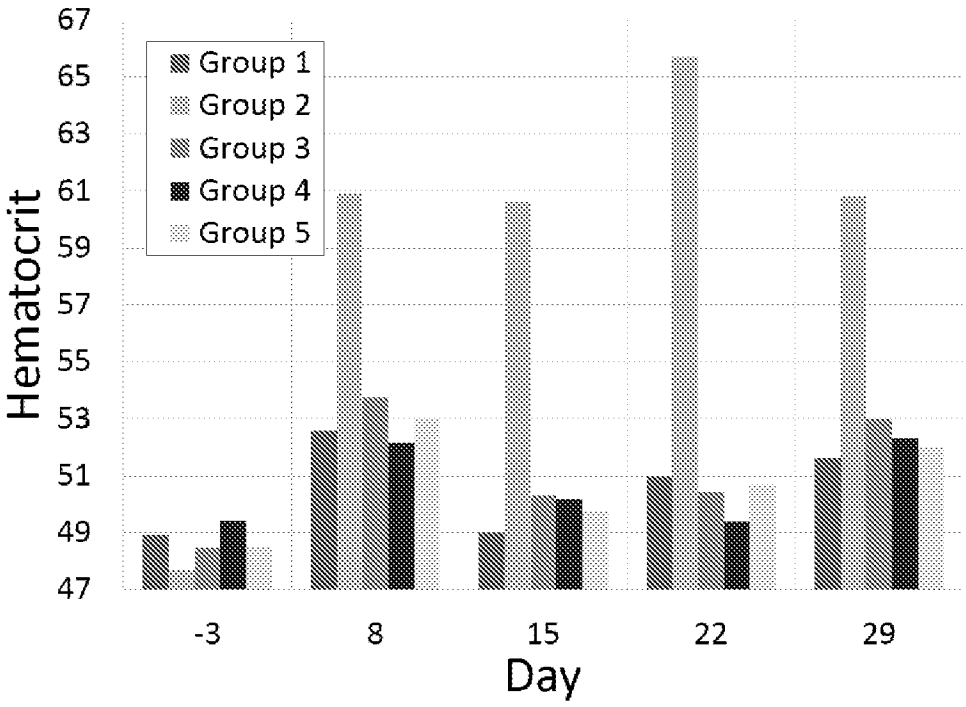

50
40
30
20
10
0
PTH (pg/mL)
N.D.
Neg.
+RNA

FIG. 32


67
65
63
61
59
57
55
53
51
49
47
Hematocrit
Group 1
Group 2
Group 3
Group 4
Group 5
-3
8
15
22
29
Day

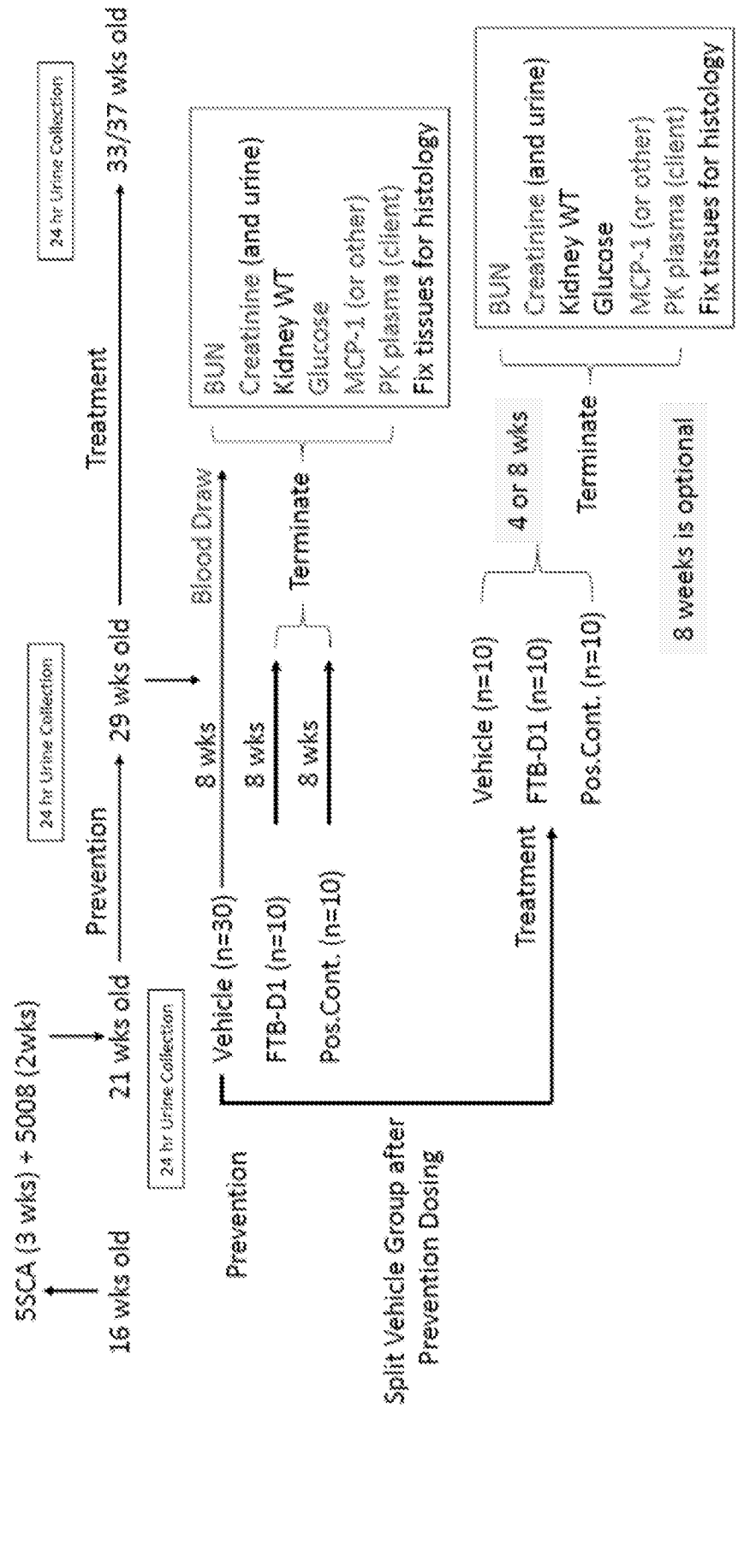

5SCA (3 wks) + 5008 (2wks)
16 wks old
21 wks old
24 hr Urine Collection
Prevention
29 wks old
24 hr Urine Collection
Treatment
33/37 wks old
24 hr Urine Collection
Prevention
Vehicle (n=30)
FTB-D1 (n=10)
Pos.Cont. (n=10)
8 wks
8 wks
8 wks
Blood Draw
Terminate
BUN
Creatinine (and urine)
Kidney WT
Glucose
MCP-1 (or other)
PK plasma (client)
Fix tissues for histology
Split Vehicle Group after Prevention Dosing
Treatment
Vehicle (n=10)
FTB-D1 (n=10)
Pos.Cont. (n=10)
4 or 8 wks
Terminate
BUN
Creatinine (and urine)
Kidney WT
Glucose
MCP-1 (or other)
PK plasma (client)
Fix tissues for histology
8 weeks is optional

FIG. 33

FIG. 34

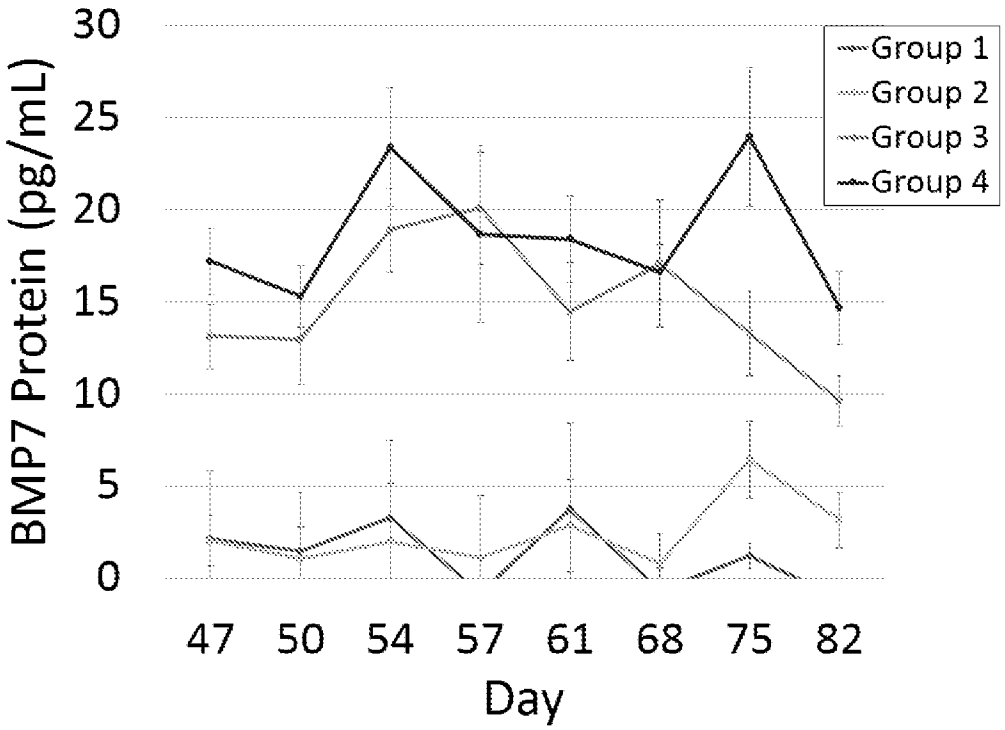

30
25
20
15
10
5
0
BMP7 Protein (pg/mL)
47
50
54
57
61
68
75
82
Day
Group 1
Group 2
Group 3
Group 4

FIG. 35

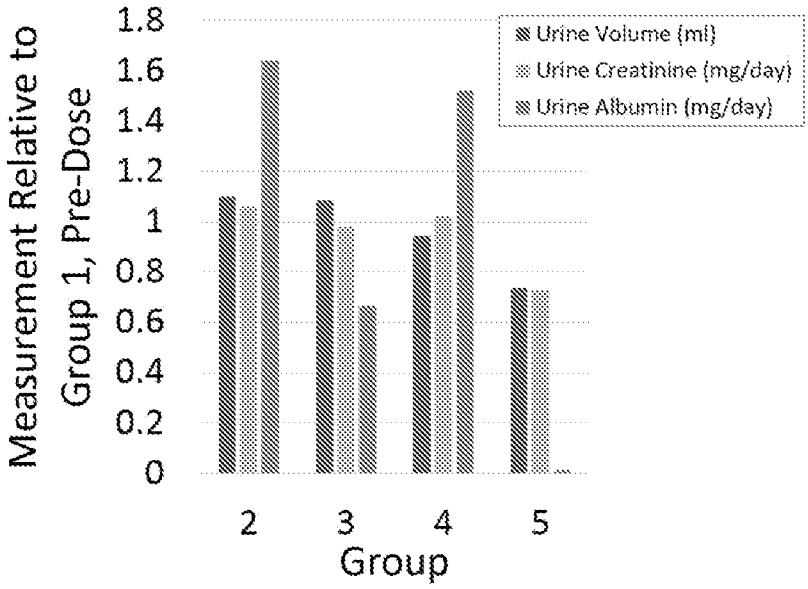
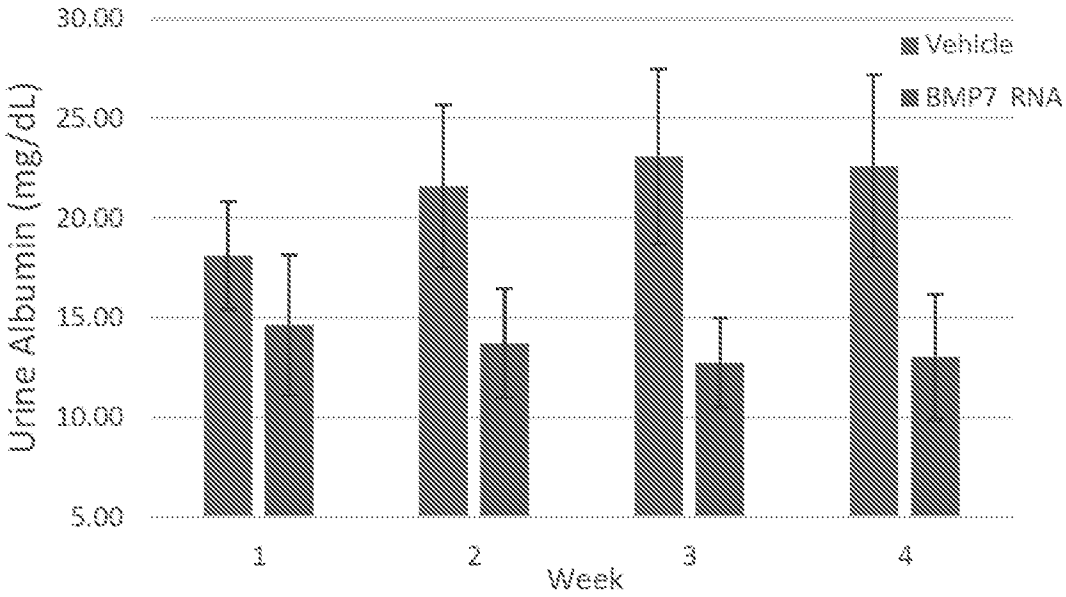

Measurement Relative to Group 1, Pre-Dose
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
2
3
4
5
Group
Urine Volume (ml)
Urine Creatinine (mg/day)
Urine Albumin (mg/day)

FIG. 36


30.00
25.00
20.00
15.00
10.00
5.00
Urine Albumin (mg/dL)
Vehicle
BMP7 RNA
1
2
3
4
Week

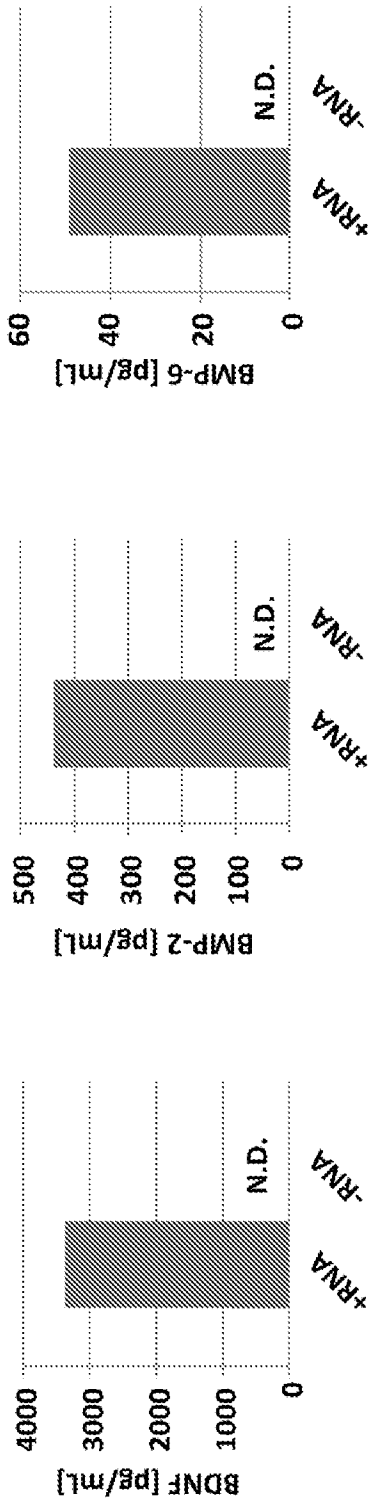

A.
BDNF [pg/mL]
4000
3000
2000
1000
0
N.D.
+RNA
-RNA
B.
BMP-2 [pg/mL]
500
400
300
200
100
0
N.D.
+RNA
-RNA
C.
BMP-6 [pg/mL]
60
40
20
0
N.D.
+RNA
-RNA

FIG. 37

FIG. 37 (continued)

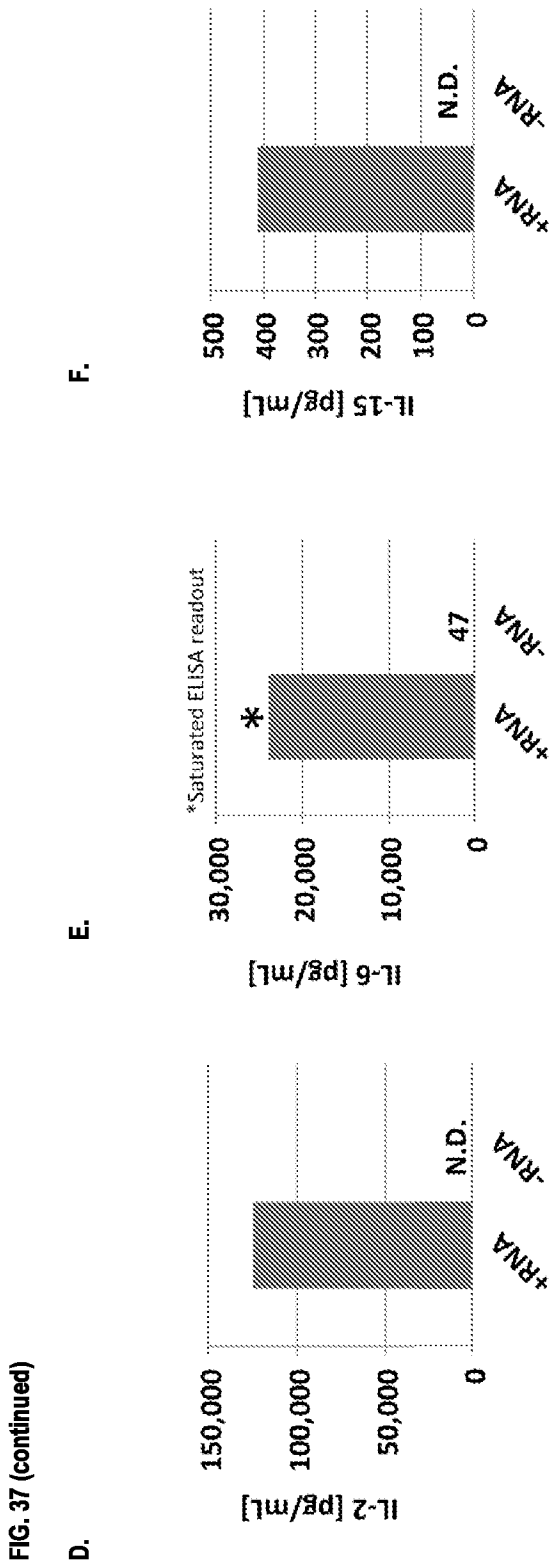


FIG. 37 (continued)

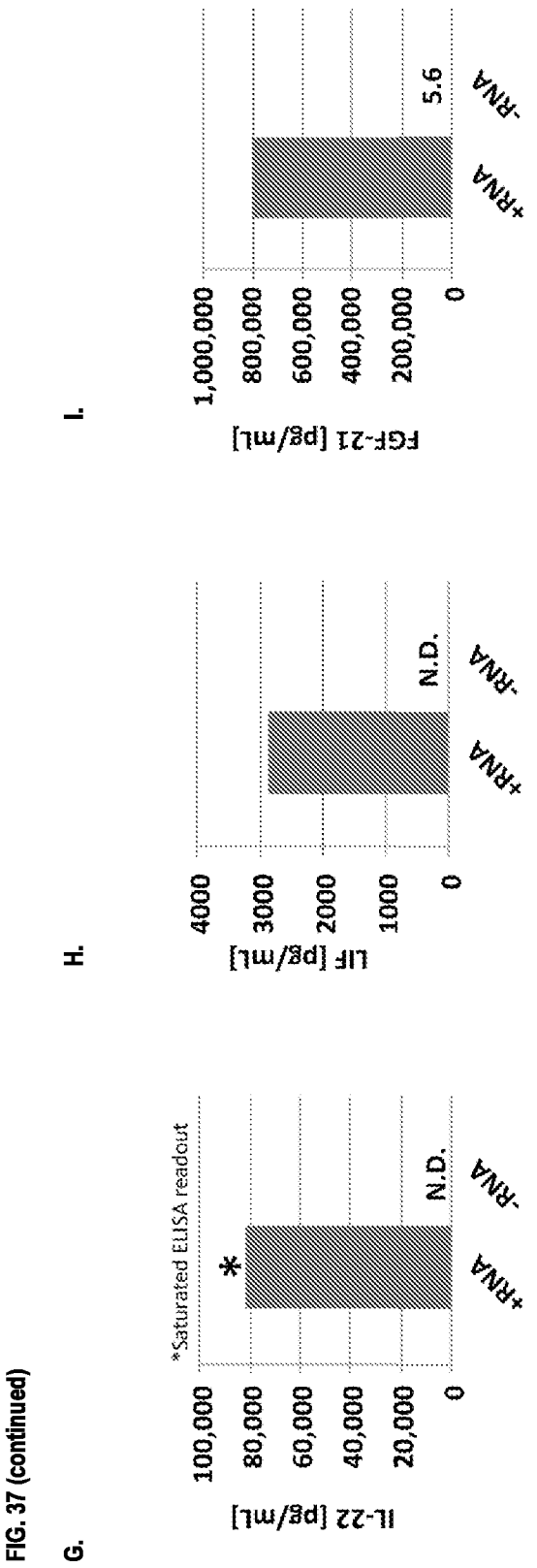
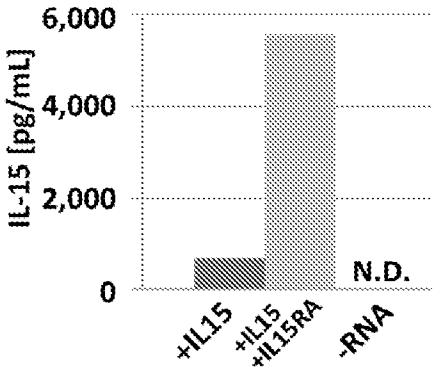


FIG. 38



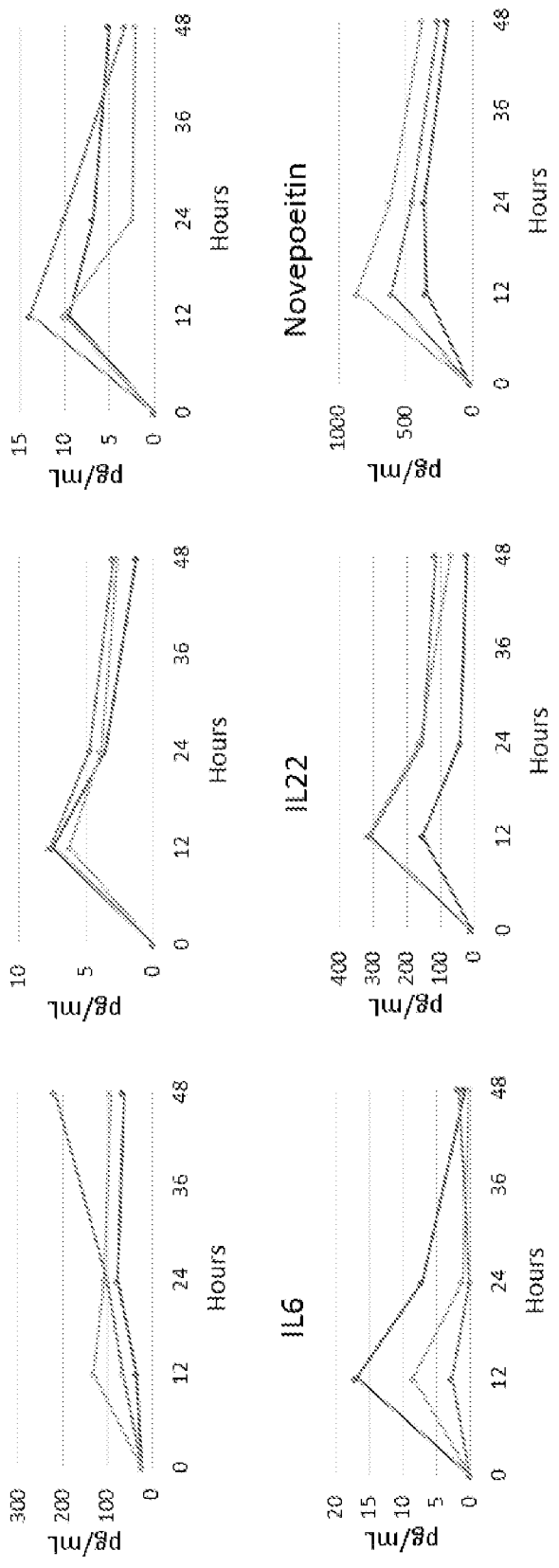

FGF21
pg/mL
300
200
100
0
0
12
24
36
48
Hours
IL15
pg/mL
10
5
0
0
12
24
36
48
Hours
IL15+IL15R
pg/mL
15
10
5
0
0
12
24
36
48
Hours
IL6
pg/mL
20
15
10
5
0
0
12
24
36
48
Hours
IL22
pg/mL
400
300
200
100
0
0
12
24
36
48
Hours
Novepoeitin
pg/mL
1000
500
0
0
12
24
36
48
Hours

FIG. 39

FIG. 40

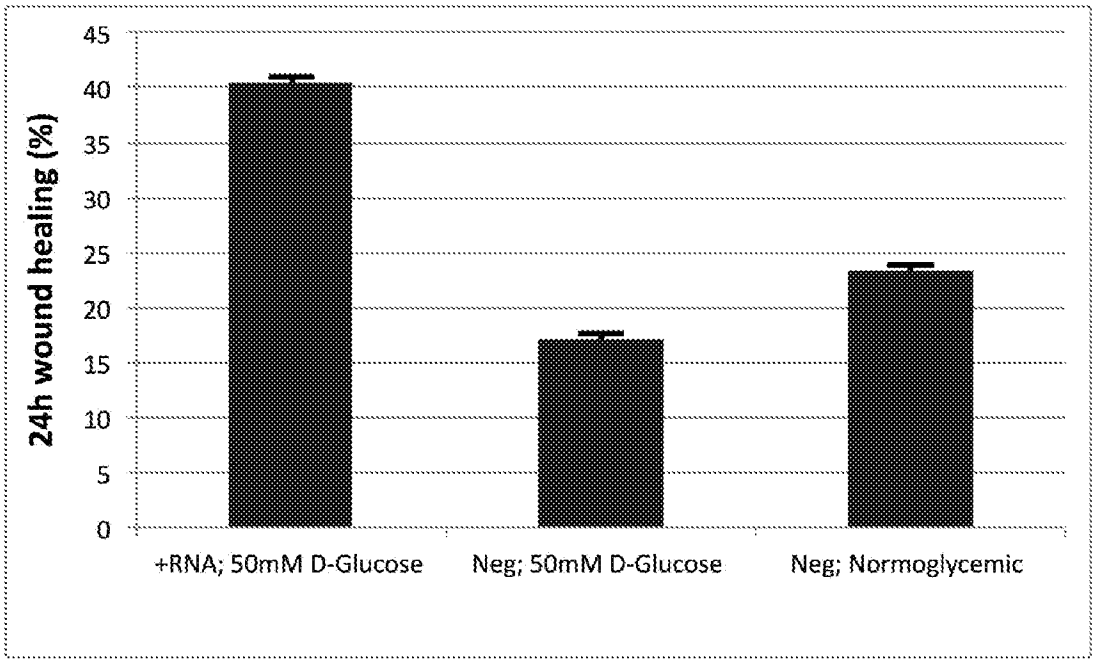

24h wound healing (%)
45
40
35
30
25
20
15
10
5
0
+RNA; 50mM D-Glucose
Neg; 50mM D-Glucose
Neg; Normoglycemic

FIG. 41

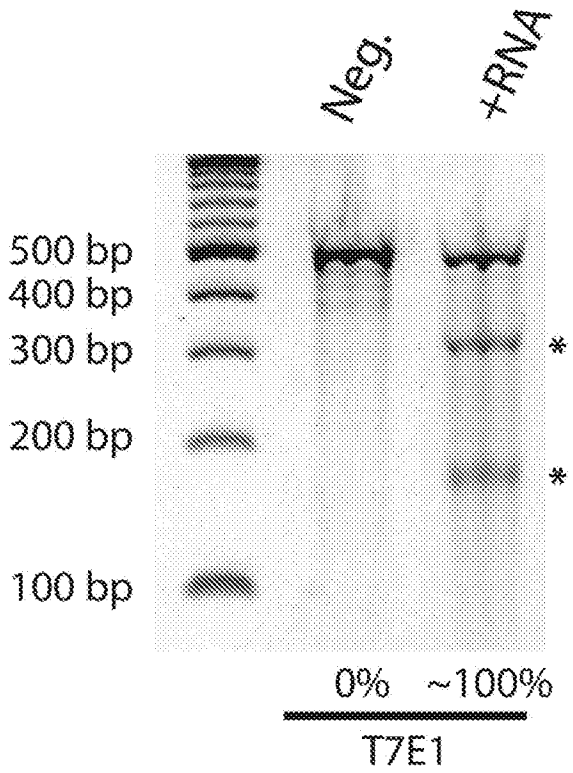

Neg.
+RNA
500 bp
400 bp
300 bp
200 bp
100 bp
*
*
0%
~100%
T7E1

FIG. 42

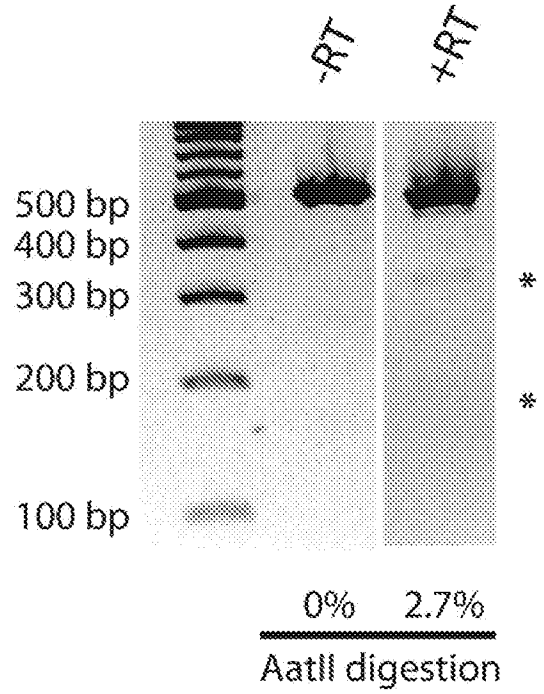

-RT
+RT
500 bp
400 bp
300 bp
200 bp
100 bp
*
*
0%
2.7%
AatII digestion

FIG. 43

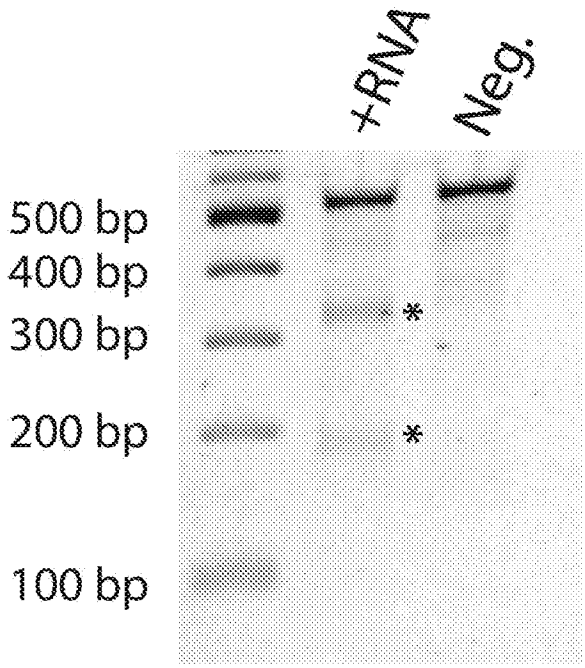

+RNA
Neg.
500 bp
400 bp
300 bp
200 bp
100 bp
*
*

FIG. 44

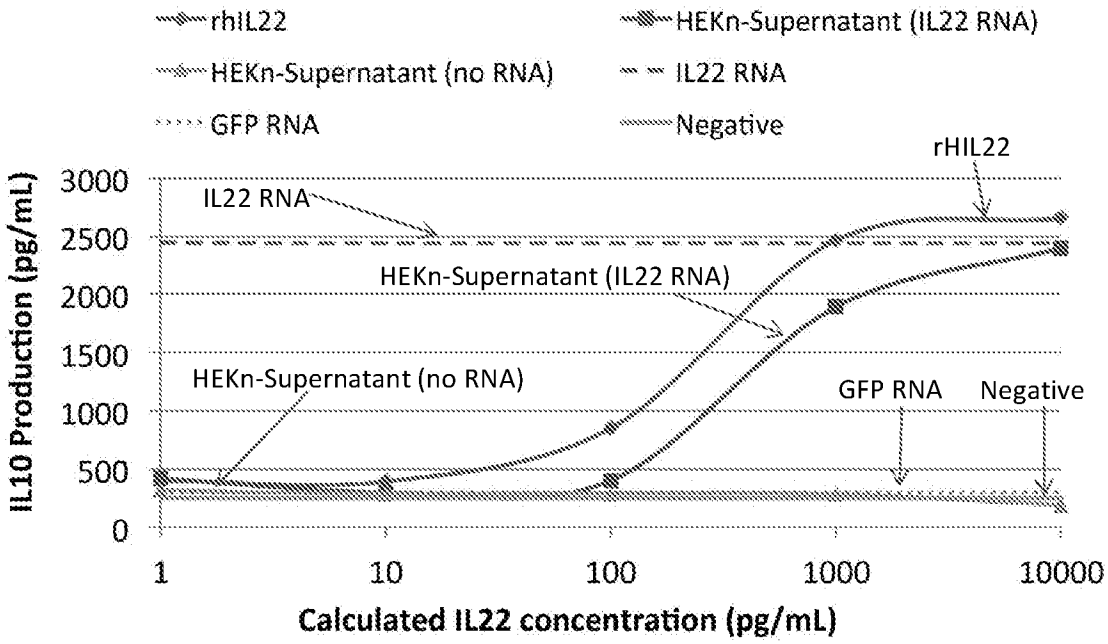

rhIL22
HEKn-Supernatant (IL22 RNA)
HEKn-Supernatant (no RNA)
IL22 RNA
GFP RNA
Negative
rHIL22
IL22 RNA
HEKn-Supernatant (IL22 RNA)
HEKn-Supernatant (no RNA)
GFP RNA
Negative
IL10 Production (pg/mL)
3000
2500
2000
1500
1000
500
0
1
10
100
1000
10000
Calculated IL22 concentration (pg/mL)

FIG. 45

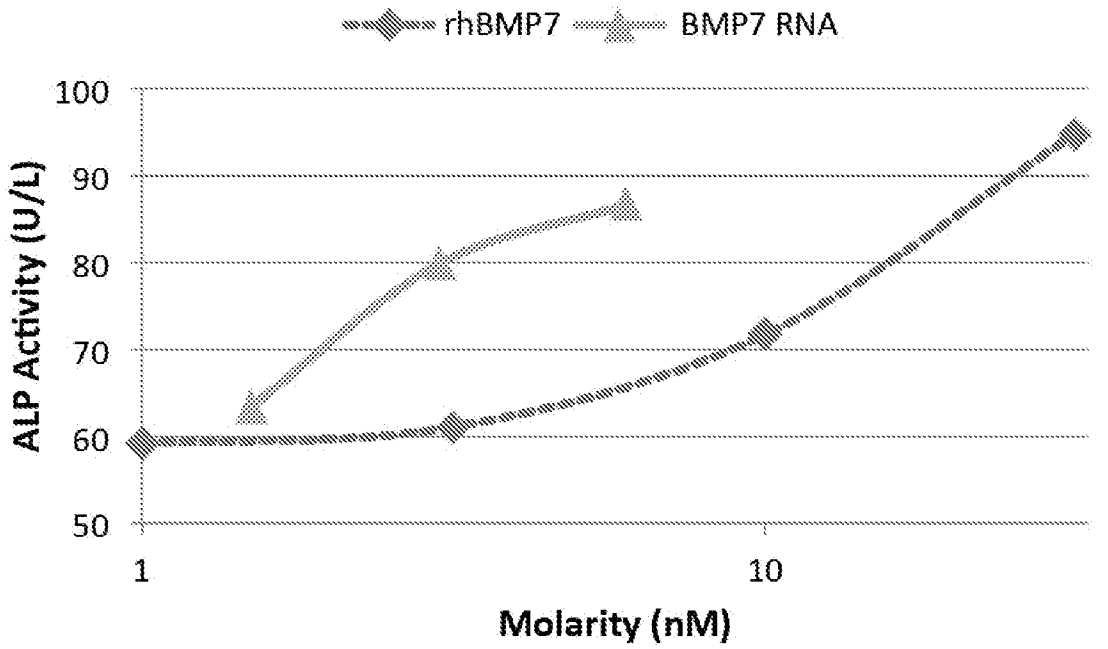

rhBMP7
BMP7 RNA
ALP Activity (U/L)
100
90
80
70
60
50
1
10
Molarity (nM)

FIG. 46

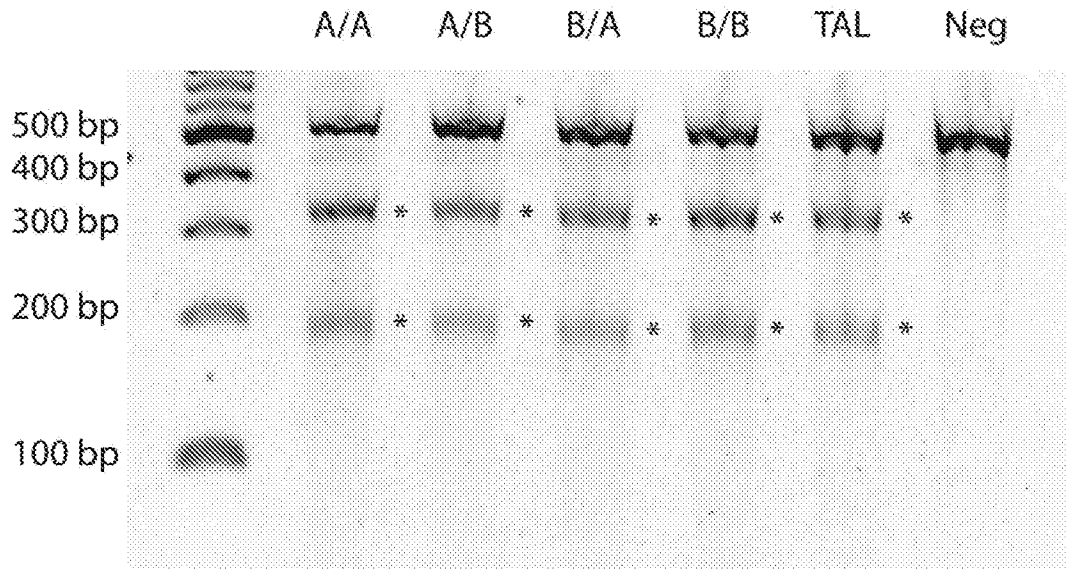

A/A
A/B
B/A
B/B
TAL
Neg
500 bp
400 bp
300 bp
200 bp
100 bp

FIG. 47

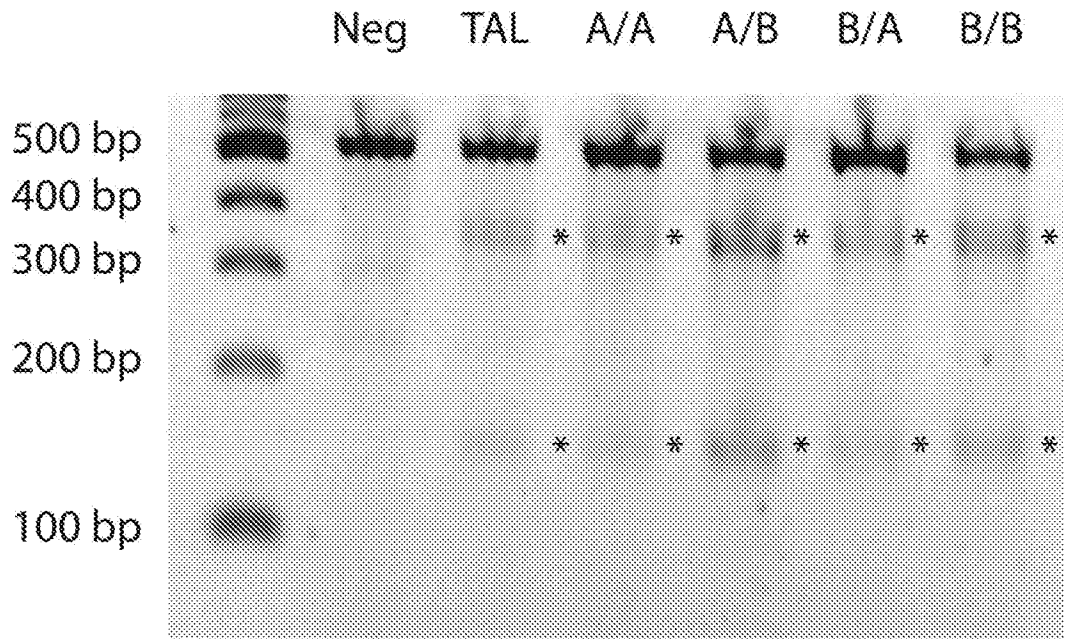

Neg
TAL
A/A
A/B
B/A
B/B
500 bp
400 bp
300 bp
200 bp
100 bp

FIG. 48

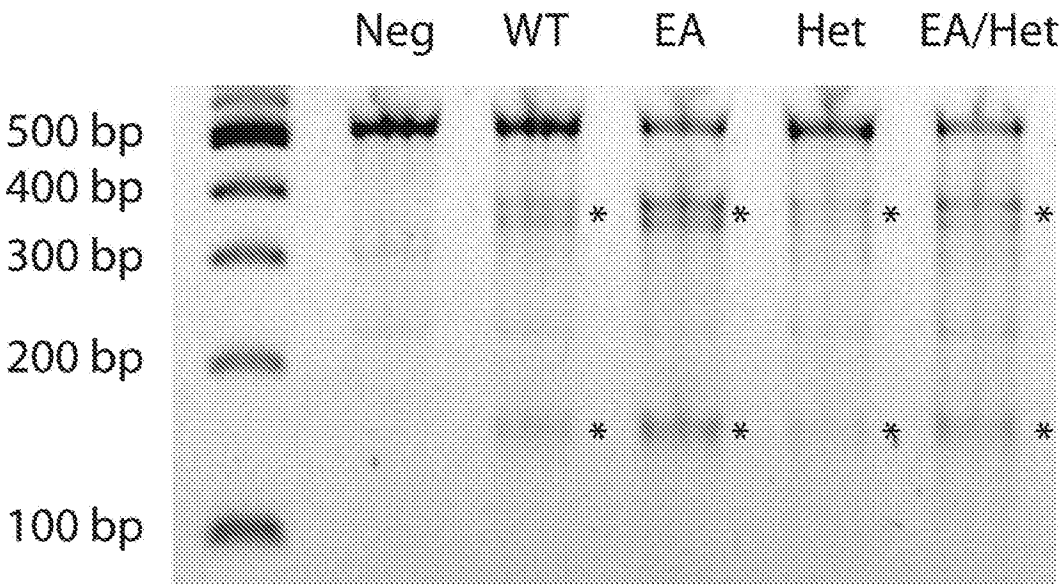


FIG. 49

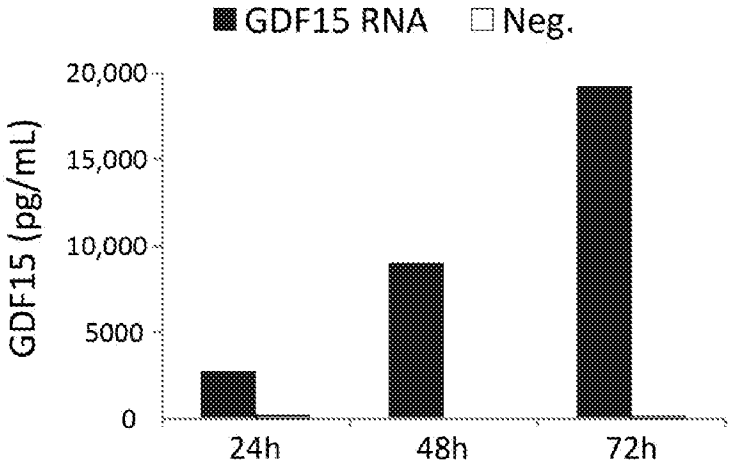
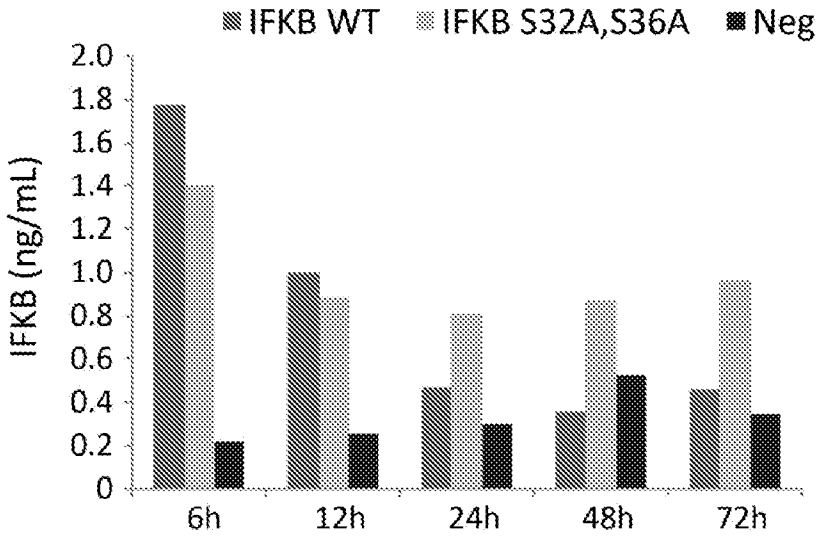

GDF15 RNA
Neg.
GDF15 (pg/mL)
20,000
15,000
10,000
5000
0
24h
48h
72h

FIG. 50


IFKB WT
IFKB S32A,S36A
Neg
IFKB (ng/mL)
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
6h
12h
24h
48h
72h

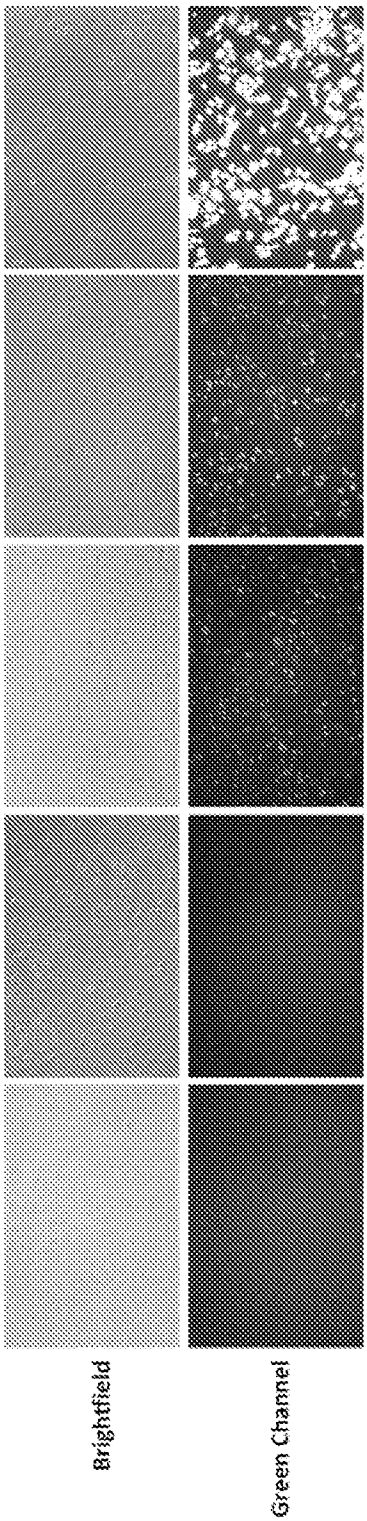

KRT5 RNA
KRT14 RNA
KRT5-GFP RNA
KRT14-GFP RNA
GFP RNA
Brightfield
Green Channel

FIG. 51

FIG. 52

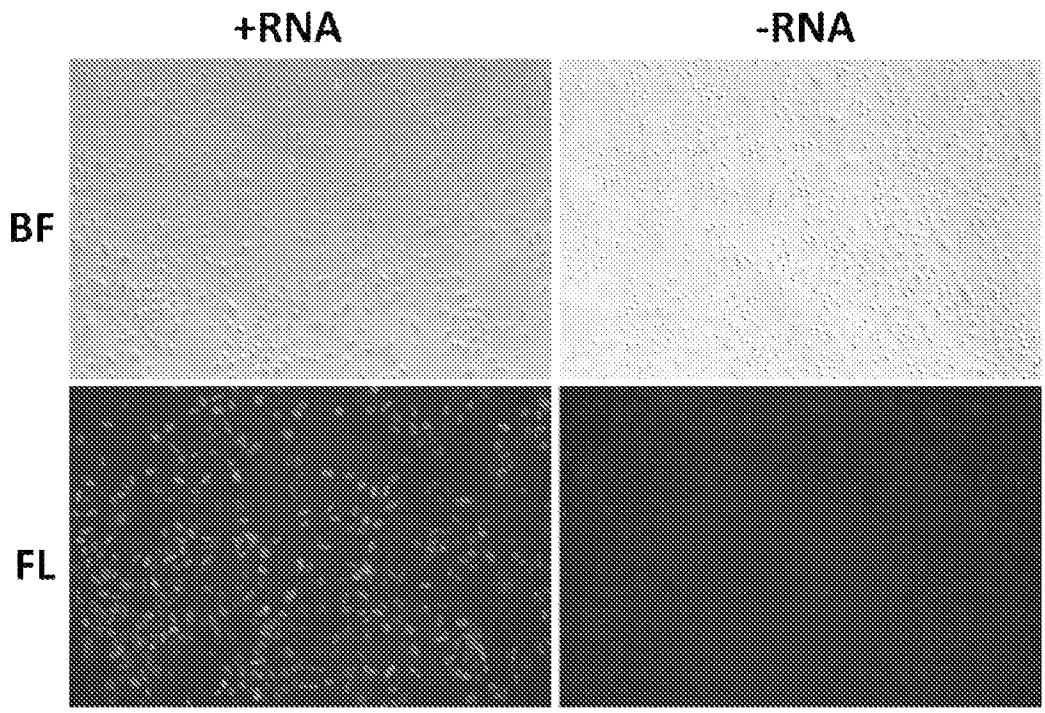

+RNA
-RNA
BF
FL

FIG. 53

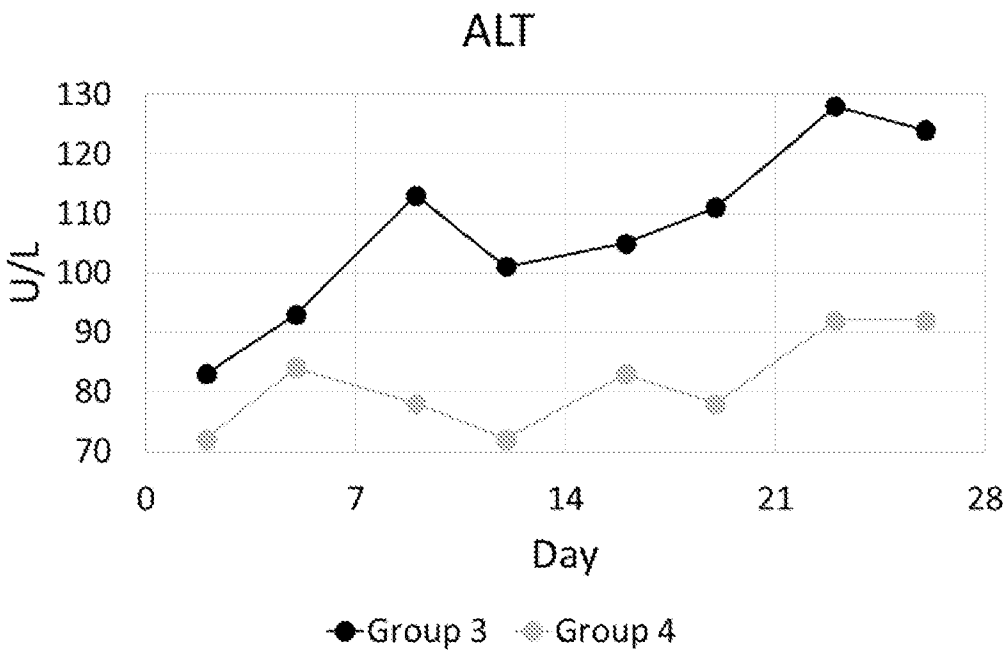

ALT
130
120
110
100
90
80
70
U/L
0
7
14
21
28
Day
Group 3
Group 4

FIG. 54

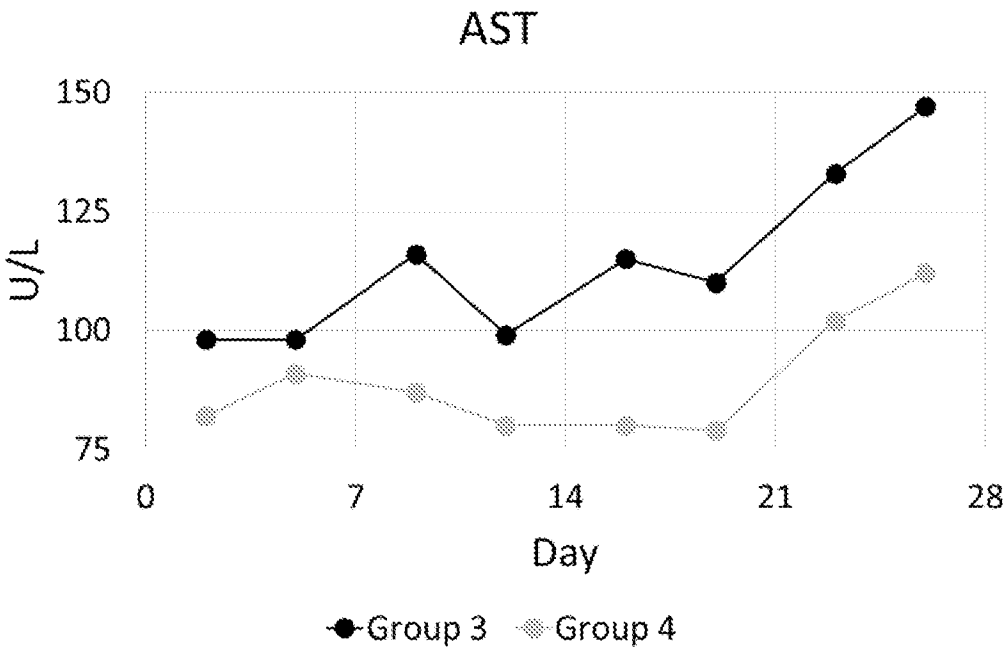

AST
150
125
100
75
U/L
0
7
14
21
28
Day
Group 3
Group 4

FIG. 55

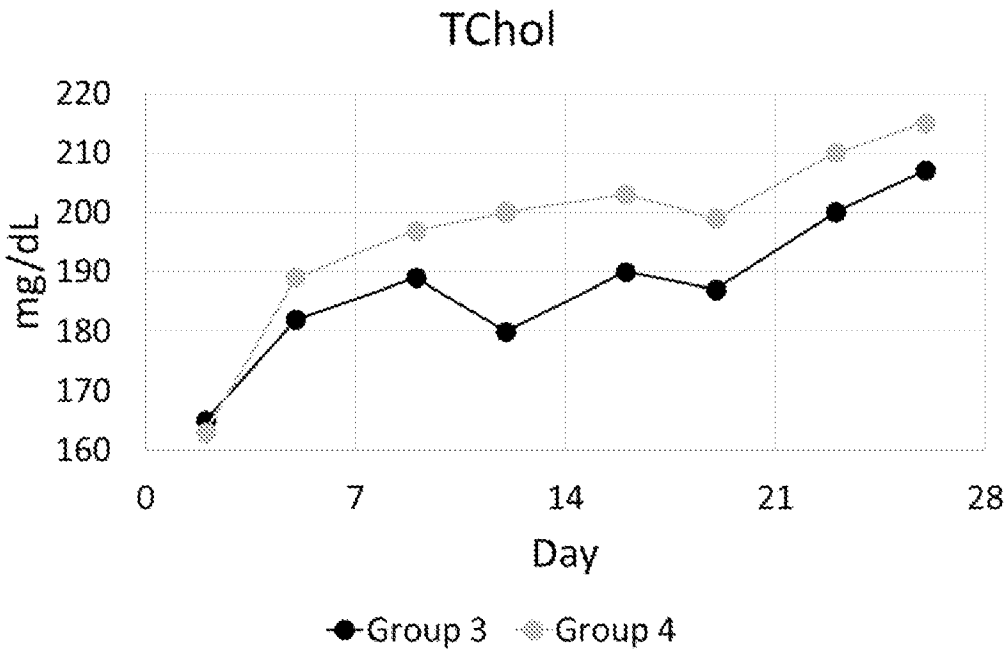

TChol
220
210
200
190
180
170
160
mg/dL
0
7
14
21
28
Day
Group 3
Group 4

FIG. 56

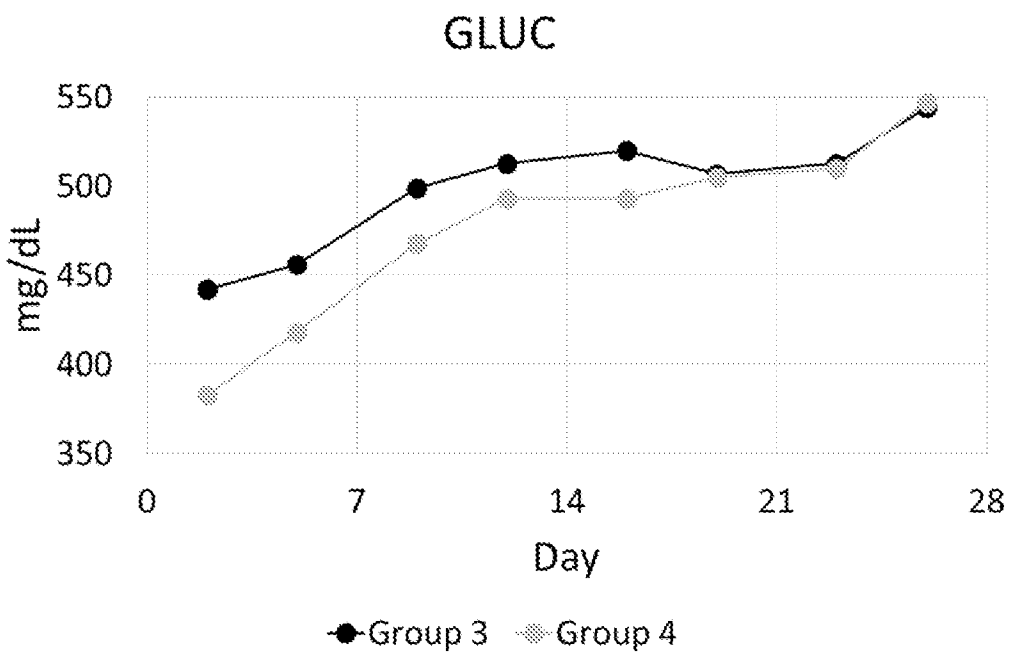

GLUC
550
500
450
400
350
mg/dL
0
7
14
21
28
Day
Group 3
Group 4

FIG. 57

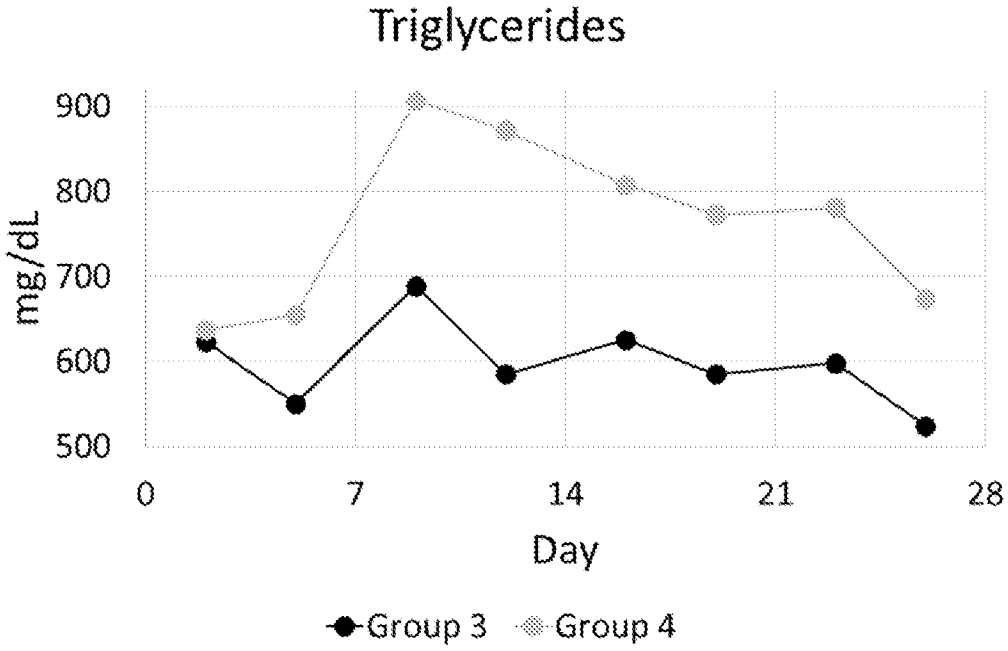

Triglycerides
900
800
700
600
500
mg/dL
0
7
14
21
28
Day
Group 3
Group 4

FIG. 58

	ALT (U/L)	AST (U/L)	TChol (mg/dL)	GLUC (mg/dL)	Trig. (mg/dL)
% Change	-24.1%	-22.3%	5.1%	-4.4%	27.8%
p-value	0.002451	0.00166	0.016834	0.037562	0.000742

FIG. 59

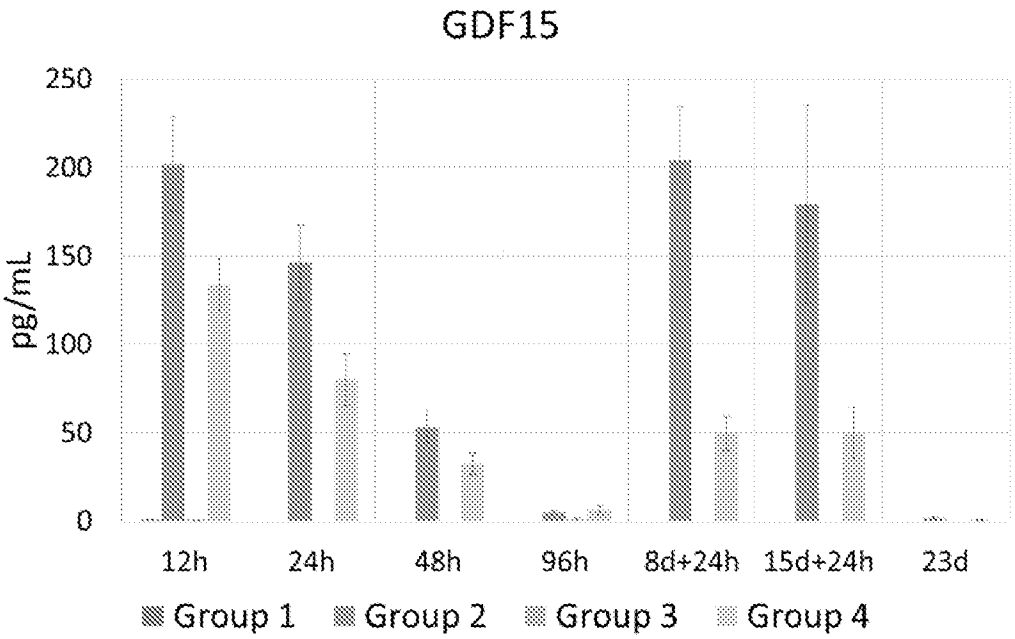


FIG. 60

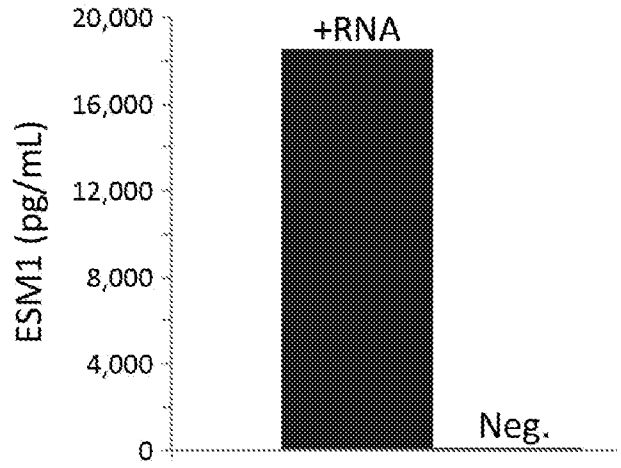

20,000
16,000
12,000
8,000
4,000
0
ESM1 (pg/mL)
+RNA
Neg.

FIG. 61

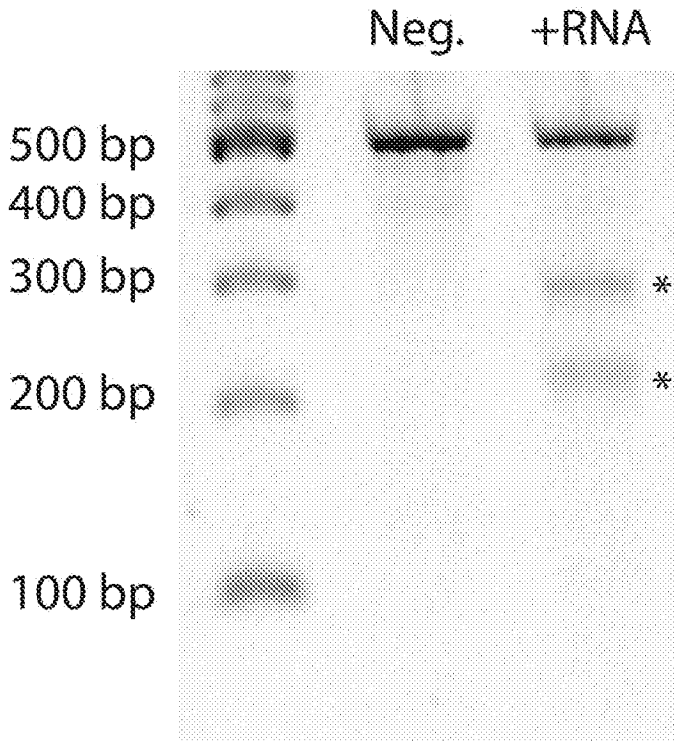
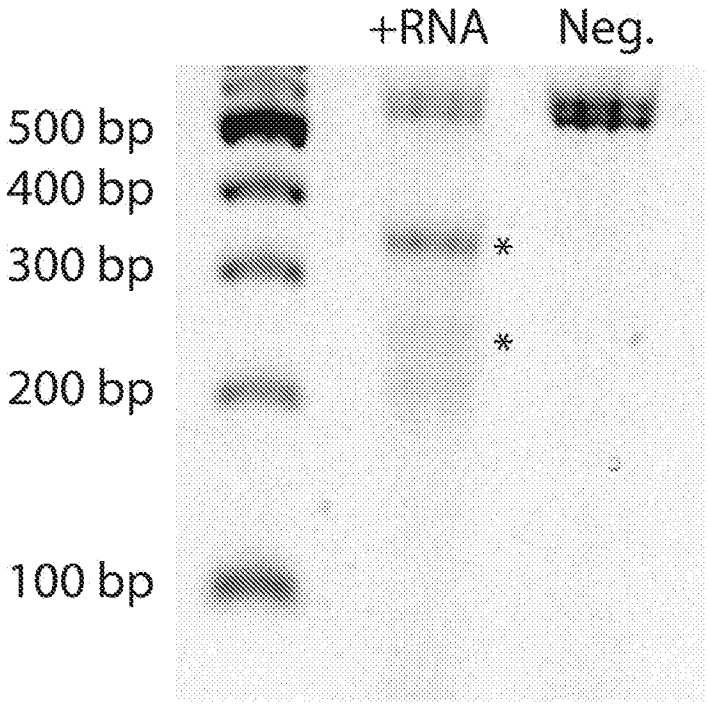

Neg.
+RNA
500 bp
400 bp
300 bp
200 bp
100 bp
*
*

FIG. 62



SEQUENCE LISTING

<110> FACTOR BIOSCIENCE INC.

<120> NUCLEIC ACID PRODUCTS AND METHODS OF ADMINISTRATION THEREOF

<130> FAB-010PC

<150> US 62/376,209
<151> 2016-08-17

<150> US 62/509,350
<151> 2017-05-22

<160> 650

<170> PatentIn version 3.5

<210> 1
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<212> PRT
<213> Homo sapiens

<400> 1

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Val Leu Glu Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr
1               5                  10                  15

Glu Leu Thr Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala
            20                  25                  30

Ser Lys Lys Lys Thr Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile
        35                  40                  45

Ser Thr Lys Ile Phe Thr Asp Glu Leu Gly Phe Ser Gly Lys His Leu
    50                  55                  60

Gly Gly Ser Asn Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala
65                  70                  75                  80

Ile Ile Leu Asp Ser Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala
                85                  90                  95

Ser His Thr Asp Ala Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg
            100                 105                 110

Lys Glu Glu Ile Lys Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu
        115                 120                 125

Asp Asn Thr Tyr Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asn Tyr
    130                 135                 140

Lys Glu Gln Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly
145                 150                 155                 160

Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr
                165                 170                 175
```

```
Gln Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn
            180                 185                 190


Ile Ser Tyr
        195


<210>  2
<211>  195
<212>  PRT
<213>  Homo sapiens

<400>  2

Val Leu Glu Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr
1               5                   10                  15


Glu Leu Thr Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala
            20                  25                  30


Ser Lys Lys Lys Thr Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile
        35                  40                  45


Ser Thr Lys Ile Phe Thr Asp Glu Leu Gly Phe Ser Gly Glu His Leu
    50                  55                  60


Gly Gly Ser Asn Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala
65                  70                  75                  80


Ile Ile Leu Asp Ser Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala
                85                  90                  95


Ser His Thr Asp Ala Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg
            100                 105                 110


Lys Glu Glu Ile Lys Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu
        115                 120                 125


Asp Asn Thr Tyr Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asn Tyr
    130                 135                 140


Lys Glu Gln Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly
145                 150                 155                 160


Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr
                165                 170                 175


Gln Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn
            180                 185                 190


Ile Ser Tyr
        195
```

<210> 3
<211> 195
<212> PRT
<213> Homo sapiens

<400> 3

Val Leu Glu Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr
1 5 10 15

Glu Leu Thr Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala
20 25 30

Ser Lys Pro Lys Thr Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile
35 40 45

Ser Thr Lys Ile Phe Thr Asp Glu Leu Gly Phe Ser Gly Lys His Leu
50 55 60

Gly Gly Ser Asn Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala
65 70 75 80

Ile Ile Leu Asp Ser Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala
85 90 95

Ser His Thr Asp Ala Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg
100 105 110

Lys Glu Glu Ile Lys Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu
115 120 125

Asp Asn Thr Tyr Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asn Tyr
130 135 140

Lys Glu Gln Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly
145 150 155 160

Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr
165 170 175

Gln Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn
180 185 190

Ile Ser Tyr
195

<210> 4
<211> 195
<212> PRT
<213> Homo sapiens

<400> 4

Val Leu Glu Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr
1 5 10 15

```
Glu Leu Thr Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala
            20                  25                  30

Ser Lys Pro Lys Thr Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile
        35                  40                  45

Ser Thr Lys Ile Phe Thr Asp Glu Leu Gly Phe Ser Gly Glu His Leu
    50                  55                  60

Gly Gly Ser Asn Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala
65                  70                  75                  80

Ile Ile Leu Asp Ser Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala
                85                  90                  95

Ser His Thr Asp Ala Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg
            100                 105                 110

Lys Glu Glu Ile Lys Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu
        115                 120                 125

Asp Asn Thr Tyr Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asn Tyr
    130                 135                 140

Lys Glu Gln Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly
145                 150                 155                 160

Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr
                165                 170                 175

Gln Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn
            180                 185                 190

Ile Ser Tyr
        195


<210>  5
<211>  191
<212>  PRT
<213>  Homo sapiens

<400>  5

Val Leu Glu Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr
1               5                   10                  15

Glu Leu Thr Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala
            20                  25                  30

Ser Lys Pro Val Glu Asn Thr Glu Phe Glu Ala Ile Ser Thr Lys Ile
        35                  40                  45
```

```
Phe Thr Asp Glu Leu Gly Phe Ser Gly Glu His Leu Gly Gly Ser Asn
    50                  55                  60

Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala Ile Ile Leu Asp
65                  70                  75                  80

Ser Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala Ser His Thr Asp
                85                  90                  95

Ala Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg Lys Glu Glu Ile
            100                 105                 110

Lys Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu Asp Asn Thr Tyr
        115                 120                 125

Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asn Tyr Lys Glu Gln Leu
    130                 135                 140

Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly Ala Leu Glu Phe
145                 150                 155                 160

Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr Gln Lys Met Ser
                165                 170                 175

Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn Ile Ser Tyr
            180                 185                 190
```

<210> 6
<211> 195
<212> PRT
<213> Homo sapiens

<400> 6

```
Val Leu Glu Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr
1               5                   10                  15

Glu Leu Thr Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala
            20                  25                  30

Ser Lys Lys Lys Thr Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile
        35                  40                  45

Ser Thr Lys Ile Phe Thr Asp Glu Leu Gly Phe Ser Gly Lys His Leu
    50                  55                  60

Gly Gly Ser Asn Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala
65                  70                  75                  80

Ile Ile Leu Asp Ser Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala
                85                  90                  95
```

```
Ser His Thr Asp Ala Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg
            100                 105                 110

Lys Glu Glu Ile Lys Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu
        115                 120                 125

Asp Asn Thr Tyr Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asp Tyr
    130                 135                 140

Lys Glu Gln Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly
145                 150                 155                 160

Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr
                165                 170                 175

Gln Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn
            180                 185                 190

Ile Ser Tyr
        195
```

<210> 7
<211> 195
<212> PRT
<213> Homo sapiens

<400> 7

```
Val Leu Glu Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr
1               5                   10                  15

Glu Leu Thr Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala
            20                  25                  30

Ser Lys Lys Lys Thr Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile
        35                  40                  45

Ser Thr Lys Ile Phe Thr Asp Glu Leu Gly Phe Ser Gly Lys His Leu
    50                  55                  60

Gly Gly Ser Asn Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala
65                  70                  75                  80

Ile Ile Leu Asp Ser Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala
                85                  90                  95

Ser His Thr Asp Ala Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg
            100                 105                 110

Lys Glu Glu Ile Lys Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu
        115                 120                 125

Asp Asn Thr Tyr Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asp Tyr
```

130 135 140

Lys Glu Gln Leu Gln Lys Phe Arg Gln Asn Thr Asn His Leu Gly Gly
145 150 155 160

Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr
165 170 175

Gln Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn
180 185 190

Ile Ser Tyr
195

<210> 8
<211> 360
<212> PRT
<213> Homo sapiens

<400> 8

Met Ala Gly His Leu Ala Ser Asp Phe Ala Phe Ser Pro Pro Pro Gly
1 5 10 15

Gly Gly Gly Asp Gly Pro Gly Gly Pro Glu Pro Gly Trp Val Asp Pro
20 25 30

Arg Thr Trp Leu Ser Phe Gln Gly Pro Pro Gly Gly Pro Gly Ile Gly
35 40 45

Pro Gly Val Gly Pro Gly Ser Glu Val Trp Gly Ile Pro Pro Cys Pro
50 55 60

Pro Pro Tyr Glu Phe Cys Gly Gly Met Ala Tyr Cys Gly Pro Gln Val
65 70 75 80

Gly Val Gly Leu Val Pro Gln Gly Gly Leu Glu Thr Ser Gln Pro Glu
85 90 95

Gly Glu Ala Gly Val Gly Val Glu Ser Asn Ser Asp Gly Ala Ser Pro
100 105 110

Glu Pro Cys Thr Val Thr Pro Gly Ala Val Lys Leu Glu Lys Glu Lys
115 120 125

Leu Glu Gln Asn Pro Glu Glu Ser Gln Asp Ile Lys Ala Leu Gln Lys
130 135 140

Glu Leu Glu Gln Phe Ala Lys Leu Leu Lys Gln Lys Arg Ile Thr Leu
145 150 155 160

Gly Tyr Thr Gln Ala Asp Val Gly Leu Thr Leu Gly Val Leu Phe Gly
165 170 175

```
Lys Val Phe Ser Gln Thr Thr Ile Cys Arg Phe Glu Ala Leu Gln Leu
            180                 185                 190

Ser Phe Lys Asn Met Cys Lys Leu Arg Pro Leu Leu Gln Lys Trp Val
        195                 200                 205

Glu Glu Ala Asp Asn Asn Glu Asn Leu Gln Glu Ile Cys Lys Ala Glu
    210                 215                 220

Thr Leu Val Gln Ala Arg Lys Arg Lys Arg Thr Ser Ile Glu Asn Arg
225                 230                 235                 240

Val Arg Gly Asn Leu Glu Asn Leu Phe Leu Gln Cys Pro Lys Pro Thr
                245                 250                 255

Leu Gln Gln Ile Ser His Ile Ala Gln Gln Leu Gly Leu Glu Lys Asp
            260                 265                 270

Val Val Arg Val Trp Phe Cys Asn Arg Arg Gln Lys Gly Lys Arg Ser
        275                 280                 285

Ser Ser Asp Tyr Ala Gln Arg Glu Asp Phe Glu Ala Ala Gly Ser Pro
    290                 295                 300

Phe Ser Gly Gly Pro Val Ser Phe Pro Leu Ala Pro Gly Pro His Phe
305                 310                 315                 320

Gly Thr Pro Gly Tyr Gly Ser Pro His Phe Thr Ala Leu Tyr Ser Ser
                325                 330                 335

Val Pro Phe Pro Glu Gly Glu Ala Phe Pro Pro Val Ser Val Thr Thr
            340                 345                 350

Leu Gly Ser Pro Met His Ser Asn
        355                 360


<210>  9
<211>  317
<212>  PRT
<213>  Homo sapiens

<400>  9

Met Tyr Asn Met Met Glu Thr Glu Leu Lys Pro Pro Gly Pro Gln Gln
1               5                   10                  15

Thr Ser Gly Gly Gly Gly Gly Asn Ser Thr Ala Ala Ala Ala Gly Gly
            20                  25                  30

Asn Gln Lys Asn Ser Pro Asp Arg Val Lys Arg Pro Met Asn Ala Phe
        35                  40                  45
```

```
Met Val Trp Ser Arg Gly Gln Arg Arg Lys Met Ala Gln Glu Asn Pro
    50                  55                  60

Lys Met His Asn Ser Glu Ile Ser Lys Arg Leu Gly Ala Glu Trp Lys
65                  70                  75                  80

Leu Leu Ser Glu Thr Glu Lys Arg Pro Phe Ile Asp Glu Ala Lys Arg
                85                  90                  95

Leu Arg Ala Leu His Met Lys Glu His Pro Asp Tyr Lys Tyr Arg Pro
            100                 105                 110

Arg Arg Lys Thr Lys Thr Leu Met Lys Lys Asp Lys Tyr Thr Leu Pro
        115                 120                 125

Gly Gly Leu Leu Ala Pro Gly Gly Asn Ser Met Ala Ser Gly Val Gly
    130                 135                 140

Val Gly Ala Gly Leu Gly Ala Gly Val Asn Gln Arg Met Asp Ser Tyr
145                 150                 155                 160

Ala His Met Asn Gly Trp Ser Asn Gly Ser Tyr Ser Met Met Gln Asp
                165                 170                 175

Gln Leu Gly Tyr Pro Gln His Pro Gly Leu Asn Ala His Gly Ala Ala
            180                 185                 190

Gln Met Gln Pro Met His Arg Tyr Asp Val Ser Ala Leu Gln Tyr Asn
        195                 200                 205

Ser Met Thr Ser Ser Gln Thr Tyr Met Asn Gly Ser Pro Thr Tyr Ser
    210                 215                 220

Met Ser Tyr Ser Gln Gln Gly Thr Pro Gly Met Ala Leu Gly Ser Met
225                 230                 235                 240

Gly Ser Val Val Lys Ser Glu Ala Ser Ser Ser Pro Pro Val Val Thr
                245                 250                 255

Ser Ser Ser His Ser Arg Ala Pro Cys Gln Ala Gly Asp Leu Arg Asp
            260                 265                 270

Met Ile Ser Met Tyr Leu Pro Gly Ala Glu Val Pro Glu Pro Ala Ala
        275                 280                 285

Pro Ser Arg Leu His Met Ser Gln His Tyr Gln Ser Gly Pro Val Pro
    290                 295                 300

Gly Thr Ala Ile Asn Gly Thr Leu Pro Leu Ser His Met
305                 310                 315
```

<210> 10
<211> 479
<212> PRT
<213> Homo sapiens

<400> 10

```
Met Arg Gln Pro Pro Gly Glu Ser Asp Met Ala Val Ser Asp Ala Leu
1               5                  10                  15

Leu Pro Ser Phe Ser Thr Phe Ala Ser Gly Pro Ala Gly Arg Glu Lys
            20                  25                  30

Thr Leu Arg Gln Ala Gly Ala Pro Asn Asn Arg Trp Arg Glu Glu Leu
        35                  40                  45

Ser His Met Lys Arg Leu Pro Pro Val Leu Pro Gly Arg Pro Tyr Asp
    50                  55                  60

Leu Ala Ala Ala Thr Val Ala Thr Asp Leu Glu Ser Gly Gly Ala Gly
65                  70                  75                  80

Ala Ala Cys Gly Gly Ser Asn Leu Ala Pro Leu Pro Arg Arg Glu Thr
                85                  90                  95

Glu Glu Phe Asn Asp Leu Leu Asp Leu Asp Phe Ile Leu Ser Asn Ser
            100                 105                 110

Leu Thr His Pro Pro Glu Ser Val Ala Ala Thr Val Ser Ser Ser Ala
        115                 120                 125

Ser Ala Ser Ser Ser Ser Ser Pro Ser Ser Ser Gly Pro Ala Ser Ala
    130                 135                 140

Pro Ser Thr Cys Ser Phe Thr Tyr Pro Ile Arg Ala Gly Asn Asp Pro
145                 150                 155                 160

Gly Val Ala Pro Gly Gly Thr Gly Gly Gly Leu Leu Tyr Gly Arg Glu
                165                 170                 175

Ser Ala Pro Pro Pro Thr Ala Pro Phe Asn Leu Ala Asp Ile Asn Asp
            180                 185                 190

Val Ser Pro Ser Gly Gly Phe Val Ala Glu Leu Leu Arg Pro Glu Leu
        195                 200                 205

Asp Pro Val Tyr Ile Pro Pro Gln Gln Pro Gln Pro Pro Gly Gly Gly
    210                 215                 220

Leu Met Gly Lys Phe Val Leu Lys Ala Ser Leu Ser Ala Pro Gly Ser
225                 230                 235                 240
```

```
Glu Tyr Gly Ser Pro Ser Val Ile Ser Val Ser Lys Gly Ser Pro Asp
                245                 250                 255

Gly Ser His Pro Val Val Val Ala Pro Tyr Asn Gly Gly Pro Pro Arg
            260                 265                 270

Thr Cys Pro Lys Ile Lys Gln Glu Ala Val Ser Ser Cys Thr His Leu
        275                 280                 285

Gly Ala Gly Pro Pro Leu Ser Asn Gly His Arg Pro Ala Ala His Asp
    290                 295                 300

Phe Pro Leu Gly Arg Gln Leu Pro Ser Arg Thr Thr Pro Thr Leu Gly
305                 310                 315                 320

Leu Glu Glu Val Leu Ser Ser Arg Asp Cys His Pro Ala Leu Pro Leu
                325                 330                 335

Pro Pro Gly Phe His Pro His Pro Gly Pro Asn Tyr Pro Ser Phe Leu
            340                 345                 350

Pro Asp Gln Met Gln Pro Gln Val Pro Pro Leu His Tyr Gln Glu Leu
        355                 360                 365

Met Pro Pro Gly Ser Cys Met Pro Glu Glu Pro Lys Pro Lys Arg Gly
    370                 375                 380

Arg Arg Ser Trp Pro Arg Lys Arg Thr Ala Thr His Thr Cys Asp Tyr
385                 390                 395                 400

Ala Gly Cys Gly Lys Thr Tyr Thr Lys Ser Ser His Leu Lys Ala His
                405                 410                 415

Leu Arg Thr His Thr Gly Glu Lys Pro Tyr His Cys Asp Trp Asp Gly
            420                 425                 430

Cys Gly Trp Lys Phe Ala Arg Ser Asp Glu Leu Thr Arg His Tyr Arg
        435                 440                 445

Lys His Thr Gly His Arg Pro Phe Gln Cys Gln Lys Cys Asp Arg Ala
    450                 455                 460

Phe Ser Arg Ser Asp His Leu Ala Leu His Met Lys Arg His Phe
465                 470                 475
```

<210> 11
<211> 454
<212> PRT
<213> Homo sapiens

<400> 11

```
Met Asp Phe Phe Arg Val Val Glu Asn Gln Gln Pro Pro Ala Thr Met
```

```
1               5                   10                  15

Pro Leu Asn Val Ser Phe Thr Asn Arg Asn Tyr Asp Leu Asp Tyr Asp
            20                  25                  30

Ser Val Gln Pro Tyr Phe Tyr Cys Asp Glu Glu Glu Asn Phe Tyr Gln
        35                  40                  45

Gln Gln Gln Gln Ser Glu Leu Gln Pro Pro Ala Pro Ser Glu Asp Ile
    50                  55                  60

Trp Lys Lys Phe Glu Leu Leu Pro Thr Pro Pro Leu Ser Pro Ser Arg
65                  70                  75                  80

Arg Ser Gly Leu Cys Ser Pro Ser Tyr Val Ala Val Thr Pro Phe Ser
                85                  90                  95

Leu Arg Gly Asp Asn Asp Gly Gly Gly Gly Ser Phe Ser Thr Ala Asp
            100                 105                 110

Gln Leu Glu Met Val Thr Glu Leu Leu Gly Gly Asp Met Val Asn Gln
        115                 120                 125

Ser Phe Ile Cys Asp Pro Asp Asp Glu Thr Phe Ile Lys Asn Ile Ile
    130                 135                 140

Ile Gln Asp Cys Met Trp Ser Gly Phe Ser Ala Ala Ala Lys Leu Val
145                 150                 155                 160

Ser Glu Lys Leu Ala Ser Tyr Gln Ala Ala Arg Lys Asp Ser Gly Ser
                165                 170                 175

Pro Asn Pro Ala Arg Gly His Ser Val Cys Ser Thr Ser Ser Leu Tyr
            180                 185                 190

Leu Gln Asp Leu Ser Ala Ala Ala Ser Glu Cys Ile Asp Pro Ser Val
        195                 200                 205

Val Phe Pro Tyr Pro Leu Asn Asp Ser Ser Ser Pro Lys Ser Cys Ala
    210                 215                 220

Ser Gln Asp Ser Ser Ala Phe Ser Pro Ser Ser Asp Ser Leu Leu Ser
225                 230                 235                 240

Ser Thr Glu Ser Ser Pro Gln Gly Ser Pro Glu Pro Leu Val Leu His
                245                 250                 255

Glu Glu Thr Pro Pro Thr Thr Ser Ser Asp Ser Glu Glu Glu Gln Glu
            260                 265                 270

Asp Glu Glu Glu Ile Asp Val Val Ser Val Glu Lys Arg Gln Ala Pro
```

275 280 285

Gly Lys Arg Ser Glu Ser Gly Ser Pro Ser Ala Gly Gly His Ser Lys
290 295 300

Pro Pro His Ser Pro Leu Val Leu Lys Arg Cys His Val Ser Thr His
305 310 315 320

Gln His Asn Tyr Ala Ala Pro Pro Ser Thr Arg Lys Asp Tyr Pro Ala
325 330 335

Ala Lys Arg Val Lys Leu Asp Ser Val Arg Val Leu Arg Gln Ile Ser
340 345 350

Asn Asn Arg Lys Cys Thr Ser Pro Arg Ser Ser Asp Thr Glu Glu Asn
355 360 365

Val Lys Arg Arg Thr His Asn Val Leu Glu Arg Gln Arg Arg Asn Glu
370 375 380

Leu Lys Arg Ser Phe Phe Ala Leu Arg Asp Gln Ile Pro Glu Leu Glu
385 390 395 400

Asn Asn Glu Lys Ala Pro Lys Val Val Ile Leu Lys Lys Ala Thr Ala
405 410 415

Tyr Ile Leu Ser Val Gln Ala Glu Glu Gln Lys Leu Ile Ser Glu Glu
420 425 430

Asp Leu Leu Arg Lys Arg Arg Glu Gln Leu Lys His Lys Leu Glu Gln
435 440 445

Leu Arg Asn Ser Cys Ala
450

<210> 12
<211> 191
<212> DNA
<213> Homo sapiens

<400> 12
ttgaatcgcg ggacccgttg gcagaggtgg cggcggcggc atgggtgccc cgacgttgcc 60

ccctgcctgg cagccctttc tcaaggacca ccgcatctct acattcaaga actggccctt 120

cttggagggc tgcgcctgca ccccggagcg ggtgagactg cccggcctcc tggggtcccc 180

cacgcccgcc t 191

<210> 13
<211> 190
<212> DNA
<213> Homo sapiens

<400> 13

ggctgccacg tccactcacg agctgtgctg tcccttgcag atggccgagg ctggcttcat 60

ccactgcccc actgagaacg agccagactt ggcccagtgt ttcttctgct tcaaggagct 120

ggaaggctgg gagccagatg acgaccccat gtaagtcttc tctggccagc ctcgatgggc 180

tttgttttga 190

<210> 14
<211> 198
<212> DNA
<213> Homo sapiens

<400> 14
cccttcagct gcctttccgc tgttgttttg atttttctag agaggaacat aaaaagcatt 60

cgtccggttg cgctttcctt tctgtcaaga agcagtttga agaattaacc cttggtgaat 120

ttttgaaact ggacagagaa agagccaaga acaaaattgt atgtattggg aataagaact 180

gctcaaaccc tgttcaat 198

<210> 15
<211> 170
<212> DNA
<213> Homo sapiens

<400> 15
gctctggttt cagtgtcatg tgtctattct ttatttccag gcaaaggaaa ccaacaataa 60

gaagaaagaa tttgaggaaa ctgcggagaa agtgcgccgt gccatcgagc agctggctgc 120

catggattga ggcctctggc cggagctgcc tggtcccaga gtggctgcac 170

<210> 16
<211> 20
<212> DNA
<213> Homo sapiens

<400> 16
ttgccccctg cctggcagcc 20

<210> 17
<211> 20
<212> DNA
<213> Homo sapiens

<400> 17
ttcttgaatg tagagatgcg 20

<210> 18
<211> 20
<212> DNA
<213> Homo sapiens

<400> 18
tgggtgcccc gacgttgccc 20

<210> 19
<211> 20
<212> DNA
<213> Homo sapiens

<400> 19
tgcggtggtc cttgagaaag 20

<210> 20
<211> 20
<212> DNA
<213> Homo sapiens

<400> 20
tcaaggacca ccgcatctct 20

<210> 21
<211> 20
<212> DNA
<213> Homo sapiens

<400> 21
tgcaggcgca gccctccaag 20

<210> 22
<211> 20
<212> DNA
<213> Homo sapiens

<400> 22
tggccgaggc tggcttcatc 20

<210> 23
<211> 20
<212> DNA
<213> Homo sapiens

<400> 23
tgggccaagt ctggctcgtt 20

<210> 24
<211> 20
<212> DNA
<213> Homo sapiens

<400> 24
ttggcccagt gtttcttctg 20

<210> 25
<211> 20
<212> DNA
<213> Homo sapiens

<400> 25
tcgtcatctg gctcccagcc 20

<210> 26
<211> 20
<212> DNA
<213> Homo sapiens

<400> 26
tgcgctttcc tttctgtcaa 20

<210> 27
<211> 20
<212> DNA
<213> Homo sapiens

<400> 27
tcaaaaattc accaagggtt 20

<210> 28
<211> 297
<212> PRT
<213> Homo sapiens

<400> 28

Met Glu Asp Tyr Thr Lys Ile Glu Lys Ile Gly Glu Gly Thr Tyr Gly
1 5 10 15

Val Val Tyr Lys Gly Arg His Lys Thr Thr Gly Gln Val Val Ala Met
20 25 30

Lys Lys Ile Arg Leu Glu Ser Glu Glu Glu Gly Val Pro Ser Thr Ala
35 40 45

Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Arg His Pro Asn Ile Val
50 55 60

Ser Leu Gln Asp Val Leu Met Gln Asp Ser Arg Leu Tyr Leu Ile Phe
65 70 75 80

Glu Phe Leu Ser Met Asp Leu Lys Lys Tyr Leu Asp Ser Ile Pro Pro
85 90 95

Gly Gln Tyr Met Asp Ser Ser Leu Val Lys Ser Tyr Leu Tyr Gln Ile
100 105 110

Leu Gln Gly Ile Val Phe Cys His Ser Arg Arg Val Leu His Arg Asp
115 120 125

Leu Lys Pro Gln Asn Leu Leu Ile Asp Asp Lys Gly Thr Ile Lys Leu
130 135 140

Ala Asp Phe Gly Leu Ala Arg Ala Phe Gly Ile Pro Ile Arg Val Tyr
145 150 155 160

Thr His Glu Val Val Thr Leu Trp Tyr Arg Ser Pro Glu Val Leu Leu
165 170 175

Gly Ser Ala Arg Tyr Ser Thr Pro Val Asp Ile Trp Ser Ile Gly Thr
180 185 190

Ile Phe Ala Glu Leu Ala Thr Lys Lys Pro Leu Phe His Gly Asp Ser
195 200 205

```
Glu Ile Asp Gln Leu Phe Arg Ile Phe Arg Ala Leu Gly Thr Pro Asn
    210                 215                 220

Asn Glu Val Trp Pro Glu Val Glu Ser Leu Gln Asp Tyr Lys Asn Thr
225                 230                 235                 240

Phe Pro Lys Trp Lys Pro Gly Ser Leu Ala Ser His Val Lys Asn Leu
                245                 250                 255

Asp Glu Asn Gly Leu Asp Leu Leu Ser Lys Met Leu Ile Tyr Asp Pro
            260                 265                 270

Ala Lys Arg Ile Ser Gly Lys Met Ala Leu Asn His Pro Tyr Phe Asn
        275                 280                 285

Asp Leu Asp Asn Gln Ile Lys Lys Met
    290                 295
```

<210> 29
<211> 298
<212> PRT
<213> Homo sapiens

<400> 29

```
Met Glu Asn Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly
1               5                   10                  15

Val Val Tyr Lys Ala Arg Asn Lys Leu Thr Gly Glu Val Val Ala Leu
            20                  25                  30

Lys Lys Ile Arg Leu Asp Thr Glu Thr Glu Gly Val Pro Ser Thr Ala
        35                  40                  45

Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Asn His Pro Asn Ile Val
    50                  55                  60

Lys Leu Leu Asp Val Ile His Thr Glu Asn Lys Leu Tyr Leu Val Phe
65                  70                  75                  80

Glu Phe Leu His Gln Asp Leu Lys Lys Phe Met Asp Ala Ser Ala Leu
                85                  90                  95

Thr Gly Ile Pro Leu Pro Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu
            100                 105                 110

Gln Gly Leu Ala Phe Cys His Ser His Arg Val Leu His Arg Asp Leu
        115                 120                 125

Lys Pro Gln Asn Leu Leu Ile Asn Thr Glu Gly Ala Ile Lys Leu Ala
    130                 135                 140

Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Val Arg Thr Tyr Thr
```

145 150 155 160

His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly
165 170 175

Cys Lys Tyr Tyr Ser Thr Ala Val Asp Ile Trp Ser Leu Gly Cys Ile
180 185 190

Phe Ala Glu Met Val Thr Arg Arg Ala Leu Phe Pro Gly Asp Ser Glu
195 200 205

Ile Asp Gln Leu Phe Arg Ile Phe Arg Thr Leu Gly Thr Pro Asp Glu
210 215 220

Val Val Trp Pro Gly Val Thr Ser Met Pro Asp Tyr Lys Pro Ser Phe
225 230 235 240

Pro Lys Trp Ala Arg Gln Asp Phe Ser Lys Val Val Pro Pro Leu Asp
245 250 255

Glu Asp Gly Arg Ser Leu Leu Ser Gln Met Leu His Tyr Asp Pro Asn
260 265 270

Lys Arg Ile Ser Ala Lys Ala Ala Leu Ala His Pro Phe Phe Gln Asp
275 280 285

Val Thr Lys Pro Val Pro His Leu Arg Leu
290 295

<210> 30
<211> 305
<212> PRT
<213> Homo sapiens

<400> 30

Met Asp Met Phe Gln Lys Val Glu Lys Ile Gly Glu Gly Thr Tyr Gly
1 5 10 15

Val Val Tyr Lys Ala Lys Asn Arg Glu Thr Gly Gln Leu Val Ala Leu
20 25 30

Lys Lys Ile Arg Leu Asp Leu Glu Met Glu Gly Val Pro Ser Thr Ala
35 40 45

Ile Arg Glu Ile Ser Leu Leu Lys Glu Leu Lys His Pro Asn Ile Val
50 55 60

Arg Leu Leu Asp Val Val His Asn Glu Arg Lys Leu Tyr Leu Val Phe
65 70 75 80

Glu Phe Leu Ser Gln Asp Leu Lys Lys Tyr Met Asp Ser Thr Pro Gly
85 90 95

```
Ser Glu Leu Pro Leu His Leu Ile Lys Ser Tyr Leu Phe Gln Leu Leu
            100                 105                 110

Gln Gly Val Ser Phe Cys His Ser His Arg Val Ile His Arg Asp Leu
        115                 120                 125

Lys Pro Gln Asn Leu Leu Ile Asn Glu Leu Gly Ala Ile Lys Leu Ala
    130                 135                 140

Asp Phe Gly Leu Ala Arg Ala Phe Gly Val Pro Leu Arg Thr Tyr Thr
145                 150                 155                 160

His Glu Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Ile Leu Leu Gly
                165                 170                 175

Ser Lys Phe Tyr Thr Thr Ala Val Asp Ile Trp Ser Ile Gly Cys Ile
            180                 185                 190

Phe Ala Glu Met Val Thr Arg Lys Ala Leu Phe Pro Gly Asp Ser Glu
        195                 200                 205

Ile Asp Gln Leu Phe Arg Ile Phe Arg Met Leu Gly Thr Pro Ser Glu
    210                 215                 220

Asp Thr Trp Pro Gly Val Thr Gln Leu Pro Asp Tyr Lys Gly Ser Phe
225                 230                 235                 240

Pro Lys Trp Thr Arg Lys Gly Leu Glu Glu Ile Val Pro Asn Leu Glu
                245                 250                 255

Pro Glu Gly Arg Asp Leu Leu Met Gln Leu Leu Gln Tyr Asp Pro Ser
            260                 265                 270

Gln Arg Ile Thr Ala Lys Thr Ala Leu Ala His Pro Tyr Phe Ser Ser
        275                 280                 285

Pro Glu Pro Ser Pro Ala Ala Arg Gln Tyr Val Leu Gln Arg Phe Arg
    290                 295                 300

His
305


<210>  31
<211>  303
<212>  PRT
<213>  Homo sapiens

<400>  31

Met Ala Thr Ser Arg Tyr Glu Pro Val Ala Glu Ile Gly Val Gly Ala
1               5                   10                  15
```

```
Tyr Gly Thr Val Tyr Lys Ala Arg Asp Pro His Ser Gly His Phe Val
            20                  25                  30

Ala Leu Lys Ser Val Arg Val Pro Asn Gly Gly Gly Gly Gly Gly Gly
        35                  40                  45

Leu Pro Ile Ser Thr Val Arg Glu Val Ala Leu Leu Arg Arg Leu Glu
    50                  55                  60

Ala Phe Glu His Pro Asn Val Val Arg Leu Met Asp Val Cys Ala Thr
65                  70                  75                  80

Ser Arg Thr Asp Arg Glu Ile Lys Val Thr Leu Val Phe Glu His Val
                85                  90                  95

Asp Gln Asp Leu Arg Thr Tyr Leu Asp Lys Ala Pro Pro Pro Gly Leu
            100                 105                 110

Pro Ala Glu Thr Ile Lys Asp Leu Met Arg Gln Phe Leu Arg Gly Leu
        115                 120                 125

Asp Phe Leu His Ala Asn Cys Ile Val His Arg Asp Leu Lys Pro Glu
    130                 135                 140

Asn Ile Leu Val Thr Ser Gly Gly Thr Val Lys Leu Ala Asp Phe Gly
145                 150                 155                 160

Leu Ala Arg Ile Tyr Ser Tyr Gln Met Ala Leu Thr Pro Val Val Val
                165                 170                 175

Thr Leu Trp Tyr Arg Ala Pro Glu Val Leu Leu Gln Ser Thr Tyr Ala
            180                 185                 190

Thr Pro Val Asp Met Trp Ser Val Gly Cys Ile Phe Ala Glu Met Phe
        195                 200                 205

Arg Arg Lys Pro Leu Phe Cys Gly Asn Ser Glu Ala Asp Gln Leu Gly
    210                 215                 220

Lys Ile Phe Asp Leu Ile Gly Leu Pro Pro Glu Asp Asp Trp Pro Arg
225                 230                 235                 240

Asp Val Ser Leu Pro Arg Gly Ala Phe Pro Pro Arg Gly Pro Arg Pro
                245                 250                 255

Val Gln Ser Val Val Pro Glu Met Glu Glu Ser Gly Ala Gln Leu Leu
            260                 265                 270

Leu Glu Met Leu Thr Phe Asn Pro His Lys Arg Ile Ser Ala Phe Arg
        275                 280                 285
```

```
Ala Leu Gln His Ser Tyr Leu His Lys Asp Glu Gly Asn Pro Glu
    290                 295                 300


<210>  32
<211>  292
<212>  PRT
<213>  Homo sapiens

<400>  32

Met Gln Lys Tyr Glu Lys Leu Glu Lys Ile Gly Glu Gly Thr Tyr Gly
1               5                   10                  15


Thr Val Phe Lys Ala Lys Asn Arg Glu Thr His Glu Ile Val Ala Leu
            20                  25                  30


Lys Arg Val Arg Leu Asp Asp Asp Asp Glu Gly Val Pro Ser Ser Ala
        35                  40                  45


Leu Arg Glu Ile Cys Leu Leu Lys Glu Leu Lys His Lys Asn Ile Val
    50                  55                  60


Arg Leu His Asp Val Leu His Ser Asp Lys Lys Leu Thr Leu Val Phe
65                  70                  75                  80


Glu Phe Cys Asp Gln Asp Leu Lys Lys Tyr Phe Asp Ser Cys Asn Gly
                85                  90                  95


Asp Leu Asp Pro Glu Ile Val Lys Ser Phe Leu Phe Gln Leu Leu Lys
            100                 105                 110


Gly Leu Gly Phe Cys His Ser Arg Asn Val Leu His Arg Asp Leu Lys
        115                 120                 125


Pro Gln Asn Leu Leu Ile Asn Arg Asn Gly Glu Leu Lys Leu Ala Asp
    130                 135                 140


Phe Gly Leu Ala Arg Ala Phe Gly Ile Pro Val Arg Cys Tyr Ser Ala
145                 150                 155                 160


Glu Val Val Thr Leu Trp Tyr Arg Pro Pro Asp Val Leu Phe Gly Ala
                165                 170                 175


Lys Leu Tyr Ser Thr Ser Ile Asp Met Trp Ser Ala Gly Cys Ile Phe
            180                 185                 190


Ala Glu Leu Ala Asn Ala Gly Arg Pro Leu Phe Pro Gly Asn Asp Val
        195                 200                 205


Asp Asp Gln Leu Lys Arg Ile Phe Arg Leu Leu Gly Thr Pro Thr Glu
    210                 215                 220
```

```
Glu Gln Trp Pro Ser Met Thr Lys Leu Pro Asp Tyr Lys Pro Tyr Pro
225                 230                 235                 240


Met Tyr Pro Ala Thr Thr Ser Leu Val Asn Val Val Pro Lys Leu Asn
                245                 250                 255


Ala Thr Gly Arg Asp Leu Leu Gln Asn Leu Leu Lys Cys Asn Pro Val
            260                 265                 270


Gln Arg Ile Ser Ala Glu Glu Ala Leu Gln His Pro Tyr Phe Ser Asp
        275                 280                 285


Phe Cys Pro Pro
    290


<210>  33
<211>  326
<212>  PRT
<213>  Homo sapiens

<400>  33

Met Glu Lys Asp Gly Leu Cys Arg Ala Asp Gln Gln Tyr Glu Cys Val
1               5                   10                  15


Ala Glu Ile Gly Glu Gly Ala Tyr Gly Lys Val Phe Lys Ala Arg Asp
            20                  25                  30


Leu Lys Asn Gly Gly Arg Phe Val Ala Leu Lys Arg Val Arg Val Gln
        35                  40                  45


Thr Gly Glu Glu Gly Met Pro Leu Ser Thr Ile Arg Glu Val Ala Val
    50                  55                  60


Leu Arg His Leu Glu Thr Phe Glu His Pro Asn Val Val Arg Leu Phe
65                  70                  75                  80


Asp Val Cys Thr Val Ser Arg Thr Asp Arg Glu Thr Lys Leu Thr Leu
                85                  90                  95


Val Phe Glu His Val Asp Gln Asp Leu Thr Thr Tyr Leu Asp Lys Val
            100                 105                 110


Pro Glu Pro Gly Val Pro Thr Glu Thr Ile Lys Asp Met Met Phe Gln
        115                 120                 125


Leu Leu Arg Gly Leu Asp Phe Leu His Ser His Arg Val Val His Arg
    130                 135                 140


Asp Leu Lys Pro Gln Asn Ile Leu Val Thr Ser Ser Gly Gln Ile Lys
145                 150                 155                 160


Leu Ala Asp Phe Gly Leu Ala Arg Ile Tyr Ser Phe Gln Met Ala Leu
```

165 170 175

Thr Ser Val Val Val Thr Leu Trp Tyr Arg Ala Pro Glu Val Leu Leu
180 185 190

Gln Ser Ser Tyr Ala Thr Pro Val Asp Leu Trp Ser Val Gly Cys Ile
195 200 205

Phe Ala Glu Met Phe Arg Arg Lys Pro Leu Phe Arg Gly Ser Ser Asp
210 215 220

Val Asp Gln Leu Gly Lys Ile Leu Asp Val Ile Gly Leu Pro Gly Glu
225 230 235 240

Glu Asp Trp Pro Arg Asp Val Ala Leu Pro Arg Gln Ala Phe His Ser
245 250 255

Lys Ser Ala Gln Pro Ile Glu Lys Phe Val Thr Asp Ile Asp Glu Leu
260 265 270

Gly Lys Asp Leu Leu Leu Lys Cys Leu Thr Phe Asn Pro Ala Lys Arg
275 280 285

Ile Ser Ala Tyr Ser Ala Leu Ser His Pro Tyr Phe Gln Asp Leu Glu
290 295 300

Arg Cys Lys Glu Asn Leu Asp Ser His Leu Pro Pro Ser Gln Asn Thr
305 310 315 320

Ser Glu Leu Asn Thr Ala
325

<210> 34
<211> 142
<212> PRT
<213> Homo sapiens

<400> 34

Met Gly Ala Pro Thr Leu Pro Pro Ala Trp Gln Pro Phe Leu Lys Asp
1 5 10 15

His Arg Ile Ser Thr Phe Lys Asn Trp Pro Phe Leu Glu Gly Cys Ala
20 25 30

Cys Thr Pro Glu Arg Met Ala Glu Ala Gly Phe Ile His Cys Pro Thr
35 40 45

Glu Asn Glu Pro Asp Leu Ala Gln Cys Phe Phe Cys Phe Lys Glu Leu
50 55 60

Glu Gly Trp Glu Pro Asp Asp Asp Pro Ile Glu Glu His Lys Lys His
65 70 75 80

```
Ser Ser Gly Cys Ala Phe Leu Ser Val Lys Lys Gln Phe Glu Glu Leu
                85                  90                  95

Thr Leu Gly Glu Phe Leu Lys Leu Asp Arg Glu Arg Ala Lys Asn Lys
            100                 105                 110

Ile Ala Lys Glu Thr Asn Asn Lys Lys Lys Glu Phe Glu Glu Thr Ala
        115                 120                 125

Glu Lys Val Arg Arg Ala Ile Glu Gln Leu Ala Ala Met Asp
    130                 135                 140


<210>  35
<211>  826
<212>  PRT
<213>  Homo sapiens

<400>  35

Met Glu Gly Ala Gly Gly Ala Asn Asp Lys Lys Lys Ile Ser Ser Glu
1               5                   10                  15

Arg Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser Arg Arg Ser Lys
            20                  25                  30

Glu Ser Glu Val Phe Tyr Glu Leu Ala His Gln Leu Pro Leu Pro His
        35                  40                  45

Asn Val Ser Ser His Leu Asp Lys Ala Ser Val Met Arg Leu Thr Ile
    50                  55                  60

Ser Tyr Leu Arg Val Arg Lys Leu Leu Asp Ala Gly Asp Leu Asp Ile
65                  70                  75                  80

Glu Asp Asp Met Lys Ala Gln Met Asn Cys Phe Tyr Leu Lys Ala Leu
                85                  90                  95

Asp Gly Phe Val Met Val Leu Thr Asp Asp Gly Asp Met Ile Tyr Ile
            100                 105                 110

Ser Asp Asn Val Asn Lys Tyr Met Gly Leu Thr Gln Phe Glu Leu Thr
        115                 120                 125

Gly His Ser Val Phe Asp Phe Thr His Pro Cys Asp His Glu Glu Met
    130                 135                 140

Arg Glu Met Leu Thr His Arg Asn Gly Leu Val Lys Lys Gly Lys Glu
145                 150                 155                 160

Gln Asn Thr Gln Arg Ser Phe Phe Leu Arg Met Lys Cys Thr Leu Thr
                165                 170                 175
```

```
Ser Arg Gly Arg Thr Met Asn Ile Lys Ser Ala Thr Trp Lys Val Leu
            180                 185                 190

His Cys Thr Gly His Ile His Val Tyr Asp Thr Asn Ser Asn Gln Pro
        195                 200                 205

Gln Cys Gly Tyr Lys Lys Pro Pro Met Thr Cys Leu Val Leu Ile Cys
    210                 215                 220

Glu Pro Ile Pro His Pro Ser Asn Ile Glu Ile Pro Leu Asp Ser Lys
225                 230                 235                 240

Thr Phe Leu Ser Arg His Ser Leu Asp Met Lys Phe Ser Tyr Cys Asp
                245                 250                 255

Glu Arg Ile Thr Glu Leu Met Gly Tyr Glu Pro Glu Glu Leu Leu Gly
            260                 265                 270

Arg Ser Ile Tyr Glu Tyr Tyr His Ala Leu Asp Ser Asp His Leu Thr
        275                 280                 285

Lys Thr His His Asp Met Phe Thr Lys Gly Gln Val Thr Thr Gly Gln
    290                 295                 300

Tyr Arg Met Leu Ala Lys Arg Gly Gly Tyr Val Trp Val Glu Thr Gln
305                 310                 315                 320

Ala Thr Val Ile Tyr Asn Thr Lys Asn Ser Gln Pro Gln Cys Ile Val
                325                 330                 335

Cys Val Asn Tyr Val Val Ser Gly Ile Ile Gln His Asp Leu Ile Phe
            340                 345                 350

Ser Leu Gln Gln Thr Glu Cys Val Leu Lys Pro Val Glu Ser Ser Asp
        355                 360                 365

Met Lys Met Thr Gln Leu Phe Thr Lys Val Glu Ser Glu Asp Thr Ser
    370                 375                 380

Ser Leu Phe Asp Lys Leu Lys Lys Glu Pro Asp Ala Leu Thr Leu Leu
385                 390                 395                 400

Ala Pro Ala Ala Gly Asp Thr Ile Ile Ser Leu Asp Phe Gly Ser Asn
                405                 410                 415

Asp Thr Glu Thr Asp Asp Gln Gln Leu Glu Glu Val Pro Leu Tyr Asn
            420                 425                 430

Asp Val Met Leu Pro Ser Pro Asn Glu Lys Leu Gln Asn Ile Asn Leu
        435                 440                 445
```

```
Ala Met Ser Pro Leu Pro Thr Ala Glu Thr Pro Lys Pro Leu Arg Ser
    450                 455                 460

Ser Ala Asp Pro Ala Leu Asn Gln Glu Val Ala Leu Lys Leu Glu Pro
465                 470                 475                 480

Asn Pro Glu Ser Leu Glu Leu Ser Phe Thr Met Pro Gln Ile Gln Asp
                485                 490                 495

Gln Thr Pro Ser Pro Ser Asp Gly Ser Thr Arg Gln Ser Ser Pro Glu
            500                 505                 510

Pro Asn Ser Pro Ser Glu Tyr Cys Phe Tyr Val Asp Ser Asp Met Val
        515                 520                 525

Asn Glu Phe Lys Leu Glu Leu Val Glu Lys Leu Phe Ala Glu Asp Thr
    530                 535                 540

Glu Ala Lys Asn Pro Phe Ser Thr Gln Asp Thr Asp Leu Asp Leu Glu
545                 550                 555                 560

Met Leu Ala Pro Tyr Ile Pro Met Asp Asp Asp Phe Gln Leu Arg Ser
                565                 570                 575

Phe Asp Gln Leu Ser Pro Leu Glu Ser Ser Ser Ala Ser Pro Glu Ser
            580                 585                 590

Ala Ser Pro Gln Ser Thr Val Thr Val Phe Gln Gln Thr Gln Ile Gln
        595                 600                 605

Glu Pro Thr Ala Asn Ala Thr Thr Thr Thr Ala Thr Thr Asp Glu Leu
    610                 615                 620

Lys Thr Val Thr Lys Asp Arg Met Glu Asp Ile Lys Ile Leu Ile Ala
625                 630                 635                 640

Ser Pro Ser Pro Thr His Ile His Lys Glu Thr Thr Ser Ala Thr Ser
                645                 650                 655

Ser Pro Tyr Arg Asp Thr Gln Ser Arg Thr Ala Ser Pro Asn Arg Ala
            660                 665                 670

Gly Lys Gly Val Ile Glu Gln Thr Glu Lys Ser His Pro Arg Ser Pro
        675                 680                 685

Asn Val Leu Ser Val Ala Leu Ser Gln Arg Thr Thr Val Pro Glu Glu
    690                 695                 700

Glu Leu Asn Pro Lys Ile Leu Ala Leu Gln Asn Ala Gln Arg Lys Arg
705                 710                 715                 720
```

```
Lys Met Glu His Asp Gly Ser Leu Phe Gln Ala Val Gly Ile Gly Thr
                725                 730                 735

Leu Leu Gln Gln Pro Asp Asp His Ala Ala Thr Thr Ser Leu Ser Trp
            740                 745                 750

Lys Arg Val Lys Gly Cys Lys Ser Ser Glu Gln Asn Gly Met Glu Gln
        755                 760                 765

Lys Thr Ile Ile Leu Ile Pro Ser Asp Leu Ala Cys Arg Leu Leu Gly
    770                 775                 780

Gln Ser Met Asp Glu Ser Gly Leu Pro Gln Leu Thr Ser Tyr Asp Cys
785                 790                 795                 800

Glu Val Asn Ala Pro Ile Gln Gly Ser Arg Asn Leu Leu Gln Gly Glu
                805                 810                 815

Glu Leu Leu Arg Ala Leu Asp Gln Val Asn
            820                 825


<210>  36
<211>  449
<212>  PRT
<213>  Homo sapiens

<400>  36

Met Gly Arg Val Gly Gly Met Ala Gln Pro Met Gly Arg Ala Gly Ala
1               5                   10                  15

Pro Lys Pro Met Gly Arg Ala Gly Ser Ala Arg Arg Gly Arg Phe Lys
            20                  25                  30

Gly Cys Trp Ser Glu Gly Ser Pro Val His Pro Val Pro Ala Val Leu
        35                  40                  45

Ser Trp Leu Leu Ala Leu Leu Arg Cys Ala Ser Thr Met Leu Ser Leu
    50                  55                  60

Arg Val Pro Leu Ala Pro Ile Thr Asp Pro Gln Gln Leu Gln Leu Ser
65                  70                  75                  80

Pro Leu Lys Gly Leu Ser Leu Val Asp Lys Glu Asn Thr Pro Pro Ala
                85                  90                  95

Leu Ser Gly Thr Arg Val Leu Ala Ser Lys Thr Ala Arg Arg Ile Phe
            100                 105                 110

Gln Glu Pro Thr Glu Pro Lys Thr Lys Ala Ala Ala Pro Gly Val Glu
        115                 120                 125
```

```
Asp Glu Pro Leu Leu Arg Glu Asn Pro Arg Arg Phe Val Ile Phe Pro
    130                 135                 140

Ile Glu Tyr His Asp Ile Trp Gln Met Tyr Lys Lys Ala Glu Ala Ser
145                 150                 155                 160

Phe Trp Thr Ala Glu Glu Val Asp Leu Ser Lys Asp Ile Gln His Trp
                165                 170                 175

Glu Ser Leu Lys Pro Glu Glu Arg Tyr Phe Ile Ser His Val Leu Ala
            180                 185                 190

Phe Phe Ala Ala Ser Asp Gly Ile Val Asn Glu Asn Leu Val Glu Arg
        195                 200                 205

Phe Ser Gln Glu Val Gln Ile Thr Glu Ala Arg Cys Phe Tyr Gly Phe
    210                 215                 220

Gln Ile Ala Met Glu Asn Ile His Ser Glu Met Tyr Ser Leu Leu Ile
225                 230                 235                 240

Asp Thr Tyr Ile Lys Asp Pro Lys Glu Arg Glu Phe Leu Phe Asn Ala
                245                 250                 255

Ile Glu Thr Met Pro Cys Val Lys Lys Lys Ala Asp Trp Ala Leu Arg
            260                 265                 270

Trp Ile Gly Asp Lys Glu Ala Thr Tyr Gly Glu Arg Val Val Ala Phe
        275                 280                 285

Ala Ala Val Glu Gly Ile Phe Phe Ser Gly Ser Phe Ala Ser Ile Phe
    290                 295                 300

Trp Leu Lys Lys Arg Gly Leu Met Pro Gly Leu Thr Phe Ser Asn Glu
305                 310                 315                 320

Leu Ile Ser Arg Asp Glu Gly Leu His Cys Asp Phe Ala Cys Leu Met
                325                 330                 335

Phe Lys His Leu Val His Lys Pro Ser Glu Glu Arg Val Arg Glu Ile
            340                 345                 350

Ile Ile Asn Ala Val Arg Ile Glu Gln Glu Phe Leu Thr Glu Ala Leu
        355                 360                 365

Pro Val Lys Leu Ile Gly Met Asn Cys Thr Leu Met Lys Gln Tyr Ile
    370                 375                 380

Glu Phe Val Ala Asp Arg Leu Met Leu Glu Leu Gly Phe Ser Lys Val
385                 390                 395                 400
```

Phe Arg Val Glu Asn Pro Phe Asp Phe Met Glu Asn Ile Ser Leu Glu
405 410 415

Gly Lys Thr Asn Phe Phe Glu Lys Arg Val Gly Glu Tyr Gln Arg Met
420 425 430

Gly Val Met Ser Ser Pro Thr Glu Asn Ser Phe Thr Leu Asp Ala Asp
435 440 445

Phe

<210> 37
<211> 188
<212> PRT
<213> Homo sapiens

<400> 37

Met Thr Glu Tyr Lys Leu Val Val Val Gly Ala Gly Gly Val Gly Lys
1 5 10 15

Ser Ala Leu Thr Ile Gln Leu Ile Gln Asn His Phe Val Asp Glu Tyr
20 25 30

Asp Pro Thr Ile Glu Asp Ser Tyr Arg Lys Gln Val Val Ile Asp Gly
35 40 45

Glu Thr Cys Leu Leu Asp Ile Leu Asp Thr Ala Gly Gln Glu Glu Tyr
50 55 60

Ser Ala Met Arg Asp Gln Tyr Met Arg Thr Gly Glu Gly Phe Leu Cys
65 70 75 80

Val Phe Ala Ile Asn Asn Thr Lys Ser Phe Glu Asp Ile His His Tyr
85 90 95

Arg Glu Gln Ile Lys Arg Val Lys Asp Ser Glu Asp Val Pro Met Val
100 105 110

Leu Val Gly Asn Lys Cys Asp Leu Pro Ser Arg Thr Val Asp Thr Lys
115 120 125

Gln Ala Gln Asp Leu Ala Arg Ser Tyr Gly Ile Pro Phe Ile Glu Thr
130 135 140

Ser Ala Lys Thr Arg Gln Gly Val Asp Asp Ala Phe Tyr Thr Leu Val
145 150 155 160

Arg Glu Ile Arg Lys His Lys Glu Lys Met Ser Lys Asp Gly Lys Lys
165 170 175

Lys Lys Lys Lys Ser Lys Thr Lys Cys Val Ile Met

180 185

<210> 38
<211> 1210
<212> PRT
<213> Homo sapiens

<400> 38

Met Arg Pro Ser Gly Thr Ala Gly Ala Ala Leu Leu Ala Leu Leu Ala
1 5 10 15

Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln
20 25 30

Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe
35 40 45

Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn
50 55 60

Leu Glu Ile Thr Tyr Val Gln Arg Asn Tyr Asp Leu Ser Phe Leu Lys
65 70 75 80

Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
85 90 95

Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr
100 105 110

Tyr Glu Asn Ser Tyr Ala Leu Ala Val Leu Ser Asn Tyr Asp Ala Asn
115 120 125

Lys Thr Gly Leu Lys Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu
130 135 140

His Gly Ala Val Arg Phe Ser Asn Asn Pro Ala Leu Cys Asn Val Glu
145 150 155 160

Ser Ile Gln Trp Arg Asp Ile Val Ser Ser Asp Phe Leu Ser Asn Met
165 170 175

Ser Met Asp Phe Gln Asn His Leu Gly Ser Cys Gln Lys Cys Asp Pro
180 185 190

Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala Gly Glu Glu Asn Cys Gln
195 200 205

Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser Gly Arg Cys Arg
210 215 220

Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys
225 230 235 240

```
Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg Lys Phe Arg Asp
                245                 250                 255

Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met Leu Tyr Asn Pro
            260                 265                 270

Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys Tyr Ser Phe Gly
        275                 280                 285

Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His
    290                 295                 300

Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr Glu Met Glu Glu
305                 310                 315                 320

Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro Cys Arg Lys Val
                325                 330                 335

Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu Ser Ile Asn
            340                 345                 350

Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile Ser Gly Asp
        355                 360                 365

Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe Thr His Thr
    370                 375                 380

Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr Val Lys Glu
385                 390                 395                 400

Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn Arg Thr Asp
                405                 410                 415

Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
            420                 425                 430

His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr Ser Leu
        435                 440                 445

Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile Ile Ser
    450                 455                 460

Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu
465                 470                 475                 480

Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu
                485                 490                 495

Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro
            500                 505                 510
```

```
Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser Cys Arg Asn
        515                 520                 525

Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu Leu Glu Gly
    530                 535                 540

Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
545                 550                 555                 560

Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
                565                 570                 575

Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
            580                 585                 590

Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp
        595                 600                 605

Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys
    610                 615                 620

Thr Tyr Gly Cys Thr Gly Pro Gly Leu Glu Gly Cys Pro Thr Asn Gly
625                 630                 635                 640

Pro Lys Ile Pro Ser Ile Ala Thr Gly Met Val Gly Ala Leu Leu Leu
                645                 650                 655

Leu Leu Val Val Ala Leu Gly Ile Gly Leu Phe Met Arg Arg Arg His
            660                 665                 670

Ile Val Arg Lys Arg Thr Leu Arg Arg Leu Leu Gln Glu Arg Glu Leu
        675                 680                 685

Val Glu Pro Leu Thr Pro Ser Gly Glu Ala Pro Asn Gln Ala Leu Leu
    690                 695                 700

Arg Ile Leu Lys Glu Thr Glu Phe Lys Lys Ile Lys Val Leu Gly Ser
705                 710                 715                 720

Gly Ala Phe Gly Thr Val Tyr Lys Gly Leu Trp Ile Pro Glu Gly Glu
                725                 730                 735

Lys Val Lys Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser
            740                 745                 750

Pro Lys Ala Asn Lys Glu Ile Leu Asp Glu Ala Tyr Val Met Ala Ser
        755                 760                 765

Val Asp Asn Pro His Val Cys Arg Leu Leu Gly Ile Cys Leu Thr Ser
    770                 775                 780
```

```
Thr Val Gln Leu Ile Thr Gln Leu Met Pro Phe Gly Cys Leu Leu Asp
785                 790                 795                 800

Tyr Val Arg Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn
                805                 810                 815

Trp Cys Val Gln Ile Ala Lys Gly Met Asn Tyr Leu Glu Asp Arg Arg
            820                 825                 830

Leu Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Lys Thr Pro
        835                 840                 845

Gln His Val Lys Ile Thr Asp Phe Gly Leu Ala Lys Leu Leu Gly Ala
    850                 855                 860

Glu Glu Lys Glu Tyr His Ala Glu Gly Gly Lys Val Pro Ile Lys Trp
865                 870                 875                 880

Met Ala Leu Glu Ser Ile Leu His Arg Ile Tyr Thr His Gln Ser Asp
                885                 890                 895

Val Trp Ser Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ser
            900                 905                 910

Lys Pro Tyr Asp Gly Ile Pro Ala Ser Glu Ile Ser Ser Ile Leu Glu
        915                 920                 925

Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr
    930                 935                 940

Met Ile Met Val Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys
945                 950                 955                 960

Phe Arg Glu Leu Ile Ile Glu Phe Ser Lys Met Ala Arg Asp Pro Gln
                965                 970                 975

Arg Tyr Leu Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro
            980                 985                 990

Thr Asp Ser Asn Phe Tyr Arg Ala  Leu Met Asp Glu Glu  Asp Met Asp
        995                 1000                1005

Asp Val  Val Asp Ala Asp Glu  Tyr Leu Ile Pro Gln  Gln Gly Phe
    1010                1015                1020

Phe Ser  Ser Pro Ser Thr Ser  Arg Thr Pro Leu Leu  Ser Ser Leu
    1025                1030                1035

Ser Ala  Thr Ser Asn Asn Ser  Thr Val Ala Cys Ile  Asp Arg Asn
    1040                1045                1050
```

Gly Leu Gln Ser Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg
1055 1060 1065

Tyr Ser Ser Asp Pro Thr Gly Ala Leu Thr Glu Asp Ser Ile Asp
1070 1075 1080

Asp Thr Phe Leu Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro
1085 1090 1095

Lys Arg Pro Ala Gly Ser Val Gln Asn Pro Val Tyr His Asn Gln
1100 1105 1110

Pro Leu Asn Pro Ala Pro Ser Arg Asp Pro His Tyr Gln Asp Pro
1115 1120 1125

His Ser Thr Ala Val Gly Asn Pro Glu Tyr Leu Asn Thr Val Gln
1130 1135 1140

Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro Ala His Trp Ala
1145 1150 1155

Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp Tyr Gln
1160 1165 1170

Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe Lys
1175 1180 1185

Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln
1190 1195 1200

Ser Ser Glu Phe Ile Gly Ala
1205 1210

<210> 39
<211> 454
<212> PRT
<213> Homo sapiens

<400> 39

Met Asp Phe Phe Arg Val Val Glu Asn Gln Gln Pro Pro Ala Thr Met
1 5 10 15

Pro Leu Asn Val Ser Phe Thr Asn Arg Asn Tyr Asp Leu Asp Tyr Asp
20 25 30

Ser Val Gln Pro Tyr Phe Tyr Cys Asp Glu Glu Glu Asn Phe Tyr Gln
35 40 45

Gln Gln Gln Gln Ser Glu Leu Gln Pro Pro Ala Pro Ser Glu Asp Ile
50 55 60

```
Trp Lys Lys Phe Glu Leu Leu Pro Thr Pro Pro Leu Ser Pro Ser Arg
65                  70                  75                  80

Arg Ser Gly Leu Cys Ser Pro Ser Tyr Val Ala Val Thr Pro Phe Ser
                85                  90                  95

Leu Arg Gly Asp Asn Asp Gly Gly Gly Gly Ser Phe Ser Thr Ala Asp
            100                 105                 110

Gln Leu Glu Met Val Thr Glu Leu Leu Gly Gly Asp Met Val Asn Gln
        115                 120                 125

Ser Phe Ile Cys Asp Pro Asp Asp Glu Thr Phe Ile Lys Asn Ile Ile
    130                 135                 140

Ile Gln Asp Cys Met Trp Ser Gly Phe Ser Ala Ala Ala Lys Leu Val
145                 150                 155                 160

Ser Glu Lys Leu Ala Ser Tyr Gln Ala Ala Arg Lys Asp Ser Gly Ser
                165                 170                 175

Pro Asn Pro Ala Arg Gly His Ser Val Cys Ser Thr Ser Ser Leu Tyr
            180                 185                 190

Leu Gln Asp Leu Ser Ala Ala Ala Ser Glu Cys Ile Asp Pro Ser Val
        195                 200                 205

Val Phe Pro Tyr Pro Leu Asn Asp Ser Ser Ser Pro Lys Ser Cys Ala
    210                 215                 220

Ser Gln Asp Ser Ser Ala Phe Ser Pro Ser Ser Asp Ser Leu Leu Ser
225                 230                 235                 240

Ser Thr Glu Ser Ser Pro Gln Gly Ser Pro Glu Pro Leu Val Leu His
                245                 250                 255

Glu Glu Thr Pro Pro Thr Thr Ser Ser Asp Ser Glu Glu Glu Gln Glu
            260                 265                 270

Asp Glu Glu Glu Ile Asp Val Val Ser Val Glu Lys Arg Gln Ala Pro
        275                 280                 285

Gly Lys Arg Ser Glu Ser Gly Ser Pro Ser Ala Gly Gly His Ser Lys
    290                 295                 300

Pro Pro His Ser Pro Leu Val Leu Lys Arg Cys His Val Ser Thr His
305                 310                 315                 320

Gln His Asn Tyr Ala Ala Pro Pro Ser Thr Arg Lys Asp Tyr Pro Ala
                325                 330                 335
```

```
Ala Lys Arg Val Lys Leu Asp Ser Val Arg Val Leu Arg Gln Ile Ser
            340                 345                 350

Asn Asn Arg Lys Cys Thr Ser Pro Arg Ser Ser Asp Thr Glu Glu Asn
        355                 360                 365

Val Lys Arg Arg Thr His Asn Val Leu Glu Arg Gln Arg Arg Asn Glu
    370                 375                 380

Leu Lys Arg Ser Phe Phe Ala Leu Arg Asp Gln Ile Pro Glu Leu Glu
385                 390                 395                 400

Asn Asn Glu Lys Ala Pro Lys Val Val Ile Leu Lys Lys Ala Thr Ala
                405                 410                 415

Tyr Ile Leu Ser Val Gln Ala Glu Glu Gln Lys Leu Ile Ser Glu Glu
            420                 425                 430

Asp Leu Leu Arg Lys Arg Arg Glu Gln Leu Lys His Lys Leu Glu Gln
        435                 440                 445

Leu Arg Asn Ser Cys Ala
    450
```

<210> 40
<211> 889
<212> PRT
<213> Homo sapiens

<400> 40

```
Met Glu Glu Gly Ala Pro Arg Gln Pro Gly Pro Ser Gln Trp Pro Pro
1               5                   10                  15

Glu Asp Glu Lys Glu Val Ile Arg Arg Ala Ile Gln Lys Glu Leu Lys
            20                  25                  30

Ile Lys Glu Gly Val Glu Asn Leu Arg Arg Val Ala Thr Asp Arg Arg
        35                  40                  45

His Leu Gly His Val Gln Gln Leu Leu Arg Ser Ser Asn Arg Arg Leu
    50                  55                  60

Glu Gln Leu His Gly Glu Leu Arg Glu Leu His Ala Arg Ile Leu Leu
65                  70                  75                  80

Pro Gly Pro Gly Pro Gly Pro Ala Glu Pro Val Ala Ser Gly Pro Arg
                85                  90                  95

Pro Trp Ala Glu Gln Leu Arg Ala Arg His Leu Glu Ala Leu Arg Arg
            100                 105                 110
```

```
Gln Leu His Val Glu Leu Lys Val Lys Gln Gly Ala Glu Asn Met Thr
        115                 120                 125

His Thr Cys Ala Ser Gly Thr Pro Lys Glu Arg Lys Leu Leu Ala Ala
    130                 135                 140

Ala Gln Gln Met Leu Arg Asp Ser Gln Leu Lys Val Ala Leu Leu Arg
145                 150                 155                 160

Met Lys Ile Ser Ser Leu Glu Ala Ser Gly Ser Pro Glu Pro Gly Pro
                165                 170                 175

Glu Leu Leu Ala Glu Glu Leu Gln His Arg Leu His Val Glu Ala Ala
            180                 185                 190

Val Ala Glu Gly Ala Lys Asn Val Val Lys Leu Leu Ser Ser Arg Arg
        195                 200                 205

Thr Gln Asp Arg Lys Ala Leu Ala Glu Ala Gln Ala Gln Leu Gln Glu
    210                 215                 220

Ser Ser Gln Lys Leu Asp Leu Leu Arg Leu Ala Leu Glu Gln Leu Leu
225                 230                 235                 240

Glu Gln Leu Pro Pro Ala His Pro Leu Arg Ser Arg Val Thr Arg Glu
                245                 250                 255

Leu Arg Ala Ala Val Pro Gly Tyr Pro Gln Pro Ser Gly Thr Pro Val
            260                 265                 270

Lys Pro Thr Ala Leu Thr Gly Thr Leu Gln Val Arg Leu Leu Gly Cys
        275                 280                 285

Glu Gln Leu Leu Thr Ala Val Pro Gly Arg Ser Pro Ala Ala Ala Leu
    290                 295                 300

Ala Ser Ser Pro Ser Glu Gly Trp Leu Arg Thr Lys Ala Lys His Gln
305                 310                 315                 320

Arg Gly Arg Gly Glu Leu Ala Ser Glu Val Leu Ala Val Leu Lys Val
                325                 330                 335

Asp Asn Arg Val Val Gly Gln Thr Gly Trp Gly Gln Val Ala Glu Gln
            340                 345                 350

Ser Trp Asp Gln Thr Phe Val Ile Pro Leu Glu Arg Ala Arg Glu Leu
        355                 360                 365

Glu Ile Gly Val His Trp Arg Asp Trp Arg Gln Leu Cys Gly Val Ala
    370                 375                 380
```

```
Phe Leu Arg Leu Glu Asp Phe Leu Asp Asn Ala Cys His Gln Leu Ser
385                 390                 395                 400

Leu Ser Leu Val Pro Gln Gly Leu Leu Phe Ala Gln Val Thr Phe Cys
                405                 410                 415

Asp Pro Val Ile Glu Arg Arg Pro Arg Leu Gln Arg Gln Glu Arg Ile
            420                 425                 430

Phe Ser Lys Arg Arg Gly Gln Asp Phe Leu Arg Ala Ser Gln Met Asn
        435                 440                 445

Leu Gly Met Ala Ala Trp Gly Arg Leu Val Met Asn Leu Leu Pro Pro
    450                 455                 460

Cys Ser Ser Pro Ser Thr Ile Ser Pro Pro Lys Gly Cys Pro Arg Thr
465                 470                 475                 480

Pro Thr Thr Leu Arg Glu Ala Ser Asp Pro Ala Thr Pro Ser Asn Phe
                485                 490                 495

Leu Pro Lys Lys Thr Pro Leu Gly Glu Glu Met Thr Pro Pro Pro Lys
            500                 505                 510

Pro Pro Arg Leu Tyr Leu Pro Gln Glu Pro Thr Ser Glu Glu Thr Pro
        515                 520                 525

Arg Thr Lys Arg Pro His Met Glu Pro Arg Thr Arg Arg Gly Pro Ser
    530                 535                 540

Pro Pro Ala Ser Pro Thr Arg Lys Pro Pro Arg Leu Gln Asp Phe Arg
545                 550                 555                 560

Cys Leu Ala Val Leu Gly Arg Gly His Phe Gly Lys Val Leu Leu Val
                565                 570                 575

Gln Phe Lys Gly Thr Gly Lys Tyr Tyr Ala Ile Lys Ala Leu Lys Lys
            580                 585                 590

Gln Glu Val Leu Ser Arg Asp Glu Ile Glu Ser Leu Tyr Cys Glu Lys
        595                 600                 605

Arg Ile Leu Glu Ala Val Gly Cys Thr Gly His Pro Phe Leu Leu Ser
    610                 615                 620

Leu Leu Ala Cys Phe Gln Thr Ser Ser His Ala Cys Phe Val Thr Glu
625                 630                 635                 640

Phe Val Pro Gly Gly Asp Leu Met Met Gln Ile His Glu Asp Val Phe
                645                 650                 655
```

```
Pro Glu Pro Gln Ala Arg Phe Tyr Val Ala Cys Val Val Leu Gly Leu
            660                 665                 670

Gln Phe Leu His Glu Lys Lys Ile Ile Tyr Arg Asp Leu Lys Leu Asp
        675                 680                 685

Asn Leu Leu Leu Asp Ala Gln Gly Phe Leu Lys Ile Ala Asp Phe Gly
    690                 695                 700

Leu Cys Lys Glu Gly Ile Gly Phe Gly Asp Arg Thr Ser Thr Phe Cys
705                 710                 715                 720

Gly Thr Pro Glu Phe Leu Ala Pro Glu Val Leu Thr Gln Glu Ala Tyr
                725                 730                 735

Thr Arg Ala Val Asp Trp Trp Gly Leu Gly Val Leu Leu Tyr Glu Met
            740                 745                 750

Leu Val Gly Glu Cys Pro Phe Pro Gly Asp Thr Glu Glu Glu Val Phe
        755                 760                 765

Asp Cys Ile Val Asn Met Asp Ala Pro Tyr Pro Gly Phe Leu Ser Val
    770                 775                 780

Gln Gly Leu Glu Phe Ile Gln Lys Leu Leu Gln Lys Cys Pro Glu Lys
785                 790                 795                 800

Arg Leu Gly Ala Gly Glu Gln Asp Ala Glu Glu Ile Lys Val Gln Pro
                805                 810                 815

Phe Phe Arg Thr Thr Asn Trp Gln Ala Leu Leu Ala Arg Thr Ile Gln
            820                 825                 830

Pro Pro Phe Val Pro Thr Leu Cys Gly Pro Ala Asp Leu Arg Tyr Phe
        835                 840                 845

Glu Gly Glu Phe Thr Gly Leu Pro Pro Ala Leu Thr Pro Pro Ala Pro
    850                 855                 860

His Ser Leu Leu Thr Ala Arg Gln Gln Ala Ala Phe Arg Asp Phe Asp
865                 870                 875                 880

Phe Val Ser Glu Arg Phe Leu Glu Pro
                885
```

<210> 41
<211> 1056
<212> PRT
<213> Homo sapiens

<400> 41

```
Met Ala Ser Gln Pro Asn Ser Ser Ala Lys Lys Lys Glu Glu Lys Gly
```

1 5 10 15

Lys Asn Ile Gln Val Val Val Arg Cys Arg Pro Phe Asn Leu Ala Glu
20 25 30

Arg Lys Ala Ser Ala His Ser Ile Val Glu Cys Asp Pro Val Arg Lys
35 40 45

Glu Val Ser Val Arg Thr Gly Gly Leu Ala Asp Lys Ser Ser Arg Lys
50 55 60

Thr Tyr Thr Phe Asp Met Val Phe Gly Ala Ser Thr Lys Gln Ile Asp
65 70 75 80

Val Tyr Arg Ser Val Val Cys Pro Ile Leu Asp Glu Val Ile Met Gly
85 90 95

Tyr Asn Cys Thr Ile Phe Ala Tyr Gly Gln Thr Gly Thr Gly Lys Thr
100 105 110

Phe Thr Met Glu Gly Glu Arg Ser Pro Asn Glu Glu Tyr Thr Trp Glu
115 120 125

Glu Asp Pro Leu Ala Gly Ile Ile Pro Arg Thr Leu His Gln Ile Phe
130 135 140

Glu Lys Leu Thr Asp Asn Gly Thr Glu Phe Ser Val Lys Val Ser Leu
145 150 155 160

Leu Glu Ile Tyr Asn Glu Glu Leu Phe Asp Leu Leu Asn Pro Ser Ser
165 170 175

Asp Val Ser Glu Arg Leu Gln Met Phe Asp Asp Pro Arg Asn Lys Arg
180 185 190

Gly Val Ile Ile Lys Gly Leu Glu Glu Ile Thr Val His Asn Lys Asp
195 200 205

Glu Val Tyr Gln Ile Leu Glu Lys Gly Ala Ala Lys Arg Thr Thr Ala
210 215 220

Ala Thr Leu Met Asn Ala Tyr Ser Ser Arg Ser His Ser Val Phe Ser
225 230 235 240

Val Thr Ile His Met Lys Glu Thr Thr Ile Asp Gly Glu Glu Leu Val
245 250 255

Lys Ile Gly Lys Leu Asn Leu Val Asp Leu Ala Gly Ser Glu Asn Ile
260 265 270

Gly Arg Ser Gly Ala Val Asp Lys Arg Ala Arg Glu Ala Gly Asn Ile

275 280 285

Asn Gln Ser Leu Leu Thr Leu Gly Arg Val Ile Thr Ala Leu Val Glu
290 295 300

Arg Thr Pro His Val Pro Tyr Arg Glu Ser Lys Leu Thr Arg Ile Leu
305 310 315 320

Gln Asp Ser Leu Gly Gly Arg Thr Arg Thr Ser Ile Ile Ala Thr Ile
325 330 335

Ser Pro Ala Ser Leu Asn Leu Glu Glu Thr Leu Ser Thr Leu Glu Tyr
340 345 350

Ala His Arg Ala Lys Asn Ile Leu Asn Lys Pro Glu Val Asn Gln Lys
355 360 365

Leu Thr Lys Lys Ala Leu Ile Lys Glu Tyr Thr Glu Glu Ile Glu Arg
370 375 380

Leu Lys Arg Asp Leu Ala Ala Ala Arg Glu Lys Asn Gly Val Tyr Ile
385 390 395 400

Ser Glu Glu Asn Phe Arg Val Met Ser Gly Lys Leu Thr Val Gln Glu
405 410 415

Glu Gln Ile Val Glu Leu Ile Glu Lys Ile Gly Ala Val Glu Glu Glu
420 425 430

Leu Asn Arg Val Thr Glu Leu Phe Met Asp Asn Lys Asn Glu Leu Asp
435 440 445

Gln Cys Lys Ser Asp Leu Gln Asn Lys Thr Gln Glu Leu Glu Thr Thr
450 455 460

Gln Lys His Leu Gln Glu Thr Lys Leu Gln Leu Val Lys Glu Glu Tyr
465 470 475 480

Ile Thr Ser Ala Leu Glu Ser Thr Glu Glu Lys Leu His Asp Ala Ala
485 490 495

Ser Lys Leu Leu Asn Thr Val Glu Glu Thr Thr Lys Asp Val Ser Gly
500 505 510

Leu His Ser Lys Leu Asp Arg Lys Lys Ala Val Asp Gln His Asn Ala
515 520 525

Glu Ala Gln Asp Ile Phe Gly Lys Asn Leu Asn Ser Leu Phe Asn Asn
530 535 540

Met Glu Glu Leu Ile Lys Asp Gly Ser Ser Lys Gln Lys Ala Met Leu

545 550 555 560

Glu Val His Lys Thr Leu Phe Gly Asn Leu Leu Ser Ser Ser Val Ser
565 570 575

Ala Leu Asp Thr Ile Thr Thr Val Ala Leu Gly Ser Leu Thr Ser Ile
580 585 590

Pro Glu Asn Val Ser Thr His Val Ser Gln Ile Phe Asn Met Ile Leu
595 600 605

Lys Glu Gln Ser Leu Ala Ala Glu Ser Lys Thr Val Leu Gln Glu Leu
610 615 620

Ile Asn Val Leu Lys Thr Asp Leu Leu Ser Ser Leu Glu Met Ile Leu
625 630 635 640

Ser Pro Thr Val Val Ser Ile Leu Lys Ile Asn Ser Gln Leu Lys His
645 650 655

Ile Phe Lys Thr Ser Leu Thr Val Ala Asp Lys Ile Glu Asp Gln Lys
660 665 670

Lys Glu Leu Asp Gly Phe Leu Ser Ile Leu Cys Asn Asn Leu His Glu
675 680 685

Leu Gln Glu Asn Thr Ile Cys Ser Leu Val Glu Ser Gln Lys Gln Cys
690 695 700

Gly Asn Leu Thr Glu Asp Leu Lys Thr Ile Lys Gln Thr His Ser Gln
705 710 715 720

Glu Leu Cys Lys Leu Met Asn Leu Trp Thr Glu Arg Phe Cys Ala Leu
725 730 735

Glu Glu Lys Cys Glu Asn Ile Gln Lys Pro Leu Ser Ser Val Gln Glu
740 745 750

Asn Ile Gln Gln Lys Ser Lys Asp Ile Val Asn Lys Met Thr Phe His
755 760 765

Ser Gln Lys Phe Cys Ala Asp Ser Asp Gly Phe Ser Gln Glu Leu Arg
770 775 780

Asn Phe Asn Gln Glu Gly Thr Lys Leu Val Glu Glu Ser Val Lys His
785 790 795 800

Ser Asp Lys Leu Asn Gly Asn Leu Glu Lys Ile Ser Gln Glu Thr Glu
805 810 815

Gln Arg Cys Glu Ser Leu Asn Thr Arg Thr Val Tyr Phe Ser Glu Gln

820 825 830

Trp Val Ser Ser Leu Asn Glu Arg Glu Gln Glu Leu His Asn Leu Leu
835 840 845

Glu Val Val Ser Gln Cys Cys Glu Ala Ser Ser Ser Asp Ile Thr Glu
850 855 860

Lys Ser Asp Gly Arg Lys Ala Ala His Glu Lys Gln His Asn Ile Phe
865 870 875 880

Leu Asp Gln Met Thr Ile Asp Glu Asp Lys Leu Ile Ala Gln Asn Leu
885 890 895

Glu Leu Asn Glu Thr Ile Lys Ile Gly Leu Thr Lys Leu Asn Cys Phe
900 905 910

Leu Glu Gln Asp Leu Lys Leu Asp Ile Pro Thr Gly Thr Thr Pro Gln
915 920 925

Arg Lys Ser Tyr Leu Tyr Pro Ser Thr Leu Val Arg Thr Glu Pro Arg
930 935 940

Glu His Leu Leu Asp Gln Leu Lys Arg Lys Gln Pro Glu Leu Leu Met
945 950 955 960

Met Leu Asn Cys Ser Glu Asn Asn Lys Glu Glu Thr Ile Pro Asp Val
965 970 975

Asp Val Glu Glu Ala Val Leu Gly Gln Tyr Thr Glu Glu Pro Leu Ser
980 985 990

Gln Glu Pro Ser Val Asp Ala Gly Val Asp Cys Ser Ser Ile Gly Gly
995 1000 1005

Val Pro Phe Phe Gln His Lys Lys Ser His Gly Lys Asp Lys Glu
1010 1015 1020

Asn Arg Gly Ile Asn Thr Leu Glu Arg Ser Lys Val Glu Glu Thr
1025 1030 1035

Thr Glu His Leu Val Thr Lys Ser Arg Leu Pro Leu Arg Ala Gln
1040 1045 1050

Ile Asn Leu
1055

<210> 42
<211> 2825
<212> PRT
<213> Homo sapiens

<400> 42

```
Met Tyr Ala Ser Leu Gly Ser Gly Pro Val Ala Pro Leu Pro Ala Ser
1               5                  10                  15

Val Pro Pro Ser Val Leu Gly Ser Trp Ser Thr Gly Gly Ser Arg Ser
            20                  25                  30

Cys Val Arg Gln Glu Thr Lys Ser Pro Gly Gly Ala Arg Thr Ser Gly
        35                  40                  45

His Trp Ala Ser Val Trp Gln Glu Val Leu Lys Gln Leu Gln Gly Ser
    50                  55                  60

Ile Glu Asp Glu Ala Met Ala Ser Ser Gly Gln Ile Asp Leu Leu Glu
65                  70                  75                  80

Arg Leu Lys Glu Leu Asn Leu Asp Ser Ser Asn Phe Pro Gly Val Lys
                85                  90                  95

Leu Arg Ser Lys Met Ser Leu Arg Ser Tyr Gly Ser Arg Glu Gly Ser
            100                 105                 110

Val Ser Ser Arg Ser Gly Glu Cys Ser Pro Val Pro Met Gly Ser Phe
        115                 120                 125

Pro Arg Arg Gly Phe Val Asn Gly Ser Arg Glu Ser Thr Gly Tyr Leu
    130                 135                 140

Glu Glu Leu Glu Lys Glu Arg Ser Leu Leu Leu Ala Asp Leu Asp Lys
145                 150                 155                 160

Glu Glu Lys Glu Lys Asp Trp Tyr Tyr Ala Gln Leu Gln Asn Leu Thr
                165                 170                 175

Lys Arg Ile Asp Ser Leu Pro Leu Thr Glu Asn Phe Ser Leu Gln Thr
            180                 185                 190

Asp Met Thr Arg Arg Gln Leu Glu Tyr Glu Ala Arg Gln Ile Arg Val
        195                 200                 205

Ala Met Glu Glu Gln Leu Gly Thr Cys Gln Asp Met Glu Lys Arg Ala
    210                 215                 220

Gln Arg Ser Ser Gln Asn Lys His Glu Thr Gly Ser His Asp Ala Glu
225                 230                 235                 240

Arg Gln Asn Glu Gly Gln Gly Val Gly Glu Ile Asn Met Ala Thr Ser
                245                 250                 255

Gly Asn Gly Gln Gly Ser Thr Thr Arg Met Asp His Glu Thr Ala Ser
            260                 265                 270
```

```
Val Leu Ser Ser Ser Ser Thr His Ser Ala Pro Arg Arg Leu Thr Ser
        275                 280                 285

His Leu Gly Thr Lys Val Glu Met Val Tyr Ser Leu Leu Ser Met Leu
    290                 295                 300

Gly Thr His Asp Lys Asp Asp Met Ser Arg Thr Leu Leu Ala Met Ser
305                 310                 315                 320

Ser Ser Gln Asp Ser Cys Ile Ser Met Arg Gln Ser Gly Cys Leu Pro
                325                 330                 335

Leu Leu Ile Gln Leu Leu His Gly Asn Asp Lys Asp Ser Val Leu Leu
            340                 345                 350

Gly Asn Ser Arg Gly Ser Lys Glu Ala Arg Ala Arg Ala Ser Ala Ala
        355                 360                 365

Leu His Asn Ile Ile His Ser Gln Pro Asp Asp Lys Arg Gly Arg Arg
    370                 375                 380

Glu Ile Arg Val Leu His Leu Leu Glu Gln Ile Arg Ala Tyr Cys Glu
385                 390                 395                 400

Thr Cys Trp Glu Trp Gln Glu Ala His Glu Pro Gly Met Asp Gln Asp
                405                 410                 415

Lys Asn Pro Met Pro Ala Pro Val Glu His Gln Ile Cys Pro Ala Val
            420                 425                 430

Cys Val Leu Met Lys Leu Ser Phe Asp Glu Glu His Arg His Ala Met
        435                 440                 445

Asn Glu Leu Gly Gly Leu Gln Ala Ile Ala Glu Leu Leu Gln Val Asp
    450                 455                 460

Cys Glu Met Tyr Gly Leu Thr Asn Asp His Tyr Ser Ile Thr Leu Arg
465                 470                 475                 480

Arg Tyr Ala Gly Met Ala Leu Thr Asn Leu Thr Phe Gly Asp Val Ala
                485                 490                 495

Asn Lys Ala Thr Leu Cys Ser Met Lys Gly Cys Met Arg Ala Leu Val
            500                 505                 510

Ala Gln Leu Lys Ser Glu Ser Glu Asp Leu Gln Gln Val Ile Ala Ser
        515                 520                 525

Val Leu Arg Asn Leu Ser Trp Arg Ala Asp Val Asn Ser Lys Lys Thr
    530                 535                 540
```

```
Leu Arg Glu Val Gly Ser Val Lys Ala Leu Met Glu Cys Ala Leu Glu
545                 550                 555                 560

Val Lys Lys Glu Ser Thr Leu Lys Ser Val Leu Ser Ala Leu Trp Asn
                565                 570                 575

Leu Ser Ala His Cys Thr Glu Asn Lys Ala Asp Ile Cys Ala Val Asp
            580                 585                 590

Gly Ala Leu Ala Phe Leu Val Gly Thr Leu Thr Tyr Arg Ser Gln Thr
        595                 600                 605

Asn Thr Leu Ala Ile Ile Glu Ser Gly Gly Gly Ile Leu Arg Asn Val
    610                 615                 620

Ser Ser Leu Ile Ala Thr Asn Glu Asp His Arg Gln Ile Leu Arg Glu
625                 630                 635                 640

Asn Asn Cys Leu Gln Thr Leu Leu Gln His Leu Lys Ser His Ser Leu
                645                 650                 655

Thr Ile Val Ser Asn Ala Cys Gly Thr Leu Trp Asn Leu Ser Ala Arg
            660                 665                 670

Asn Pro Lys Asp Gln Glu Ala Leu Trp Asp Met Gly Ala Val Ser Met
        675                 680                 685

Leu Lys Asn Leu Ile His Ser Lys His Lys Met Ile Ala Met Gly Ser
    690                 695                 700

Ala Ala Ala Leu Arg Asn Leu Met Ala Asn Arg Pro Ala Lys Tyr Lys
705                 710                 715                 720

Asp Ala Asn Ile Met Ser Pro Gly Ser Ser Leu Pro Ser Leu His Val
                725                 730                 735

Arg Lys Gln Lys Ala Leu Glu Ala Glu Leu Asp Ala Gln His Leu Ser
            740                 745                 750

Glu Thr Phe Asp Asn Ile Asp Asn Leu Ser Pro Lys Ala Ser His Arg
        755                 760                 765

Ser Lys Gln Arg His Lys Gln Ser Leu Tyr Gly Asp Tyr Val Phe Asp
    770                 775                 780

Thr Asn Arg His Asp Asp Asn Arg Ser Asp Asn Phe Asn Thr Gly Asn
785                 790                 795                 800

Met Thr Val Leu Ser Pro Tyr Leu Asn Thr Thr Val Leu Pro Ser Ser
                805                 810                 815
```

```
Ser Ser Ser Arg Gly Ser Leu Asp Ser Ser Arg Ser Glu Lys Asp Arg
            820                 825                 830

Ser Leu Glu Arg Glu Arg Gly Ile Gly Leu Gly Asn Tyr His Pro Ala
        835                 840                 845

Thr Glu Asn Pro Gly Thr Ser Ser Lys Arg Gly Leu Gln Ile Ser Thr
    850                 855                 860

Thr Ala Ala Gln Ile Ala Lys Val Met Glu Glu Val Ser Ala Ile His
865                 870                 875                 880

Thr Ser Gln Glu Asp Arg Ser Ser Gly Ser Thr Thr Glu Leu His Cys
                885                 890                 895

Val Thr Asp Glu Arg Asn Ala Leu Arg Arg Ser Ser Ala Ala His Thr
            900                 905                 910

His Ser Asn Thr Tyr Asn Phe Thr Lys Ser Glu Asn Ser Asn Arg Thr
        915                 920                 925

Cys Ser Met Pro Tyr Ala Lys Leu Glu Tyr Lys Arg Ser Ser Asn Asp
    930                 935                 940

Ser Leu Asn Ser Val Ser Ser Ser Asp Gly Tyr Gly Lys Arg Gly Gln
945                 950                 955                 960

Met Lys Pro Ser Ile Glu Ser Tyr Ser Glu Asp Asp Glu Ser Lys Phe
                965                 970                 975

Cys Ser Tyr Gly Gln Tyr Pro Ala Asp Leu Ala His Lys Ile His Ser
            980                 985                 990

Ala Asn His Met Asp Asp Asn Asp  Gly Glu Leu Asp Thr  Pro Ile Asn
        995                 1000                1005

Tyr Ser  Leu Lys Tyr Ser Asp  Glu Gln Leu Asn Ser  Gly Arg Gln
    1010                1015                1020

Ser Pro  Ser Gln Asn Glu Arg  Trp Ala Arg Pro Lys  His Ile Ile
    1025                1030                1035

Glu Asp  Glu Ile Lys Gln Ser  Glu Gln Arg Gln Ser  Arg Asn Gln
    1040                1045                1050

Ser Thr  Thr Tyr Pro Val Tyr  Thr Glu Ser Thr Asp  Asp Lys His
    1055                1060                1065

Leu Lys  Phe Gln Pro His Phe  Gly Gln Gln Glu Cys  Val Ser Pro
    1070                1075                1080
```

```
Tyr Arg  Ser Arg Gly Ala Asn  Gly Ser Glu Thr Asn  Arg Val Gly
    1085                1090                1095

Ser Asn  His Gly Ile Asn Gln  Asn Val Ser Gln Ser  Leu Cys Gln
    1100                1105                1110

Glu Asp  Asp Tyr Glu Asp Asp  Lys Pro Thr Asn Tyr  Ser Glu Arg
    1115                1120                1125

Tyr Ser  Glu Glu Glu Gln His  Glu Glu Glu Glu Arg  Pro Thr Asn
    1130                1135                1140

Tyr Ser  Ile Lys Tyr Asn Glu  Glu Lys Arg His Val  Asp Gln Pro
    1145                1150                1155

Ile Asp  Tyr Ser Leu Lys Tyr  Ala Thr Asp Ile Pro  Ser Ser Gln
    1160                1165                1170

Lys Gln  Ser Phe Ser Phe Ser  Lys Ser Ser Ser Gly  Gln Ser Ser
    1175                1180                1185

Lys Thr  Glu His Met Ser Ser  Ser Ser Glu Asn Thr  Ser Thr Pro
    1190                1195                1200

Ser Ser  Asn Ala Lys Arg Gln  Asn Gln Leu His Pro  Ser Ser Ala
    1205                1210                1215

Gln Ser  Arg Ser Gly Gln Pro  Gln Lys Ala Ala Thr  Cys Lys Val
    1220                1225                1230

Ser Ser  Ile Asn Gln Glu Thr  Ile Gln Thr Tyr Cys  Val Glu Asp
    1235                1240                1245

Thr Pro  Ile Cys Phe Ser Arg  Cys Ser Ser Leu Ser  Ser Leu Ser
    1250                1255                1260

Ser Ala  Glu Asp Glu Ile Gly  Cys Asn Gln Thr Thr  Gln Glu Ala
    1265                1270                1275

Asp Ser  Ala Asn Thr Leu Gln  Ile Ala Glu Ile Lys  Glu Lys Ile
    1280                1285                1290

Gly Thr  Arg Ser Ala Glu Asp  Pro Val Ser Glu Val  Pro Ala Val
    1295                1300                1305

Ser Gln  His Pro Arg Thr Lys  Ser Ser Arg Leu Gln  Gly Ser Ser
    1310                1315                1320

Leu Ser  Ser Glu Ser Ala Arg  His Lys Ala Val Glu  Phe Ser Ser
    1325                1330                1335
```

```
Gly Ala  Lys Ser Pro Ser Lys  Ser Gly Ala Gln Thr  Pro Lys Ser
    1340                 1345                 1350

Pro Pro  Glu His Tyr Val Gln  Glu Thr Pro Leu Met  Phe Ser Arg
    1355                 1360                 1365

Cys Thr  Ser Val Ser Ser Leu  Asp Ser Phe Glu Ser  Arg Ser Ile
    1370                 1375                 1380

Ala Ser  Ser Val Gln Ser Glu  Pro Cys Ser Gly Met  Val Ser Gly
    1385                 1390                 1395

Ile Ile  Ser Pro Ser Asp Leu  Pro Asp Ser Pro Gly  Gln Thr Met
    1400                 1405                 1410

Pro Pro  Ser Arg Ser Lys Thr  Pro Pro Pro Pro Pro  Gln Thr Ala
    1415                 1420                 1425

Gln Thr  Lys Arg Glu Val Pro  Lys Asn Lys Ala Pro  Thr Ala Glu
    1430                 1435                 1440

Lys Arg  Glu Ser Gly Pro Lys  Gln Ala Ala Val Asn  Ala Ala Val
    1445                 1450                 1455

Gln Arg  Val Gln Val Leu Pro  Asp Ala Asp Thr Leu  Leu His Phe
    1460                 1465                 1470

Ala Thr  Glu Ser Thr Pro Asp  Gly Phe Ser Cys Ser  Ser Ser Leu
    1475                 1480                 1485

Ser Ala  Leu Ser Leu Asp Glu  Pro Phe Ile Gln Lys  Asp Val Glu
    1490                 1495                 1500

Leu Arg  Ile Met Pro Pro Val  Gln Glu Asn Asp Asn  Gly Asn Glu
    1505                 1510                 1515

Thr Glu  Ser Glu Gln Pro Lys  Glu Ser Asn Glu Asn  Gln Glu Lys
    1520                 1525                 1530

Glu Ala  Glu Lys Thr Ile Asp  Ser Glu Lys Asp Leu  Leu Asp Asp
    1535                 1540                 1545

Ser Asp  Asp Asp Asp Ile Glu  Ile Leu Glu Glu Cys  Ile Ile Ser
    1550                 1555                 1560

Ala Met  Pro Thr Lys Ser Ser  Arg Lys Ala Lys Lys  Pro Ala Gln
    1565                 1570                 1575

Thr Ala  Ser Lys Leu Pro Pro  Pro Val Ala Arg Lys  Pro Ser Gln
    1580                 1585                 1590
```

```
Leu Pro  Val Tyr Lys Leu Leu  Pro Ser Gln Asn Arg  Leu Gln Pro
    1595                1600                1605

Gln Lys  His Val Ser Phe Thr  Pro Gly Asp Asp Met  Pro Arg Val
    1610                1615                1620

Tyr Cys  Val Glu Gly Thr Pro  Ile Asn Phe Ser Thr  Ala Thr Ser
    1625                1630                1635

Leu Ser  Asp Leu Thr Ile Glu  Ser Pro Pro Asn Glu  Leu Ala Ala
    1640                1645                1650

Gly Glu  Gly Val Arg Gly Gly  Ala Gln Ser Gly Glu  Phe Glu Lys
    1655                1660                1665

Arg Asp  Thr Ile Pro Thr Glu  Gly Arg Ser Thr Asp  Glu Ala Gln
    1670                1675                1680

Gly Gly  Lys Thr Ser Ser Val  Thr Ile Pro Glu Leu  Asp Asp Asn
    1685                1690                1695

Lys Ala  Glu Glu Gly Asp Ile  Leu Ala Glu Cys Ile  Asn Ser Ala
    1700                1705                1710

Met Pro  Lys Gly Lys Ser His  Lys Pro Phe Arg Val  Lys Lys Ile
    1715                1720                1725

Met Asp  Gln Val Gln Gln Ala  Ser Ala Ser Ser Ser  Ala Pro Asn
    1730                1735                1740

Lys Asn  Gln Leu Asp Gly Lys  Lys Lys Lys Pro Thr  Ser Pro Val
    1745                1750                1755

Lys Pro  Ile Pro Gln Asn Thr  Glu Tyr Arg Thr Arg  Val Arg Lys
    1760                1765                1770

Asn Ala  Asp Ser Lys Asn Asn  Leu Asn Ala Glu Arg  Val Phe Ser
    1775                1780                1785

Asp Asn  Lys Asp Ser Lys Lys  Gln Asn Leu Lys Asn  Asn Ser Lys
    1790                1795                1800

Val Phe  Asn Asp Lys Leu Pro  Asn Asn Glu Asp Arg  Val Arg Gly
    1805                1810                1815

Ser Phe  Ala Phe Asp Ser Pro  His His Tyr Thr Pro  Ile Glu Gly
    1820                1825                1830

Thr Pro  Tyr Cys Phe Ser Arg  Asn Asp Ser Leu Ser  Ser Leu Asp
    1835                1840                1845
```

```
Phe Asp  Asp Asp Asp Val Asp  Leu Ser Arg Glu Lys  Ala Glu Leu
    1850                 1855                 1860

Arg Lys  Ala Lys Glu Asn Lys  Glu Ser Glu Ala Lys  Val Thr Ser
    1865                 1870                 1875

His Thr  Glu Leu Thr Ser Asn  Gln Gln Ser Ala Asn  Lys Thr Gln
    1880                 1885                 1890

Ala Ile  Ala Lys Gln Pro Ile  Asn Arg Gly Gln Pro  Lys Pro Ile
    1895                 1900                 1905

Leu Gln  Lys Gln Ser Thr Phe  Pro Gln Ser Ser Lys  Asp Ile Pro
    1910                 1915                 1920

Asp Arg  Gly Ala Ala Thr Asp  Glu Lys Leu Gln Asn  Phe Ala Ile
    1925                 1930                 1935

Glu Asn  Thr Pro Val Cys Phe  Ser His Asn Ser Ser  Leu Ser Ser
    1940                 1945                 1950

Leu Ser  Asp Ile Asp Gln Glu  Asn Asn Asn Lys Glu  Asn Glu Pro
    1955                 1960                 1965

Ile Lys  Glu Thr Glu Pro Pro  Asp Ser Gln Gly Glu  Pro Ser Lys
    1970                 1975                 1980

Pro Gln  Ala Ser Gly Tyr Ala  Pro Lys Ser Phe His  Val Glu Asp
    1985                 1990                 1995

Thr Pro  Val Cys Phe Ser Arg  Asn Ser Ser Leu Ser  Ser Leu Ser
    2000                 2005                 2010

Ile Asp  Ser Glu Asp Asp Leu  Leu Gln Glu Cys Ile  Ser Ser Ala
    2015                 2020                 2025

Met Pro  Lys Lys Lys Lys Pro  Ser Arg Leu Lys Gly  Asp Asn Glu
    2030                 2035                 2040

Lys His  Ser Pro Arg Asn Met  Gly Gly Ile Leu Gly  Glu Asp Leu
    2045                 2050                 2055

Thr Leu  Asp Leu Lys Asp Ile  Gln Arg Pro Asp Ser  Glu His Gly
    2060                 2065                 2070

Leu Ser  Pro Asp Ser Glu Asn  Phe Asp Trp Lys Ala  Ile Gln Glu
    2075                 2080                 2085

Gly Ala  Asn Ser Ile Val Ser  Ser Leu His Gln Ala  Ala Ala Ala
    2090                 2095                 2100
```

```
Ala Cys  Leu Ser Arg Gln Ala  Ser Ser Asp Ser Asp  Ser Ile Leu
    2105                2110                2115

Ser Leu  Lys Ser Gly Ile Ser  Leu Gly Ser Pro Phe  His Leu Thr
    2120                2125                2130

Pro Asp  Gln Glu Glu Lys Pro  Phe Thr Ser Asn Lys  Gly Pro Arg
    2135                2140                2145

Ile Leu  Lys Pro Gly Glu Lys  Ser Thr Leu Glu Thr  Lys Lys Ile
    2150                2155                2160

Glu Ser  Glu Ser Lys Gly Ile  Lys Gly Gly Lys Lys  Val Tyr Lys
    2165                2170                2175

Ser Leu  Ile Thr Gly Lys Val  Arg Ser Asn Ser Glu  Ile Ser Gly
    2180                2185                2190

Gln Met  Lys Gln Pro Leu Gln  Ala Asn Met Pro Ser  Ile Ser Arg
    2195                2200                2205

Gly Arg  Thr Met Ile His Ile  Pro Gly Val Arg Asn  Ser Ser Ser
    2210                2215                2220

Ser Thr  Ser Pro Val Ser Lys  Lys Gly Pro Pro Leu  Lys Thr Pro
    2225                2230                2235

Ala Ser  Lys Ser Pro Ser Glu  Gly Gln Thr Ala Thr  Thr Ser Pro
    2240                2245                2250

Arg Gly  Ala Lys Pro Ser Val  Lys Ser Glu Leu Ser  Pro Val Ala
    2255                2260                2265

Arg Gln  Thr Ser Gln Ile Gly  Gly Ser Ser Lys Ala  Pro Ser Arg
    2270                2275                2280

Ser Gly  Ser Arg Asp Ser Thr  Pro Ser Arg Pro Ala  Gln Gln Pro
    2285                2290                2295

Leu Ser  Arg Pro Ile Gln Ser  Pro Gly Arg Asn Ser  Ile Ser Pro
    2300                2305                2310

Gly Arg  Asn Gly Ile Ser Pro  Pro Asn Lys Leu Ser  Gln Leu Pro
    2315                2320                2325

Arg Thr  Ser Ser Pro Ser Thr  Ala Ser Thr Lys Ser  Ser Gly Ser
    2330                2335                2340

Gly Lys  Met Ser Tyr Thr Ser  Pro Gly Arg Gln Met  Ser Gln Gln
    2345                2350                2355
```

```
Asn Leu  Thr Lys Gln Thr Gly  Leu Ser Lys Asn Ala  Ser Ser Ile
    2360                 2365                 2370

Pro Arg  Ser Glu Ser Ala Ser  Lys Gly Leu Asn Gln  Met Asn Asn
    2375                 2380                 2385

Gly Asn  Gly Ala Asn Lys Lys  Val Glu Leu Ser Arg  Met Ser Ser
    2390                 2395                 2400

Thr Lys  Ser Ser Gly Ser Glu  Ser Asp Arg Ser Glu  Arg Pro Val
    2405                 2410                 2415

Leu Val  Arg Gln Ser Thr Phe  Ile Lys Glu Ala Pro  Ser Pro Thr
    2420                 2425                 2430

Leu Arg  Arg Lys Leu Glu Glu  Ser Ala Ser Phe Glu  Ser Leu Ser
    2435                 2440                 2445

Pro Ser  Ser Arg Pro Ala Ser  Pro Thr Arg Ser Gln  Ala Gln Thr
    2450                 2455                 2460

Pro Val  Leu Ser Pro Ser Leu  Pro Asp Met Ser Leu  Ser Thr His
    2465                 2470                 2475

Ser Ser  Val Gln Ala Gly Gly  Trp Arg Lys Leu Pro  Pro Asn Leu
    2480                 2485                 2490

Ser Pro  Thr Ile Glu Tyr Asn  Asp Gly Arg Pro Ala  Lys Arg His
    2495                 2500                 2505

Asp Ile  Ala Arg Ser His Ser  Glu Ser Pro Ser Arg  Leu Pro Ile
    2510                 2515                 2520

Asn Arg  Ser Gly Thr Trp Lys  Arg Glu His Ser Lys  His Ser Ser
    2525                 2530                 2535

Ser Leu  Pro Arg Val Ser Thr  Trp Arg Arg Thr Gly  Ser Ser Ser
    2540                 2545                 2550

Ser Ile  Leu Ser Ala Ser Ser  Glu Ser Ser Glu Lys  Ala Lys Ser
    2555                 2560                 2565

Glu Asp  Glu Lys His Val Asn  Ser Ile Ser Gly Thr  Lys Gln Ser
    2570                 2575                 2580

Lys Glu  Asn Gln Val Ser Ala  Lys Gly Thr Trp Arg  Lys Ile Lys
    2585                 2590                 2595

Glu Asn  Glu Phe Ser Pro Thr  Asn Ser Thr Ser Gln  Thr Val Ser
    2600                 2605                 2610
```

```
Ser Gly  Ala Thr Asn Gly Ala  Glu Ser Lys Thr Leu  Ile Tyr Gln
    2615                 2620                 2625

Met Ala  Pro Ala Val Ser Lys  Thr Glu Asp Val Trp  Val Arg Ile
    2630                 2635                 2640

Glu Asp  Cys Pro Ile Asn Asn  Pro Arg Ser Gly Arg  Ser Pro Thr
    2645                 2650                 2655

Gly Asn  Thr Pro Pro Val Ile  Asp Ser Val Ser Glu  Lys Ala Asn
    2660                 2665                 2670

Pro Asn  Ile Lys Asp Ser Lys  Asp Asn Gln Ala Lys  Gln Asn Val
    2675                 2680                 2685

Gly Asn  Gly Ser Val Pro Met  Arg Thr Val Gly Leu  Glu Asn Arg
    2690                 2695                 2700

Leu Asn  Ser Phe Ile Gln Val  Asp Ala Pro Asp Gln  Lys Gly Thr
    2705                 2710                 2715

Glu Ile  Lys Pro Gly Gln Asn  Asn Pro Val Pro Val  Ser Glu Thr
    2720                 2725                 2730

Asn Glu  Ser Ser Ile Val Glu  Arg Thr Pro Phe Ser  Ser Ser Ser
    2735                 2740                 2745

Ser Ser  Lys His Ser Ser Pro  Ser Gly Thr Val Ala  Ala Arg Val
    2750                 2755                 2760

Thr Pro  Phe Asn Tyr Asn Pro  Ser Pro Arg Lys Ser  Ser Ala Asp
    2765                 2770                 2775

Ser Thr  Ser Ala Arg Pro Ser  Gln Ile Pro Thr Pro  Val Asn Asn
    2780                 2785                 2790

Asn Thr  Lys Lys Arg Asp Ser  Lys Thr Asp Ser Thr  Glu Ser Ser
    2795                 2800                 2805

Gly Thr  Gln Ser Pro Lys Arg  His Ser Gly Ser Tyr  Leu Val Thr
    2810                 2815                 2820

Ser Val
    2825
```

<210> 43
<211> 1863
<212> PRT
<213> Homo sapiens

<400> 43

```
Met Asp Leu Ser Ala Leu Arg Val Glu Glu Val Gln Asn Val Ile Asn
1               5                  10                  15

Ala Met Gln Lys Ile Leu Glu Cys Pro Ile Cys Leu Glu Leu Ile Lys
            20                  25                  30

Glu Pro Val Ser Thr Lys Cys Asp His Ile Phe Cys Lys Phe Cys Met
        35                  40                  45

Leu Lys Leu Leu Asn Gln Lys Lys Gly Pro Ser Gln Cys Pro Leu Cys
    50                  55                  60

Lys Asn Asp Ile Thr Lys Arg Ser Leu Gln Glu Ser Thr Arg Phe Ser
65                  70                  75                  80

Gln Leu Val Glu Glu Leu Leu Lys Ile Ile Cys Ala Phe Gln Leu Asp
                85                  90                  95

Thr Gly Leu Glu Tyr Ala Asn Ser Tyr Asn Phe Ala Lys Lys Glu Asn
            100                 105                 110

Asn Ser Pro Glu His Leu Lys Asp Glu Val Ser Ile Ile Gln Ser Met
        115                 120                 125

Gly Tyr Arg Asn Arg Ala Lys Arg Leu Leu Gln Ser Glu Pro Glu Asn
    130                 135                 140

Pro Ser Leu Gln Glu Thr Ser Leu Ser Val Gln Leu Ser Asn Leu Gly
145                 150                 155                 160

Thr Val Arg Thr Leu Arg Thr Lys Gln Arg Ile Gln Pro Gln Lys Thr
                165                 170                 175

Ser Val Tyr Ile Glu Leu Gly Ser Asp Ser Ser Glu Asp Thr Val Asn
            180                 185                 190

Lys Ala Thr Tyr Cys Ser Val Gly Asp Gln Glu Leu Leu Gln Ile Thr
        195                 200                 205

Pro Gln Gly Thr Arg Asp Glu Ile Ser Leu Asp Ser Ala Lys Lys Ala
    210                 215                 220

Ala Cys Glu Phe Ser Glu Thr Asp Val Thr Asn Thr Glu His His Gln
225                 230                 235                 240

Pro Ser Asn Asn Asp Leu Asn Thr Thr Glu Lys Arg Ala Ala Glu Arg
                245                 250                 255

His Pro Glu Lys Tyr Gln Gly Ser Ser Val Ser Asn Leu His Val Glu
            260                 265                 270
```

```
Pro Cys Gly Thr Asn Thr His Ala Ser Ser Leu Gln His Glu Asn Ser
        275                 280                 285

Ser Leu Leu Leu Thr Lys Asp Arg Met Asn Val Glu Lys Ala Glu Phe
    290                 295                 300

Cys Asn Lys Ser Lys Gln Pro Gly Leu Ala Arg Ser Gln His Asn Arg
305                 310                 315                 320

Trp Ala Gly Ser Lys Glu Thr Cys Asn Asp Arg Arg Thr Pro Ser Thr
                325                 330                 335

Glu Lys Lys Val Asp Leu Asn Ala Asp Pro Leu Cys Glu Arg Lys Glu
            340                 345                 350

Trp Asn Lys Gln Lys Leu Pro Cys Ser Glu Asn Pro Arg Asp Thr Glu
        355                 360                 365

Asp Val Pro Trp Ile Thr Leu Asn Ser Ser Ile Gln Lys Val Asn Glu
    370                 375                 380

Trp Phe Ser Arg Ser Asp Glu Leu Leu Gly Ser Asp Asp Ser His Asp
385                 390                 395                 400

Gly Glu Ser Glu Ser Asn Ala Lys Val Ala Asp Val Leu Asp Val Leu
                405                 410                 415

Asn Glu Val Asp Glu Tyr Ser Gly Ser Ser Glu Lys Ile Asp Leu Leu
            420                 425                 430

Ala Ser Asp Pro His Glu Ala Leu Ile Cys Lys Ser Glu Arg Val His
        435                 440                 445

Ser Lys Ser Val Glu Ser Asn Ile Glu Asp Lys Ile Phe Gly Lys Thr
    450                 455                 460

Tyr Arg Lys Lys Ala Ser Leu Pro Asn Leu Ser His Val Thr Glu Asn
465                 470                 475                 480

Leu Ile Ile Gly Ala Phe Val Thr Glu Pro Gln Ile Ile Gln Glu Arg
                485                 490                 495

Pro Leu Thr Asn Lys Leu Lys Arg Lys Arg Arg Pro Thr Ser Gly Leu
            500                 505                 510

His Pro Glu Asp Phe Ile Lys Lys Ala Asp Leu Ala Val Gln Lys Thr
        515                 520                 525

Pro Glu Met Ile Asn Gln Gly Thr Asn Gln Thr Glu Gln Asn Gly Gln
    530                 535                 540
```

```
Val Met Asn Ile Thr Asn Ser Gly His Glu Asn Lys Thr Lys Gly Asp
545                 550                 555                 560

Ser Ile Gln Asn Glu Lys Asn Pro Asn Pro Ile Glu Ser Leu Glu Lys
                565                 570                 575

Glu Ser Ala Phe Lys Thr Lys Ala Glu Pro Ile Ser Ser Ser Ile Ser
            580                 585                 590

Asn Met Glu Leu Glu Leu Asn Ile His Asn Ser Lys Ala Pro Lys Lys
        595                 600                 605

Asn Arg Leu Arg Arg Lys Ser Ser Thr Arg His Ile His Ala Leu Glu
    610                 615                 620

Leu Val Val Ser Arg Asn Leu Ser Pro Pro Asn Cys Thr Glu Leu Gln
625                 630                 635                 640

Ile Asp Ser Cys Ser Ser Ser Glu Glu Ile Lys Lys Lys Lys Tyr Asn
                645                 650                 655

Gln Met Pro Val Arg His Ser Arg Asn Leu Gln Leu Met Glu Gly Lys
            660                 665                 670

Glu Pro Ala Thr Gly Ala Lys Lys Ser Asn Lys Pro Asn Glu Gln Thr
        675                 680                 685

Ser Lys Arg His Asp Ser Asp Thr Phe Pro Glu Leu Lys Leu Thr Asn
    690                 695                 700

Ala Pro Gly Ser Phe Thr Lys Cys Ser Asn Thr Ser Glu Leu Lys Glu
705                 710                 715                 720

Phe Val Asn Pro Ser Leu Pro Arg Glu Glu Lys Glu Glu Lys Leu Glu
                725                 730                 735

Thr Val Lys Val Ser Asn Asn Ala Glu Asp Pro Lys Asp Leu Met Leu
            740                 745                 750

Ser Gly Glu Arg Val Leu Gln Thr Glu Arg Ser Val Glu Ser Ser Ser
        755                 760                 765

Ile Ser Leu Val Pro Gly Thr Asp Tyr Gly Thr Gln Glu Ser Ile Ser
    770                 775                 780

Leu Leu Glu Val Ser Thr Leu Gly Lys Ala Lys Thr Glu Pro Asn Lys
785                 790                 795                 800

Cys Val Ser Gln Cys Ala Ala Phe Glu Asn Pro Lys Gly Leu Ile His
                805                 810                 815
```

```
Gly Cys Ser Lys Asp Asn Arg Asn Asp Thr Glu Gly Phe Lys Tyr Pro
            820                 825                 830

Leu Gly His Glu Val Asn His Ser Arg Glu Thr Ser Ile Glu Met Glu
        835                 840                 845

Glu Ser Glu Leu Asp Ala Gln Tyr Leu Gln Asn Thr Phe Lys Val Ser
    850                 855                 860

Lys Arg Gln Ser Phe Ala Pro Phe Ser Asn Pro Gly Asn Ala Glu Glu
865                 870                 875                 880

Glu Cys Ala Thr Phe Ser Ala His Ser Gly Ser Leu Lys Lys Gln Ser
                885                 890                 895

Pro Lys Val Thr Phe Glu Cys Glu Gln Lys Glu Glu Asn Gln Gly Lys
            900                 905                 910

Asn Glu Ser Asn Ile Lys Pro Val Gln Thr Val Asn Ile Thr Ala Gly
        915                 920                 925

Phe Pro Val Val Gly Gln Lys Asp Lys Pro Val Asp Asn Ala Lys Cys
    930                 935                 940

Ser Ile Lys Gly Gly Ser Arg Phe Cys Leu Ser Ser Gln Phe Arg Gly
945                 950                 955                 960

Asn Glu Thr Gly Leu Ile Thr Pro Asn Lys His Gly Leu Leu Gln Asn
                965                 970                 975

Pro Tyr Arg Ile Pro Pro Leu Phe Pro Ile Lys Ser Phe Val Lys Thr
            980                 985                 990

Lys Cys Lys Lys Asn Leu Leu Glu  Glu Asn Phe Glu Glu  His Ser Met
        995                 1000                1005

Ser Pro  Glu Arg Glu Met Gly  Asn Glu Asn Ile Pro  Ser Thr Val
    1010                1015                1020

Ser Thr  Ile Ser Arg Asn Asn  Ile Arg Glu Asn Val  Phe Lys Glu
    1025                1030                1035

Ala Ser  Ser Ser Asn Ile Asn  Glu Val Gly Ser Ser  Thr Asn Glu
    1040                1045                1050

Val Gly  Ser Ser Ile Asn Glu  Ile Gly Ser Ser Asp  Glu Asn Ile
    1055                1060                1065

Gln Ala  Glu Leu Gly Arg Asn  Arg Gly Pro Lys Leu  Asn Ala Met
    1070                1075                1080
```

```
Leu Arg  Leu Gly Val Leu Gln  Pro Glu Val Tyr Lys  Gln Ser Leu
    1085                1090                1095

Pro Gly  Ser Asn Cys Lys His  Pro Glu Ile Lys Lys  Gln Glu Tyr
    1100                1105                1110

Glu Glu  Val Val Gln Thr Val  Asn Thr Asp Phe Ser  Pro Tyr Leu
    1115                1120                1125

Ile Ser  Asp Asn Leu Glu Gln  Pro Met Gly Ser Ser  His Ala Ser
    1130                1135                1140

Gln Val  Cys Ser Glu Thr Pro  Asp Asp Leu Leu Asp  Asp Gly Glu
    1145                1150                1155

Ile Lys  Glu Asp Thr Ser Phe  Ala Glu Asn Asp Ile  Lys Glu Ser
    1160                1165                1170

Ser Ala  Val Phe Ser Lys Ser  Val Gln Lys Gly Glu  Leu Ser Arg
    1175                1180                1185

Ser Pro  Ser Pro Phe Thr His  Thr His Leu Ala Gln  Gly Tyr Arg
    1190                1195                1200

Arg Gly  Ala Lys Lys Leu Glu  Ser Ser Glu Glu Asn  Leu Ser Ser
    1205                1210                1215

Glu Asp  Glu Glu Leu Pro Cys  Phe Gln His Leu Leu  Phe Gly Lys
    1220                1225                1230

Val Asn  Asn Ile Pro Ser Gln  Ser Thr Arg His Ser  Thr Val Ala
    1235                1240                1245

Thr Glu  Cys Leu Ser Lys Asn  Thr Glu Glu Asn Leu  Leu Ser Leu
    1250                1255                1260

Lys Asn  Ser Leu Asn Asp Cys  Ser Asn Gln Val Ile  Leu Ala Lys
    1265                1270                1275

Ala Ser  Gln Glu His His Leu  Ser Glu Glu Thr Lys  Cys Ser Ala
    1280                1285                1290

Ser Leu  Phe Ser Ser Gln Cys  Ser Glu Leu Glu Asp  Leu Thr Ala
    1295                1300                1305

Asn Thr  Asn Thr Gln Asp Pro  Phe Leu Ile Gly Ser  Ser Lys Gln
    1310                1315                1320

Met Arg  His Gln Ser Glu Ser  Gln Gly Val Gly Leu  Ser Asp Lys
    1325                1330                1335
```

```
Glu Leu  Val Ser Asp Asp Glu  Glu Arg Gly Thr Gly  Leu Glu Glu
    1340                1345                1350

Asn Asn  Gln Glu Glu Gln Ser  Met Asp Ser Asn Leu  Gly Glu Ala
    1355                1360                1365

Ala Ser  Gly Cys Glu Ser Glu  Thr Ser Val Ser Glu  Asp Cys Ser
    1370                1375                1380

Gly Leu  Ser Ser Gln Ser Asp  Ile Leu Thr Thr Gln  Gln Arg Asp
    1385                1390                1395

Thr Met  Gln His Asn Leu Ile  Lys Leu Gln Gln Glu  Met Ala Glu
    1400                1405                1410

Leu Glu  Ala Val Leu Glu Gln  His Gly Ser Gln Pro  Ser Asn Ser
    1415                1420                1425

Tyr Pro  Ser Ile Ile Ser Asp  Ser Ser Ala Leu Glu  Asp Leu Arg
    1430                1435                1440

Asn Pro  Glu Gln Ser Thr Ser  Glu Lys Ala Val Leu  Thr Ser Gln
    1445                1450                1455

Lys Ser  Ser Glu Tyr Pro Ile  Ser Gln Asn Pro Glu  Gly Leu Ser
    1460                1465                1470

Ala Asp  Lys Phe Glu Val Ser  Ala Asp Ser Ser Thr  Ser Lys Asn
    1475                1480                1485

Lys Glu  Pro Gly Val Glu Arg  Ser Ser Pro Ser Lys  Cys Pro Ser
    1490                1495                1500

Leu Asp  Asp Arg Trp Tyr Met  His Ser Cys Ser Gly  Ser Leu Gln
    1505                1510                1515

Asn Arg  Asn Tyr Pro Ser Gln  Glu Glu Leu Ile Lys  Val Val Asp
    1520                1525                1530

Val Glu  Glu Gln Gln Leu Glu  Glu Ser Gly Pro His  Asp Leu Thr
    1535                1540                1545

Glu Thr  Ser Tyr Leu Pro Arg  Gln Asp Leu Glu Gly  Thr Pro Tyr
    1550                1555                1560

Leu Glu  Ser Gly Ile Ser Leu  Phe Ser Asp Asp Pro  Glu Ser Asp
    1565                1570                1575

Pro Ser  Glu Asp Arg Ala Pro  Glu Ser Ala Arg Val  Gly Asn Ile
    1580                1585                1590
```

```
Pro Ser  Ser Thr Ser Ala Leu  Lys Val Pro Gln Leu  Lys Val Ala
    1595                 1600                 1605

Glu Ser  Ala Gln Ser Pro Ala  Ala Ala His Thr Thr  Asp Thr Ala
    1610                 1615                 1620

Gly Tyr  Asn Ala Met Glu Glu  Ser Val Ser Arg Glu  Lys Pro Glu
    1625                 1630                 1635

Leu Thr  Ala Ser Thr Glu Arg  Val Asn Lys Arg Met  Ser Met Val
    1640                 1645                 1650

Val Ser  Gly Leu Thr Pro Glu  Glu Phe Met Leu Val  Tyr Lys Phe
    1655                 1660                 1665

Ala Arg  Lys His His Ile Thr  Leu Thr Asn Leu Ile  Thr Glu Glu
    1670                 1675                 1680

Thr Thr  His Val Val Met Lys  Thr Asp Ala Glu Phe  Val Cys Glu
    1685                 1690                 1695

Arg Thr  Leu Lys Tyr Phe Leu  Gly Ile Ala Gly Gly  Lys Trp Val
    1700                 1705                 1710

Val Ser  Tyr Phe Trp Val Thr  Gln Ser Ile Lys Glu  Arg Lys Met
    1715                 1720                 1725

Leu Asn  Glu His Asp Phe Glu  Val Arg Gly Asp Val  Val Asn Gly
    1730                 1735                 1740

Arg Asn  His Gln Gly Pro Lys  Arg Ala Arg Glu Ser  Gln Asp Arg
    1745                 1750                 1755

Lys Ile  Phe Arg Gly Leu Glu  Ile Cys Cys Tyr Gly  Pro Phe Thr
    1760                 1765                 1770

Asn Met  Pro Thr Asp Gln Leu  Glu Trp Met Val Gln  Leu Cys Gly
    1775                 1780                 1785

Ala Ser  Val Val Lys Glu Leu  Ser Ser Phe Thr Leu  Gly Thr Gly
    1790                 1795                 1800

Val His  Pro Ile Val Val Val  Gln Pro Asp Ala Trp  Thr Glu Asp
    1805                 1810                 1815

Asn Gly  Phe His Ala Ile Gly  Gln Met Cys Glu Ala  Pro Val Val
    1820                 1825                 1830

Thr Arg  Glu Trp Val Leu Asp  Ser Val Ala Leu Tyr  Gln Cys Gln
    1835                 1840                 1845
```

```
Glu Leu  Asp Thr Tyr Leu Ile  Pro Gln Ile Pro His  Ser His Tyr
    1850                1855                1860


<210>  44
<211>  3418
<212>  PRT
<213>  Homo sapiens

<400>  44

Met Pro Ile Gly Ser Lys Glu Arg Pro Thr Phe Phe Glu Ile Phe Lys
1               5                   10                  15


Thr Arg Cys Asn Lys Ala Asp Leu Gly Pro Ile Ser Leu Asn Trp Phe
            20                  25                  30


Glu Glu Leu Ser Ser Glu Ala Pro Pro Tyr Asn Ser Glu Pro Ala Glu
        35                  40                  45


Glu Ser Glu His Lys Asn Asn Asn Tyr Glu Pro Asn Leu Phe Lys Thr
    50                  55                  60


Pro Gln Arg Lys Pro Ser Tyr Asn Gln Leu Ala Ser Thr Pro Ile Ile
65                  70                  75                  80


Phe Lys Glu Gln Gly Leu Thr Leu Pro Leu Tyr Gln Ser Pro Val Lys
                85                  90                  95


Glu Leu Asp Lys Phe Lys Leu Asp Leu Gly Arg Asn Val Pro Asn Ser
            100                 105                 110


Arg His Lys Ser Leu Arg Thr Val Lys Thr Lys Met Asp Gln Ala Asp
        115                 120                 125


Asp Val Ser Cys Pro Leu Leu Asn Ser Cys Leu Ser Glu Ser Pro Val
    130                 135                 140


Val Leu Gln Cys Thr His Val Thr Pro Gln Arg Asp Lys Ser Val Val
145                 150                 155                 160


Cys Gly Ser Leu Phe His Thr Pro Lys Phe Val Lys Gly Arg Gln Thr
                165                 170                 175


Pro Lys His Ile Ser Glu Ser Leu Gly Ala Glu Val Asp Pro Asp Met
            180                 185                 190


Ser Trp Ser Ser Ser Leu Ala Thr Pro Pro Thr Leu Ser Ser Thr Val
        195                 200                 205


Leu Ile Val Arg Asn Glu Glu Ala Ser Glu Thr Val Phe Pro His Asp
    210                 215                 220
```

```
Thr Thr Ala Asn Val Lys Ser Tyr Phe Ser Asn His Asp Glu Ser Leu
225                 230                 235                 240

Lys Lys Asn Asp Arg Phe Ile Ala Ser Val Thr Asp Ser Glu Asn Thr
                245                 250                 255

Asn Gln Arg Glu Ala Ala Ser His Gly Phe Gly Lys Thr Ser Gly Asn
            260                 265                 270

Ser Phe Lys Val Asn Ser Cys Lys Asp His Ile Gly Lys Ser Met Pro
        275                 280                 285

Asn Val Leu Glu Asp Glu Val Tyr Glu Thr Val Val Asp Thr Ser Glu
    290                 295                 300

Glu Asp Ser Phe Ser Leu Cys Phe Ser Lys Cys Arg Thr Lys Asn Leu
305                 310                 315                 320

Gln Lys Val Arg Thr Ser Lys Thr Arg Lys Lys Ile Phe His Glu Ala
                325                 330                 335

Asn Ala Asp Glu Cys Glu Lys Ser Lys Asn Gln Val Lys Glu Lys Tyr
            340                 345                 350

Ser Phe Val Ser Glu Val Glu Pro Asn Asp Thr Asp Pro Leu Asp Ser
        355                 360                 365

Asn Val Ala Asn Gln Lys Pro Phe Glu Ser Gly Ser Asp Lys Ile Ser
    370                 375                 380

Lys Glu Val Val Pro Ser Leu Ala Cys Glu Trp Ser Gln Leu Thr Leu
385                 390                 395                 400

Ser Gly Leu Asn Gly Ala Gln Met Glu Lys Ile Pro Leu Leu His Ile
                405                 410                 415

Ser Ser Cys Asp Gln Asn Ile Ser Glu Lys Asp Leu Leu Asp Thr Glu
            420                 425                 430

Asn Lys Arg Lys Lys Asp Phe Leu Thr Ser Glu Asn Ser Leu Pro Arg
        435                 440                 445

Ile Ser Ser Leu Pro Lys Ser Glu Lys Pro Leu Asn Glu Glu Thr Val
    450                 455                 460

Val Asn Lys Arg Asp Glu Glu Gln His Leu Glu Ser His Thr Asp Cys
465                 470                 475                 480

Ile Leu Ala Val Lys Gln Ala Ile Ser Gly Thr Ser Pro Val Ala Ser
                485                 490                 495
```

```
Ser Phe Gln Gly Ile Lys Lys Ser Ile Phe Arg Ile Arg Glu Ser Pro
            500                 505                 510

Lys Glu Thr Phe Asn Ala Ser Phe Ser Gly His Met Thr Asp Pro Asn
        515                 520                 525

Phe Lys Lys Glu Thr Glu Ala Ser Glu Ser Gly Leu Glu Ile His Thr
    530                 535                 540

Val Cys Ser Gln Lys Glu Asp Ser Leu Cys Pro Asn Leu Ile Asp Asn
545                 550                 555                 560

Gly Ser Trp Pro Ala Thr Thr Thr Gln Asn Ser Val Ala Leu Lys Asn
                565                 570                 575

Ala Gly Leu Ile Ser Thr Leu Lys Lys Lys Thr Asn Lys Phe Ile Tyr
            580                 585                 590

Ala Ile His Asp Glu Thr Ser Tyr Lys Gly Lys Lys Ile Pro Lys Asp
        595                 600                 605

Gln Lys Ser Glu Leu Ile Asn Cys Ser Ala Gln Phe Glu Ala Asn Ala
    610                 615                 620

Phe Glu Ala Pro Leu Thr Phe Ala Asn Ala Asp Ser Gly Leu Leu His
625                 630                 635                 640

Ser Ser Val Lys Arg Ser Cys Ser Gln Asn Asp Ser Glu Glu Pro Thr
                645                 650                 655

Leu Ser Leu Thr Ser Ser Phe Gly Thr Ile Leu Arg Lys Cys Ser Arg
            660                 665                 670

Asn Glu Thr Cys Ser Asn Asn Thr Val Ile Ser Gln Asp Leu Asp Tyr
        675                 680                 685

Lys Glu Ala Lys Cys Asn Lys Glu Lys Leu Gln Leu Phe Ile Thr Pro
    690                 695                 700

Glu Ala Asp Ser Leu Ser Cys Leu Gln Glu Gly Gln Cys Glu Asn Asp
705                 710                 715                 720

Pro Lys Ser Lys Lys Val Ser Asp Ile Lys Glu Glu Val Leu Ala Ala
                725                 730                 735

Ala Cys His Pro Val Gln His Ser Lys Val Glu Tyr Ser Asp Thr Asp
            740                 745                 750

Phe Gln Ser Gln Lys Ser Leu Leu Tyr Asp His Glu Asn Ala Ser Thr
        755                 760                 765
```

```
Leu Ile Leu Thr Pro Thr Ser Lys Asp Val Leu Ser Asn Leu Val Met
    770                 775                 780

Ile Ser Arg Gly Lys Glu Ser Tyr Lys Met Ser Asp Lys Leu Lys Gly
785                 790                 795                 800

Asn Asn Tyr Glu Ser Asp Val Glu Leu Thr Lys Asn Ile Pro Met Glu
                805                 810                 815

Lys Asn Gln Asp Val Cys Ala Leu Asn Glu Asn Tyr Lys Asn Val Glu
            820                 825                 830

Leu Leu Pro Pro Glu Lys Tyr Met Arg Val Ala Ser Pro Ser Arg Lys
        835                 840                 845

Val Gln Phe Asn Gln Asn Thr Asn Leu Arg Val Ile Gln Lys Asn Gln
    850                 855                 860

Glu Glu Thr Thr Ser Ile Ser Lys Ile Thr Val Asn Pro Asp Ser Glu
865                 870                 875                 880

Glu Leu Phe Ser Asp Asn Glu Asn Asn Phe Val Phe Gln Val Ala Asn
                885                 890                 895

Glu Arg Asn Asn Leu Ala Leu Gly Asn Thr Lys Glu Leu His Glu Thr
            900                 905                 910

Asp Leu Thr Cys Val Asn Glu Pro Ile Phe Lys Asn Ser Thr Met Val
        915                 920                 925

Leu Tyr Gly Asp Thr Gly Asp Lys Gln Ala Thr Gln Val Ser Ile Lys
    930                 935                 940

Lys Asp Leu Val Tyr Val Leu Ala Glu Glu Asn Lys Asn Ser Val Lys
945                 950                 955                 960

Gln His Ile Lys Met Thr Leu Gly Gln Asp Leu Lys Ser Asp Ile Ser
                965                 970                 975

Leu Asn Ile Asp Lys Ile Pro Glu Lys Asn Asn Asp Tyr Met Asn Lys
            980                 985                 990

Trp Ala Gly Leu Leu Gly Pro Ile  Ser Asn His Ser Phe  Gly Gly Ser
        995                 1000                1005

Phe Arg  Thr Ala Ser Asn Lys  Glu Ile Lys Leu Ser  Glu His Asn
    1010                1015                1020

Ile Lys  Lys Ser Lys Met Phe  Phe Lys Asp Ile Glu  Glu Gln Tyr
    1025                1030                1035
```

```
Pro Thr  Ser Leu Ala Cys Val  Glu Ile Val Asn Thr  Leu Ala Leu
    1040                1045                1050

Asp Asn  Gln Lys Lys Leu Ser  Lys Pro Gln Ser Ile  Asn Thr Val
    1055                1060                1065

Ser Ala  His Leu Gln Ser Ser  Val Val Val Ser Asp  Cys Lys Asn
    1070                1075                1080

Ser His  Ile Thr Pro Gln Met  Leu Phe Ser Lys Gln  Asp Phe Asn
    1085                1090                1095

Ser Asn  His Asn Leu Thr Pro  Ser Gln Lys Ala Glu  Ile Thr Glu
    1100                1105                1110

Leu Ser  Thr Ile Leu Glu Glu  Ser Gly Ser Gln Phe  Glu Phe Thr
    1115                1120                1125

Gln Phe  Arg Lys Pro Ser Tyr  Ile Leu Gln Lys Ser  Thr Phe Glu
    1130                1135                1140

Val Pro  Glu Asn Gln Met Thr  Ile Leu Lys Thr Thr  Ser Glu Glu
    1145                1150                1155

Cys Arg  Asp Ala Asp Leu His  Val Ile Met Asn Ala  Pro Ser Ile
    1160                1165                1170

Gly Gln  Val Asp Ser Ser Lys  Gln Phe Glu Gly Thr  Val Glu Ile
    1175                1180                1185

Lys Arg  Lys Phe Ala Gly Leu  Leu Lys Asn Asp Cys  Asn Lys Ser
    1190                1195                1200

Ala Ser  Gly Tyr Leu Thr Asp  Glu Asn Glu Val Gly  Phe Arg Gly
    1205                1210                1215

Phe Tyr  Ser Ala His Gly Thr  Lys Leu Asn Val Ser  Thr Glu Ala
    1220                1225                1230

Leu Gln  Lys Ala Val Lys Leu  Phe Ser Asp Ile Glu  Asn Ile Ser
    1235                1240                1245

Glu Glu  Thr Ser Ala Glu Val  His Pro Ile Ser Leu  Ser Ser Ser
    1250                1255                1260

Lys Cys  His Asp Ser Val Val  Ser Met Phe Lys Ile  Glu Asn His
    1265                1270                1275

Asn Asp  Lys Thr Val Ser Glu  Lys Asn Asn Lys Cys  Gln Leu Ile
    1280                1285                1290
```

```
Leu Gln  Asn Asn Ile Glu Met  Thr Thr Gly Thr Phe  Val Glu Glu
    1295                1300                1305

Ile Thr  Glu Asn Tyr Lys Arg  Asn Thr Glu Asn Glu  Asp Asn Lys
    1310                1315                1320

Tyr Thr  Ala Ala Ser Arg Asn  Ser His Asn Leu Glu  Phe Asp Gly
    1325                1330                1335

Ser Asp  Ser Ser Lys Asn Asp  Thr Val Cys Ile His  Lys Asp Glu
    1340                1345                1350

Thr Asp  Leu Leu Phe Thr Asp  Gln His Asn Ile Cys  Leu Lys Leu
    1355                1360                1365

Ser Gly  Gln Phe Met Lys Glu  Gly Asn Thr Gln Ile  Lys Glu Asp
    1370                1375                1380

Leu Ser  Asp Leu Thr Phe Leu  Glu Val Ala Lys Ala  Gln Glu Ala
    1385                1390                1395

Cys His  Gly Asn Thr Ser Asn  Lys Glu Gln Leu Thr  Ala Thr Lys
    1400                1405                1410

Thr Glu  Gln Asn Ile Lys Asp  Phe Glu Thr Ser Asp  Thr Phe Phe
    1415                1420                1425

Gln Thr  Ala Ser Gly Lys Asn  Ile Ser Val Ala Lys  Glu Ser Phe
    1430                1435                1440

Asn Lys  Ile Val Asn Phe Phe  Asp Gln Lys Pro Glu  Glu Leu His
    1445                1450                1455

Asn Phe  Ser Leu Asn Ser Glu  Leu His Ser Asp Ile  Arg Lys Asn
    1460                1465                1470

Lys Met  Asp Ile Leu Ser Tyr  Glu Glu Thr Asp Ile  Val Lys His
    1475                1480                1485

Lys Ile  Leu Lys Glu Ser Val  Pro Val Gly Thr Gly  Asn Gln Leu
    1490                1495                1500

Val Thr  Phe Gln Gly Gln Pro  Glu Arg Asp Glu Lys  Ile Lys Glu
    1505                1510                1515

Pro Thr  Leu Leu Gly Phe His  Thr Ala Ser Gly Lys  Lys Val Lys
    1520                1525                1530

Ile Ala  Lys Glu Ser Leu Asp  Lys Val Lys Asn Leu  Phe Asp Glu
    1535                1540                1545
```

```
Lys Glu  Gln Gly Thr Ser Glu  Ile Thr Ser Phe Ser  His Gln Trp
    1550                1555                1560

Ala Lys  Thr Leu Lys Tyr Arg  Glu Ala Cys Lys Asp  Leu Glu Leu
    1565                1570                1575

Ala Cys  Glu Thr Ile Glu Ile  Thr Ala Ala Pro Lys  Cys Lys Glu
    1580                1585                1590

Met Gln  Asn Ser Leu Asn Asn  Asp Lys Asn Leu Val  Ser Ile Glu
    1595                1600                1605

Thr Val  Val Pro Pro Lys Leu  Leu Ser Asp Asn Leu  Cys Arg Gln
    1610                1615                1620

Thr Glu  Asn Leu Lys Thr Ser  Lys Ser Ile Phe Leu  Lys Val Lys
    1625                1630                1635

Val His  Glu Asn Val Glu Lys  Glu Thr Ala Lys Ser  Pro Ala Thr
    1640                1645                1650

Cys Tyr  Thr Asn Gln Ser Pro  Tyr Ser Val Ile Glu  Asn Ser Ala
    1655                1660                1665

Leu Ala  Phe Tyr Thr Ser Cys  Ser Arg Lys Thr Ser  Val Ser Gln
    1670                1675                1680

Thr Ser  Leu Leu Glu Ala Lys  Lys Trp Leu Arg Glu  Gly Ile Phe
    1685                1690                1695

Asp Gly  Gln Pro Glu Arg Ile  Asn Thr Ala Asp Tyr  Val Gly Asn
    1700                1705                1710

Tyr Leu  Tyr Glu Asn Asn Ser  Asn Ser Thr Ile Ala  Glu Asn Asp
    1715                1720                1725

Lys Asn  His Leu Ser Glu Lys  Gln Asp Thr Tyr Leu  Ser Asn Ser
    1730                1735                1740

Ser Met  Ser Asn Ser Tyr Ser  Tyr His Ser Asp Glu  Val Tyr Asn
    1745                1750                1755

Asp Ser  Gly Tyr Leu Ser Lys  Asn Lys Leu Asp Ser  Gly Ile Glu
    1760                1765                1770

Pro Val  Leu Lys Asn Val Glu  Asp Gln Lys Asn Thr  Ser Phe Ser
    1775                1780                1785

Lys Val  Ile Ser Asn Val Lys  Asp Ala Asn Ala Tyr  Pro Gln Thr
    1790                1795                1800
```

```
Val Asn  Glu Asp Ile Cys Val  Glu Glu Leu Val Thr  Ser Ser Ser
    1805                 1810                 1815

Pro Cys  Lys Asn Lys Asn Ala  Ala Ile Lys Leu Ser  Ile Ser Asn
    1820                 1825                 1830

Ser Asn  Asn Phe Glu Val Gly  Pro Pro Ala Phe Arg  Ile Ala Ser
    1835                 1840                 1845

Gly Lys  Ile Val Cys Val Ser  His Glu Thr Ile Lys  Lys Val Lys
    1850                 1855                 1860

Asp Ile  Phe Thr Asp Ser Phe  Ser Lys Val Ile Lys  Glu Asn Asn
    1865                 1870                 1875

Glu Asn  Lys Ser Lys Ile Cys  Gln Thr Lys Ile Met  Ala Gly Cys
    1880                 1885                 1890

Tyr Glu  Ala Leu Asp Asp Ser  Glu Asp Ile Leu His  Asn Ser Leu
    1895                 1900                 1905

Asp Asn  Asp Glu Cys Ser Thr  His Ser His Lys Val  Phe Ala Asp
    1910                 1915                 1920

Ile Gln  Ser Glu Glu Ile Leu  Gln His Asn Gln Asn  Met Ser Gly
    1925                 1930                 1935

Leu Glu  Lys Val Ser Lys Ile  Ser Pro Cys Asp Val  Ser Leu Glu
    1940                 1945                 1950

Thr Ser  Asp Ile Cys Lys Cys  Ser Ile Gly Lys Leu  His Lys Ser
    1955                 1960                 1965

Val Ser  Ser Ala Asn Thr Cys  Gly Ile Phe Ser Thr  Ala Ser Gly
    1970                 1975                 1980

Lys Ser  Val Gln Val Ser Asp  Ala Ser Leu Gln Asn  Ala Arg Gln
    1985                 1990                 1995

Val Phe  Ser Glu Ile Glu Asp  Ser Thr Lys Gln Val  Phe Ser Lys
    2000                 2005                 2010

Val Leu  Phe Lys Ser Asn Glu  His Ser Asp Gln Leu  Thr Arg Glu
    2015                 2020                 2025

Glu Asn  Thr Ala Ile Arg Thr  Pro Glu His Leu Ile  Ser Gln Lys
    2030                 2035                 2040

Gly Phe  Ser Tyr Asn Val Val  Asn Ser Ser Ala Phe  Ser Gly Phe
    2045                 2050                 2055
```

```
Ser Thr  Ala Ser Gly Lys Gln  Val Ser Ile Leu Glu  Ser Ser Leu
    2060                 2065                 2070

His Lys  Val Lys Gly Val Leu  Glu Glu Phe Asp Leu  Ile Arg Thr
    2075                 2080                 2085

Glu His  Ser Leu His Tyr Ser  Pro Thr Ser Arg Gln  Asn Val Ser
    2090                 2095                 2100

Lys Ile  Leu Pro Arg Val Asp  Lys Arg Asn Pro Glu  His Cys Val
    2105                 2110                 2115

Asn Ser  Glu Met Glu Lys Thr  Cys Ser Lys Glu Phe  Lys Leu Ser
    2120                 2125                 2130

Asn Asn  Leu Asn Val Glu Gly  Gly Ser Ser Glu Asn  Asn His Ser
    2135                 2140                 2145

Ile Lys  Val Ser Pro Tyr Leu  Ser Gln Phe Gln Gln  Asp Lys Gln
    2150                 2155                 2160

Gln Leu  Val Leu Gly Thr Lys  Val Ser Leu Val Glu  Asn Ile His
    2165                 2170                 2175

Val Leu  Gly Lys Glu Gln Ala  Ser Pro Lys Asn Val  Lys Met Glu
    2180                 2185                 2190

Ile Gly  Lys Thr Glu Thr Phe  Ser Asp Val Pro Val  Lys Thr Asn
    2195                 2200                 2205

Ile Glu  Val Cys Ser Thr Tyr  Ser Lys Asp Ser Glu  Asn Tyr Phe
    2210                 2215                 2220

Glu Thr  Glu Ala Val Glu Ile  Ala Lys Ala Phe Met  Glu Asp Asp
    2225                 2230                 2235

Glu Leu  Thr Asp Ser Lys Leu  Pro Ser His Ala Thr  His Ser Leu
    2240                 2245                 2250

Phe Thr  Cys Pro Glu Asn Glu  Glu Met Val Leu Ser  Asn Ser Arg
    2255                 2260                 2265

Ile Gly  Lys Arg Arg Gly Glu  Pro Leu Ile Leu Val  Gly Glu Pro
    2270                 2275                 2280

Ser Ile  Lys Arg Asn Leu Leu  Asn Glu Phe Asp Arg  Ile Ile Glu
    2285                 2290                 2295

Asn Gln  Glu Lys Ser Leu Lys  Ala Ser Lys Ser Thr  Pro Asp Gly
    2300                 2305                 2310
```

```
Thr Ile  Lys Asp Arg Arg Leu  Phe Met His His Val  Ser Leu Glu
    2315                 2320                 2325

Pro Ile  Thr Cys Val Pro Phe  Arg Thr Thr Lys Glu  Arg Gln Glu
    2330                 2335                 2340

Ile Gln  Asn Pro Asn Phe Thr  Ala Pro Gly Gln Glu  Phe Leu Ser
    2345                 2350                 2355

Lys Ser  His Leu Tyr Glu His  Leu Thr Leu Glu Lys  Ser Ser Ser
    2360                 2365                 2370

Asn Leu  Ala Val Ser Gly His  Pro Phe Tyr Gln Val  Ser Ala Thr
    2375                 2380                 2385

Arg Asn  Glu Lys Met Arg His  Leu Ile Thr Thr Gly  Arg Pro Thr
    2390                 2395                 2400

Lys Val  Phe Val Pro Pro Phe  Lys Thr Lys Ser His  Phe His Arg
    2405                 2410                 2415

Val Glu  Gln Cys Val Arg Asn  Ile Asn Leu Glu Glu  Asn Arg Gln
    2420                 2425                 2430

Lys Gln  Asn Ile Asp Gly His  Gly Ser Asp Asp Ser  Lys Asn Lys
    2435                 2440                 2445

Ile Asn  Asp Asn Glu Ile His  Gln Phe Asn Lys Asn  Asn Ser Asn
    2450                 2455                 2460

Gln Ala  Ala Ala Val Thr Phe  Thr Lys Cys Glu Glu  Glu Pro Leu
    2465                 2470                 2475

Asp Leu  Ile Thr Ser Leu Gln  Asn Ala Arg Asp Ile  Gln Asp Met
    2480                 2485                 2490

Arg Ile  Lys Lys Lys Gln Arg  Gln Arg Val Phe Pro  Gln Pro Gly
    2495                 2500                 2505

Ser Leu  Tyr Leu Ala Lys Thr  Ser Thr Leu Pro Arg  Ile Ser Leu
    2510                 2515                 2520

Lys Ala  Ala Val Gly Gly Gln  Val Pro Ser Ala Cys  Ser His Lys
    2525                 2530                 2535

Gln Leu  Tyr Thr Tyr Gly Val  Ser Lys His Cys Ile  Lys Ile Asn
    2540                 2545                 2550

Ser Lys  Asn Ala Glu Ser Phe  Gln Phe His Thr Glu  Asp Tyr Phe
    2555                 2560                 2565
```

```
Gly Lys  Glu Ser Leu Trp Thr  Gly Lys Gly Ile Gln  Leu Ala Asp
    2570                 2575                 2580

Gly Gly  Trp Leu Ile Pro Ser  Asn Asp Gly Lys Ala  Gly Lys Glu
    2585                 2590                 2595

Glu Phe  Tyr Arg Ala Leu Cys  Asp Thr Pro Gly Val  Asp Pro Lys
    2600                 2605                 2610

Leu Ile  Ser Arg Ile Trp Val  Tyr Asn His Tyr Arg  Trp Ile Ile
    2615                 2620                 2625

Trp Lys  Leu Ala Ala Met Glu  Cys Ala Phe Pro Lys  Glu Phe Ala
    2630                 2635                 2640

Asn Arg  Cys Leu Ser Pro Glu  Arg Val Leu Leu Gln  Leu Lys Tyr
    2645                 2650                 2655

Arg Tyr  Asp Thr Glu Ile Asp  Arg Ser Arg Arg Ser  Ala Ile Lys
    2660                 2665                 2670

Lys Ile  Met Glu Arg Asp Asp  Thr Ala Ala Lys Thr  Leu Val Leu
    2675                 2680                 2685

Cys Val  Ser Asp Ile Ile Ser  Leu Ser Ala Asn Ile  Ser Glu Thr
    2690                 2695                 2700

Ser Ser  Asn Lys Thr Ser Ser  Ala Asp Thr Gln Lys  Val Ala Ile
    2705                 2710                 2715

Ile Glu  Leu Thr Asp Gly Trp  Tyr Ala Val Lys Ala  Gln Leu Asp
    2720                 2725                 2730

Pro Pro  Leu Leu Ala Val Leu  Lys Asn Gly Arg Leu  Thr Val Gly
    2735                 2740                 2745

Gln Lys  Ile Ile Leu His Gly  Ala Glu Leu Val Gly  Ser Pro Asp
    2750                 2755                 2760

Ala Cys  Thr Pro Leu Glu Ala  Pro Glu Ser Leu Met  Leu Lys Ile
    2765                 2770                 2775

Ser Ala  Asn Ser Thr Arg Pro  Ala Arg Trp Tyr Thr  Lys Leu Gly
    2780                 2785                 2790

Phe Phe  Pro Asp Pro Arg Pro  Phe Pro Leu Pro Leu  Ser Ser Leu
    2795                 2800                 2805

Phe Ser  Asp Gly Gly Asn Val  Gly Cys Val Asp Val  Ile Ile Gln
    2810                 2815                 2820
```

```
Arg Ala  Tyr Pro Ile Gln Trp  Met Glu Lys Thr Ser  Ser Gly Leu
    2825                 2830                 2835

Tyr Ile  Phe Arg Asn Glu Arg  Glu Glu Glu Lys Glu  Ala Ala Lys
    2840                 2845                 2850

Tyr Val  Glu Ala Gln Gln Lys  Arg Leu Glu Ala Leu  Phe Thr Lys
    2855                 2860                 2865

Ile Gln  Glu Glu Phe Glu Glu  His Glu Glu Asn Thr  Thr Lys Pro
    2870                 2875                 2880

Tyr Leu  Pro Ser Arg Ala Leu  Thr Arg Gln Gln Val  Arg Ala Leu
    2885                 2890                 2895

Gln Asp  Gly Ala Glu Leu Tyr  Glu Ala Val Lys Asn  Ala Ala Asp
    2900                 2905                 2910

Pro Ala  Tyr Leu Glu Gly Tyr  Phe Ser Glu Glu Gln  Leu Arg Ala
    2915                 2920                 2925

Leu Asn  Asn His Arg Gln Met  Leu Asn Asp Lys Lys  Gln Ala Gln
    2930                 2935                 2940

Ile Gln  Leu Glu Ile Arg Lys  Ala Met Glu Ser Ala  Glu Gln Lys
    2945                 2950                 2955

Glu Gln  Gly Leu Ser Arg Asp  Val Thr Thr Val Trp  Lys Leu Arg
    2960                 2965                 2970

Ile Val  Ser Tyr Ser Lys Lys  Glu Lys Asp Ser Val  Ile Leu Ser
    2975                 2980                 2985

Ile Trp  Arg Pro Ser Ser Asp  Leu Tyr Ser Leu Leu  Thr Glu Gly
    2990                 2995                 3000

Lys Arg  Tyr Arg Ile Tyr His  Leu Ala Thr Ser Lys  Ser Lys Ser
    3005                 3010                 3015

Lys Ser  Glu Arg Ala Asn Ile  Gln Leu Ala Ala Thr  Lys Lys Thr
    3020                 3025                 3030

Gln Tyr  Gln Gln Leu Pro Val  Ser Asp Glu Ile Leu  Phe Gln Ile
    3035                 3040                 3045

Tyr Gln  Pro Arg Glu Pro Leu  His Phe Ser Lys Phe  Leu Asp Pro
    3050                 3055                 3060

Asp Phe  Gln Pro Ser Cys Ser  Glu Val Asp Leu Ile  Gly Phe Val
    3065                 3070                 3075
```

```
Val Ser  Val Val Lys Lys Thr  Gly Leu Ala Pro Phe  Val Tyr Leu
    3080                 3085                 3090

Ser Asp  Glu Cys Tyr Asn Leu  Leu Ala Ile Lys Phe  Trp Ile Asp
    3095                 3100                 3105

Leu Asn  Glu Asp Ile Ile Lys  Pro His Met Leu Ile  Ala Ala Ser
    3110                 3115                 3120

Asn Leu  Gln Trp Arg Pro Glu  Ser Lys Ser Gly Leu  Leu Thr Leu
    3125                 3130                 3135

Phe Ala  Gly Asp Phe Ser Val  Phe Ser Ala Ser Pro  Lys Glu Gly
    3140                 3145                 3150

His Phe  Gln Glu Thr Phe Asn  Lys Met Lys Asn Thr  Val Glu Asn
    3155                 3160                 3165

Ile Asp  Ile Leu Cys Asn Glu  Ala Glu Asn Lys Leu  Met His Ile
    3170                 3175                 3180

Leu His  Ala Asn Asp Pro Lys  Trp Ser Thr Pro Thr  Lys Asp Cys
    3185                 3190                 3195

Thr Ser  Gly Pro Tyr Thr Ala  Gln Ile Ile Pro Gly  Thr Gly Asn
    3200                 3205                 3210

Lys Leu  Leu Met Ser Ser Pro  Asn Cys Glu Ile Tyr  Tyr Gln Ser
    3215                 3220                 3225

Pro Leu  Ser Leu Cys Met Ala  Lys Arg Lys Ser Val  Ser Thr Pro
    3230                 3235                 3240

Val Ser  Ala Gln Met Thr Ser  Lys Ser Cys Lys Gly  Glu Lys Glu
    3245                 3250                 3255

Ile Asp  Asp Gln Lys Asn Cys  Lys Lys Arg Arg Ala  Leu Asp Phe
    3260                 3265                 3270

Leu Ser  Arg Leu Pro Leu Pro  Pro Pro Val Ser Pro  Ile Cys Thr
    3275                 3280                 3285

Phe Val  Ser Pro Ala Ala Gln  Lys Ala Phe Gln Pro  Pro Arg Ser
    3290                 3295                 3300

Cys Gly  Thr Lys Tyr Glu Thr  Pro Ile Lys Lys Lys  Glu Leu Asn
    3305                 3310                 3315

Ser Pro  Gln Met Thr Pro Phe  Lys Lys Phe Asn Glu  Ile Ser Leu
    3320                 3325                 3330
```

Leu Glu Ser Asn Ser Ile Ala Asp Glu Glu Leu Ala Leu Ile Asn
3335 3340 3345

Thr Gln Ala Leu Leu Ser Gly Ser Thr Gly Glu Lys Gln Phe Ile
3350 3355 3360

Ser Val Ser Glu Ser Thr Arg Thr Ala Pro Thr Ser Ser Glu Asp
3365 3370 3375

Tyr Leu Arg Leu Lys Arg Arg Cys Thr Thr Ser Leu Ile Lys Glu
3380 3385 3390

Gln Glu Ser Ser Gln Ala Ser Thr Glu Glu Cys Glu Lys Asn Lys
3395 3400 3405

Gln Asp Thr Ile Thr Thr Lys Lys Tyr Ile
3410 3415

<210> 45
<211> 393
<212> PRT
<213> Homo sapiens

<400> 45

Met Glu Glu Pro Gln Ser Asp Pro Ser Val Glu Pro Pro Leu Ser Gln
1 5 10 15

Glu Thr Phe Ser Asp Leu Trp Lys Leu Leu Pro Glu Asn Asn Val Leu
20 25 30

Ser Pro Leu Pro Ser Gln Ala Met Asp Asp Leu Met Leu Ser Pro Asp
35 40 45

Asp Ile Glu Gln Trp Phe Thr Glu Asp Pro Gly Pro Asp Glu Ala Pro
50 55 60

Arg Met Pro Glu Ala Ala Pro Pro Val Ala Pro Ala Pro Ala Ala Pro
65 70 75 80

Thr Pro Ala Ala Pro Ala Pro Ala Pro Ser Trp Pro Leu Ser Ser Ser
85 90 95

Val Pro Ser Gln Lys Thr Tyr Gln Gly Ser Tyr Gly Phe Arg Leu Gly
100 105 110

Phe Leu His Ser Gly Thr Ala Lys Ser Val Thr Cys Thr Tyr Ser Pro
115 120 125

Ala Leu Asn Lys Met Phe Cys Gln Leu Ala Lys Thr Cys Pro Val Gln
130 135 140

Leu Trp Val Asp Ser Thr Pro Pro Pro Gly Thr Arg Val Arg Ala Met

145 150 155 160

Ala Ile Tyr Lys Gln Ser Gln His Met Thr Glu Val Val Arg Arg Cys
165 170 175

Pro His His Glu Arg Cys Ser Asp Ser Asp Gly Leu Ala Pro Pro Gln
180 185 190

His Leu Ile Arg Val Glu Gly Asn Leu Arg Val Glu Tyr Leu Asp Asp
195 200 205

Arg Asn Thr Phe Arg His Ser Val Val Val Pro Tyr Glu Pro Pro Glu
210 215 220

Val Gly Ser Asp Cys Thr Thr Ile His Tyr Asn Tyr Met Cys Asn Ser
225 230 235 240

Ser Cys Met Gly Gly Met Asn Arg Arg Pro Ile Leu Thr Ile Ile Thr
245 250 255

Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asn Ser Phe Glu Val
260 265 270

Arg Val Cys Ala Cys Pro Gly Arg Asp Arg Arg Thr Glu Glu Glu Asn
275 280 285

Leu Arg Lys Lys Gly Glu Pro His His Glu Leu Pro Pro Gly Ser Thr
290 295 300

Lys Arg Ala Leu Pro Asn Asn Thr Ser Ser Ser Pro Gln Pro Lys Lys
305 310 315 320

Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Gln Ile Arg Gly Arg Glu
325 330 335

Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp
340 345 350

Ala Gln Ala Gly Lys Glu Pro Gly Gly Ser Arg Ala His Ser Ser His
355 360 365

Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met
370 375 380

Phe Lys Thr Glu Gly Pro Asp Ser Asp
385 390

<210> 46
<211> 770
<212> PRT
<213> Homo sapiens

<400> 46

```
Met Leu Pro Gly Leu Ala Leu Leu Leu Leu Ala Ala Trp Thr Ala Arg
1               5                  10                  15

Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro
            20                  25                  30

Gln Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln
        35                  40                  45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
    50                  55                  60

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu
65                  70                  75                  80

Gln Ile Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr Ile Gln Asn
                85                  90                  95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
            100                 105                 110

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu
        115                 120                 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys
    130                 135                 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu
145                 150                 155                 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly Ile
                165                 170                 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
            180                 185                 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val
        195                 200                 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
    210                 215                 220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu
225                 230                 235                 240

Glu Ala Asp Asp Asp Glu Asp Asp Glu Asp Gly Asp Glu Val Glu Glu
                245                 250                 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile
            260                 265                 270
```

```
Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg
        275                 280                 285

Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile
    290                 295                 300

Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe
305                 310                 315                 320

Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr
                325                 330                 335

Cys Met Ala Val Cys Gly Ser Ala Met Ser Gln Ser Leu Leu Lys Thr
            340                 345                 350

Thr Gln Glu Pro Leu Ala Arg Asp Pro Val Lys Leu Pro Thr Thr Ala
        355                 360                 365

Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp
    370                 375                 380

Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala
385                 390                 395                 400

Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala
                405                 410                 415

Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile
            420                 425                 430

Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn
        435                 440                 445

Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met
    450                 455                 460

Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu
465                 470                 475                 480

Gln Ala Val Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys
                485                 490                 495

Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe
            500                 505                 510

Glu His Val Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser
        515                 520                 525

Gln Val Met Thr His Leu Arg Val Ile Tyr Glu Arg Met Asn Gln Ser
    530                 535                 540
```

```
Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp
545                 550                 555                 560

Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Asp Val
                565                 570                 575

Leu Ala Asn Met Ile Ser Glu Pro Arg Ile Ser Tyr Gly Asn Asp Ala
            580                 585                 590

Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro
        595                 600                 605

Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe
    610                 615                 620

Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val
625                 630                 635                 640

Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser
                645                 650                 655

Gly Leu Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Lys Met Asp
            660                 665                 670

Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu
        675                 680                 685

Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly
    690                 695                 700

Leu Met Val Gly Gly Val Val Ile Ala Thr Val Ile Val Ile Thr Leu
705                 710                 715                 720

Val Met Leu Lys Lys Lys Gln Tyr Thr Ser Ile His His Gly Val Val
                725                 730                 735

Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser Lys Met
            740                 745                 750

Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys Phe Phe Glu Gln Met
        755                 760                 765

Gln Asn
    770
```

<210> 47
<211> 3144
<212> PRT
<213> Homo sapiens

<400> 47

```
Met Ala Thr Leu Glu Lys Leu Met Lys Ala Phe Glu Ser Leu Lys Ser
1               5                  10                  15

Phe Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln
            20                  25                  30

Gln Gln Gln Gln Gln Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Pro
        35                  40                  45

Pro Pro Pro Gln Leu Pro Gln Pro Pro Pro Gln Ala Gln Pro Leu Leu
    50                  55                  60

Pro Gln Pro Gln Pro Pro Pro Pro Pro Pro Pro Pro Pro Pro Gly Pro
65                  70                  75                  80

Ala Val Ala Glu Glu Pro Leu His Arg Pro Lys Lys Glu Leu Ser Ala
                85                  90                  95

Thr Lys Lys Asp Arg Val Asn His Cys Leu Thr Ile Cys Glu Asn Ile
            100                 105                 110

Val Ala Gln Ser Val Arg Asn Ser Pro Glu Phe Gln Lys Leu Leu Gly
        115                 120                 125

Ile Ala Met Glu Leu Phe Leu Leu Cys Ser Asp Asp Ala Glu Ser Asp
    130                 135                 140

Val Arg Met Val Ala Asp Glu Cys Leu Asn Lys Val Ile Lys Ala Leu
145                 150                 155                 160

Met Asp Ser Asn Leu Pro Arg Leu Gln Leu Glu Leu Tyr Lys Glu Ile
                165                 170                 175

Lys Lys Asn Gly Ala Pro Arg Ser Leu Arg Ala Ala Leu Trp Arg Phe
            180                 185                 190

Ala Glu Leu Ala His Leu Val Arg Pro Gln Lys Cys Arg Pro Tyr Leu
        195                 200                 205

Val Asn Leu Leu Pro Cys Leu Thr Arg Thr Ser Lys Arg Pro Glu Glu
    210                 215                 220

Ser Val Gln Glu Thr Leu Ala Ala Ala Val Pro Lys Ile Met Ala Ser
225                 230                 235                 240

Phe Gly Asn Phe Ala Asn Asp Asn Glu Ile Lys Val Leu Leu Lys Ala
                245                 250                 255

Phe Ile Ala Asn Leu Lys Ser Ser Ser Pro Thr Ile Arg Arg Thr Ala
            260                 265                 270
```

```
Ala Gly Ser Ala Val Ser Ile Cys Gln His Ser Arg Arg Thr Gln Tyr
        275                 280                 285

Phe Tyr Ser Trp Leu Leu Asn Val Leu Leu Gly Leu Leu Val Pro Val
    290                 295                 300

Glu Asp Glu His Ser Thr Leu Leu Ile Leu Gly Val Leu Leu Thr Leu
305                 310                 315                 320

Arg Tyr Leu Val Pro Leu Leu Gln Gln Gln Val Lys Asp Thr Ser Leu
                325                 330                 335

Lys Gly Ser Phe Gly Val Thr Arg Lys Glu Met Glu Val Ser Pro Ser
            340                 345                 350

Ala Glu Gln Leu Val Gln Val Tyr Glu Leu Thr Leu His His Thr Gln
        355                 360                 365

His Gln Asp His Asn Val Val Thr Gly Ala Leu Glu Leu Leu Gln Gln
    370                 375                 380

Leu Phe Arg Thr Pro Pro Pro Glu Leu Leu Gln Thr Leu Thr Ala Val
385                 390                 395                 400

Gly Gly Ile Gly Gln Leu Thr Ala Ala Lys Glu Glu Ser Gly Gly Arg
                405                 410                 415

Ser Arg Ser Gly Ser Ile Val Glu Leu Ile Ala Gly Gly Gly Ser Ser
            420                 425                 430

Cys Ser Pro Val Leu Ser Arg Lys Gln Lys Gly Lys Val Leu Leu Gly
        435                 440                 445

Glu Glu Glu Ala Leu Glu Asp Asp Ser Glu Ser Arg Ser Asp Val Ser
    450                 455                 460

Ser Ser Ala Leu Thr Ala Ser Val Lys Asp Glu Ile Ser Gly Glu Leu
465                 470                 475                 480

Ala Ala Ser Ser Gly Val Ser Thr Pro Gly Ser Ala Gly His Asp Ile
                485                 490                 495

Ile Thr Glu Gln Pro Arg Ser Gln His Thr Leu Gln Ala Asp Ser Val
            500                 505                 510

Asp Leu Ala Ser Cys Asp Leu Thr Ser Ser Ala Thr Asp Gly Asp Glu
        515                 520                 525

Glu Asp Ile Leu Ser His Ser Ser Ser Gln Val Ser Ala Val Pro Ser
    530                 535                 540
```

```
Asp Pro Ala Met Asp Leu Asn Asp Gly Thr Gln Ala Ser Ser Pro Ile
545                 550                 555                 560

Ser Asp Ser Ser Gln Thr Thr Thr Glu Gly Pro Asp Ser Ala Val Thr
                565                 570                 575

Pro Ser Asp Ser Ser Glu Ile Val Leu Asp Gly Thr Asp Asn Gln Tyr
            580                 585                 590

Leu Gly Leu Gln Ile Gly Gln Pro Gln Asp Glu Asp Glu Glu Ala Thr
        595                 600                 605

Gly Ile Leu Pro Asp Glu Ala Ser Glu Ala Phe Arg Asn Ser Ser Met
    610                 615                 620

Ala Leu Gln Gln Ala His Leu Leu Lys Asn Met Ser His Cys Arg Gln
625                 630                 635                 640

Pro Ser Asp Ser Ser Val Asp Lys Phe Val Leu Arg Asp Glu Ala Thr
                645                 650                 655

Glu Pro Gly Asp Gln Glu Asn Lys Pro Cys Arg Ile Lys Gly Asp Ile
            660                 665                 670

Gly Gln Ser Thr Asp Asp Asp Ser Ala Pro Leu Val His Cys Val Arg
        675                 680                 685

Leu Leu Ser Ala Ser Phe Leu Leu Thr Gly Gly Lys Asn Val Leu Val
    690                 695                 700

Pro Asp Arg Asp Val Arg Val Ser Val Lys Ala Leu Ala Leu Ser Cys
705                 710                 715                 720

Val Gly Ala Ala Val Ala Leu His Pro Glu Ser Phe Phe Ser Lys Leu
                725                 730                 735

Tyr Lys Val Pro Leu Asp Thr Thr Glu Tyr Pro Glu Glu Gln Tyr Val
            740                 745                 750

Ser Asp Ile Leu Asn Tyr Ile Asp His Gly Asp Pro Gln Val Arg Gly
        755                 760                 765

Ala Thr Ala Ile Leu Cys Gly Thr Leu Ile Cys Ser Ile Leu Ser Arg
    770                 775                 780

Ser Arg Phe His Val Gly Asp Trp Met Gly Thr Ile Arg Thr Leu Thr
785                 790                 795                 800

Gly Asn Thr Phe Ser Leu Ala Asp Cys Ile Pro Leu Leu Arg Lys Thr
                805                 810                 815
```

```
Leu Lys Asp Glu Ser Ser Val Thr Cys Lys Leu Ala Cys Thr Ala Val
            820                 825                 830

Arg Asn Cys Val Met Ser Leu Cys Ser Ser Ser Tyr Ser Glu Leu Gly
        835                 840                 845

Leu Gln Leu Ile Ile Asp Val Leu Thr Leu Arg Asn Ser Ser Tyr Trp
    850                 855                 860

Leu Val Arg Thr Glu Leu Leu Glu Thr Leu Ala Glu Ile Asp Phe Arg
865                 870                 875                 880

Leu Val Ser Phe Leu Glu Ala Lys Ala Glu Asn Leu His Arg Gly Ala
                885                 890                 895

His His Tyr Thr Gly Leu Leu Lys Leu Gln Glu Arg Val Leu Asn Asn
            900                 905                 910

Val Val Ile His Leu Leu Gly Asp Glu Asp Pro Arg Val Arg His Val
        915                 920                 925

Ala Ala Ala Ser Leu Ile Arg Leu Val Pro Lys Leu Phe Tyr Lys Cys
    930                 935                 940

Asp Gln Gly Gln Ala Asp Pro Val Val Ala Val Ala Arg Asp Gln Ser
945                 950                 955                 960

Ser Val Tyr Leu Lys Leu Leu Met His Glu Thr Gln Pro Pro Ser His
                965                 970                 975

Phe Ser Val Ser Thr Ile Thr Arg Ile Tyr Arg Gly Tyr Asn Leu Leu
            980                 985                 990

Pro Ser Ile Thr Asp Val Thr Met  Glu Asn Asn Leu Ser  Arg Val Ile
        995                 1000                1005

Ala Ala  Val Ser His Glu Leu  Ile Thr Ser Thr Thr  Arg Ala Leu
    1010                1015                1020

Thr Phe  Gly Cys Cys Glu Ala  Leu Cys Leu Leu Ser  Thr Ala Phe
    1025                1030                1035

Pro Val  Cys Ile Trp Ser Leu  Gly Trp His Cys Gly  Val Pro Pro
    1040                1045                1050

Leu Ser  Ala Ser Asp Glu Ser  Arg Lys Ser Cys Thr  Val Gly Met
    1055                1060                1065

Ala Thr  Met Ile Leu Thr Leu  Leu Ser Ser Ala Trp  Phe Pro Leu
    1070                1075                1080
```

```
Asp Leu  Ser Ala His Gln Asp  Ala Leu Ile Leu Ala  Gly Asn Leu
    1085                1090                1095

Leu Ala  Ala Ser Ala Pro Lys  Ser Leu Arg Ser Ser  Trp Ala Ser
    1100                1105                1110

Glu Glu  Glu Ala Asn Pro Ala  Ala Thr Lys Gln Glu  Glu Val Trp
    1115                1120                1125

Pro Ala  Leu Gly Asp Arg Ala  Leu Val Pro Met Val  Glu Gln Leu
    1130                1135                1140

Phe Ser  His Leu Leu Lys Val  Ile Asn Ile Cys Ala  His Val Leu
    1145                1150                1155

Asp Asp  Val Ala Pro Gly Pro  Ala Ile Lys Ala Ala  Leu Pro Ser
    1160                1165                1170

Leu Thr  Asn Pro Pro Ser Leu  Ser Pro Ile Arg Arg  Lys Gly Lys
    1175                1180                1185

Glu Lys  Glu Pro Gly Glu Gln  Ala Ser Val Pro Leu  Ser Pro Lys
    1190                1195                1200

Lys Gly  Ser Glu Ala Ser Ala  Ala Ser Arg Gln Ser  Asp Thr Ser
    1205                1210                1215

Gly Pro  Val Thr Thr Ser Lys  Ser Ser Ser Leu Gly  Ser Phe Tyr
    1220                1225                1230

His Leu  Pro Ser Tyr Leu Lys  Leu His Asp Val Leu  Lys Ala Thr
    1235                1240                1245

His Ala  Asn Tyr Lys Val Thr  Leu Asp Leu Gln Asn  Ser Thr Glu
    1250                1255                1260

Lys Phe  Gly Gly Phe Leu Arg  Ser Ala Leu Asp Val  Leu Ser Gln
    1265                1270                1275

Ile Leu  Glu Leu Ala Thr Leu  Gln Asp Ile Gly Lys  Cys Val Glu
    1280                1285                1290

Glu Ile  Leu Gly Tyr Leu Lys  Ser Cys Phe Ser Arg  Glu Pro Met
    1295                1300                1305

Met Ala  Thr Val Cys Val Gln  Gln Leu Leu Lys Thr  Leu Phe Gly
    1310                1315                1320

Thr Asn  Leu Ala Ser Gln Phe  Asp Gly Leu Ser Ser  Asn Pro Ser
    1325                1330                1335
```

```
Lys Ser  Gln Gly Arg Ala Gln  Arg Leu Gly Ser Ser  Ser Val Arg
    1340                 1345                 1350

Pro Gly  Leu Tyr His Tyr Cys  Phe Met Ala Pro Tyr  Thr His Phe
    1355                 1360                 1365

Thr Gln  Ala Leu Ala Asp Ala  Ser Leu Arg Asn Met  Val Gln Ala
    1370                 1375                 1380

Glu Gln  Glu Asn Asp Thr Ser  Gly Trp Phe Asp Val  Leu Gln Lys
    1385                 1390                 1395

Val Ser  Thr Gln Leu Lys Thr  Asn Leu Thr Ser Val  Thr Lys Asn
    1400                 1405                 1410

Arg Ala  Asp Lys Asn Ala Ile  His Asn His Ile Arg  Leu Phe Glu
    1415                 1420                 1425

Pro Leu  Val Ile Lys Ala Leu  Lys Gln Tyr Thr Thr  Thr Thr Cys
    1430                 1435                 1440

Val Gln  Leu Gln Lys Gln Val  Leu Asp Leu Leu Ala  Gln Leu Val
    1445                 1450                 1455

Gln Leu  Arg Val Asn Tyr Cys  Leu Leu Asp Ser Asp  Gln Val Phe
    1460                 1465                 1470

Ile Gly  Phe Val Leu Lys Gln  Phe Glu Tyr Ile Glu  Val Gly Gln
    1475                 1480                 1485

Phe Arg  Glu Ser Glu Ala Ile  Ile Pro Asn Ile Phe  Phe Phe Leu
    1490                 1495                 1500

Val Leu  Leu Ser Tyr Glu Arg  Tyr His Ser Lys Gln  Ile Ile Gly
    1505                 1510                 1515

Ile Pro  Lys Ile Ile Gln Leu  Cys Asp Gly Ile Met  Ala Ser Gly
    1520                 1525                 1530

Arg Lys  Ala Val Thr His Ala  Ile Pro Ala Leu Gln  Pro Ile Val
    1535                 1540                 1545

His Asp  Leu Phe Val Leu Arg  Gly Thr Asn Lys Ala  Asp Ala Gly
    1550                 1555                 1560

Lys Glu  Leu Glu Thr Gln Lys  Glu Val Val Val Ser  Met Leu Leu
    1565                 1570                 1575

Arg Leu  Ile Gln Tyr His Gln  Val Leu Glu Met Phe  Ile Leu Val
    1580                 1585                 1590
```

```
Leu Gln  Gln Cys His Lys Glu  Asn Glu Asp Lys Trp  Lys Arg Leu
    1595                 1600                 1605

Ser Arg  Gln Ile Ala Asp Ile  Ile Leu Pro Met Leu  Ala Lys Gln
    1610                 1615                 1620

Gln Met  His Ile Asp Ser His  Glu Ala Leu Gly Val  Leu Asn Thr
    1625                 1630                 1635

Leu Phe  Glu Ile Leu Ala Pro  Ser Ser Leu Arg Pro  Val Asp Met
    1640                 1645                 1650

Leu Leu  Arg Ser Met Phe Val  Thr Pro Asn Thr Met  Ala Ser Val
    1655                 1660                 1665

Ser Thr  Val Gln Leu Trp Ile  Ser Gly Ile Leu Ala  Ile Leu Arg
    1670                 1675                 1680

Val Leu  Ile Ser Gln Ser Thr  Glu Asp Ile Val Leu  Ser Arg Ile
    1685                 1690                 1695

Gln Glu  Leu Ser Phe Ser Pro  Tyr Leu Ile Ser Cys  Thr Val Ile
    1700                 1705                 1710

Asn Arg  Leu Arg Asp Gly Asp  Ser Thr Ser Thr Leu  Glu Glu His
    1715                 1720                 1725

Ser Glu  Gly Lys Gln Ile Lys  Asn Leu Pro Glu Glu  Thr Phe Ser
    1730                 1735                 1740

Arg Phe  Leu Leu Gln Leu Val  Gly Ile Leu Leu Glu  Asp Ile Val
    1745                 1750                 1755

Thr Lys  Gln Leu Lys Val Glu  Met Ser Glu Gln Gln  His Thr Phe
    1760                 1765                 1770

Tyr Cys  Gln Glu Leu Gly Thr  Leu Leu Met Cys Leu  Ile His Ile
    1775                 1780                 1785

Phe Lys  Ser Gly Met Phe Arg  Arg Ile Thr Ala Ala  Ala Thr Arg
    1790                 1795                 1800

Leu Phe  Arg Ser Asp Gly Cys  Gly Gly Ser Phe Tyr  Thr Leu Asp
    1805                 1810                 1815

Ser Leu  Asn Leu Arg Ala Arg  Ser Met Ile Thr Thr  His Pro Ala
    1820                 1825                 1830

Leu Val  Leu Leu Trp Cys Gln  Ile Leu Leu Leu Val  Asn His Thr
    1835                 1840                 1845
```

```
Asp Tyr  Arg Trp Trp Ala Glu  Val Gln Gln Thr Pro  Lys Arg His
    1850                 1855                 1860

Ser Leu  Ser Ser Thr Lys Leu  Leu Ser Pro Gln Met  Ser Gly Glu
    1865                 1870                 1875

Glu Glu  Asp Ser Asp Leu Ala  Ala Lys Leu Gly Met  Cys Asn Arg
    1880                 1885                 1890

Glu Ile  Val Arg Arg Gly Ala  Leu Ile Leu Phe Cys  Asp Tyr Val
    1895                 1900                 1905

Cys Gln  Asn Leu His Asp Ser  Glu His Leu Thr Trp  Leu Ile Val
    1910                 1915                 1920

Asn His  Ile Gln Asp Leu Ile  Ser Leu Ser His Glu  Pro Pro Val
    1925                 1930                 1935

Gln Asp  Phe Ile Ser Ala Val  His Arg Asn Ser Ala  Ala Ser Gly
    1940                 1945                 1950

Leu Phe  Ile Gln Ala Ile Gln  Ser Arg Cys Glu Asn  Leu Ser Thr
    1955                 1960                 1965

Pro Thr  Met Leu Lys Lys Thr  Leu Gln Cys Leu Glu  Gly Ile His
    1970                 1975                 1980

Leu Ser  Gln Ser Gly Ala Val  Leu Thr Leu Tyr Val  Asp Arg Leu
    1985                 1990                 1995

Leu Cys  Thr Pro Phe Arg Val  Leu Ala Arg Met Val  Asp Ile Leu
    2000                 2005                 2010

Ala Cys  Arg Arg Val Glu Met  Leu Leu Ala Ala Asn  Leu Gln Ser
    2015                 2020                 2025

Ser Met  Ala Gln Leu Pro Met  Glu Glu Leu Asn Arg  Ile Gln Glu
    2030                 2035                 2040

Tyr Leu  Gln Ser Ser Gly Leu  Ala Gln Arg His Gln  Arg Leu Tyr
    2045                 2050                 2055

Ser Leu  Leu Asp Arg Phe Arg  Leu Ser Thr Met Gln  Asp Ser Leu
    2060                 2065                 2070

Ser Pro  Ser Pro Pro Val Ser  Ser His Pro Leu Asp  Gly Asp Gly
    2075                 2080                 2085

His Val  Ser Leu Glu Thr Val  Ser Pro Asp Lys Asp  Trp Tyr Val
    2090                 2095                 2100
```

```
His Leu  Val Lys Ser Gln Cys  Trp Thr Arg Ser Asp  Ser Ala Leu
    2105                 2110                 2115

Leu Glu  Gly Ala Glu Leu Val  Asn Arg Ile Pro Ala  Glu Asp Met
    2120                 2125                 2130

Asn Ala  Phe Met Met Asn Ser  Glu Phe Asn Leu Ser  Leu Leu Ala
    2135                 2140                 2145

Pro Cys  Leu Ser Leu Gly Met  Ser Glu Ile Ser Gly  Gly Gln Lys
    2150                 2155                 2160

Ser Ala  Leu Phe Glu Ala Ala  Arg Glu Val Thr Leu  Ala Arg Val
    2165                 2170                 2175

Ser Gly  Thr Val Gln Gln Leu  Pro Ala Val His His  Val Phe Gln
    2180                 2185                 2190

Pro Glu  Leu Pro Ala Glu Pro  Ala Ala Tyr Trp Ser  Lys Leu Asn
    2195                 2200                 2205

Asp Leu  Phe Gly Asp Ala Ala  Leu Tyr Gln Ser Leu  Pro Thr Leu
    2210                 2215                 2220

Ala Arg  Ala Leu Ala Gln Tyr  Leu Val Val Val Ser  Lys Leu Pro
    2225                 2230                 2235

Ser His  Leu His Leu Pro Pro  Glu Lys Glu Lys Asp  Ile Val Lys
    2240                 2245                 2250

Phe Val  Val Ala Thr Leu Glu  Ala Leu Ser Trp His  Leu Ile His
    2255                 2260                 2265

Glu Gln  Ile Pro Leu Ser Leu  Asp Leu Gln Ala Gly  Leu Asp Cys
    2270                 2275                 2280

Cys Cys  Leu Ala Leu Gln Leu  Pro Gly Leu Trp Ser  Val Val Ser
    2285                 2290                 2295

Ser Thr  Glu Phe Val Thr His  Ala Cys Ser Leu Ile  Tyr Cys Val
    2300                 2305                 2310

His Phe  Ile Leu Glu Ala Val  Ala Val Gln Pro Gly  Glu Gln Leu
    2315                 2320                 2325

Leu Ser  Pro Glu Arg Arg Thr  Asn Thr Pro Lys Ala  Ile Ser Glu
    2330                 2335                 2340

Glu Glu  Glu Glu Val Asp Pro  Asn Thr Gln Asn Pro  Lys Tyr Ile
    2345                 2350                 2355
```

```
Thr Ala  Ala Cys Glu Met Val  Ala Glu Met Val Glu  Ser Leu Gln
    2360                2365                2370

Ser Val  Leu Ala Leu Gly His  Lys Arg Asn Ser Gly  Val Pro Ala
    2375                2380                2385

Phe Leu  Thr Pro Leu Leu Arg  Asn Ile Ile Ile Ser  Leu Ala Arg
    2390                2395                2400

Leu Pro  Leu Val Asn Ser Tyr  Thr Arg Val Pro Pro  Leu Val Trp
    2405                2410                2415

Lys Leu  Gly Trp Ser Pro Lys  Pro Gly Gly Asp Phe  Gly Thr Ala
    2420                2425                2430

Phe Pro  Glu Ile Pro Val Glu  Phe Leu Gln Glu Lys  Glu Val Phe
    2435                2440                2445

Lys Glu  Phe Ile Tyr Arg Ile  Asn Thr Leu Gly Trp  Thr Ser Arg
    2450                2455                2460

Thr Gln  Phe Glu Glu Thr Trp  Ala Thr Leu Leu Gly  Val Leu Val
    2465                2470                2475

Thr Gln  Pro Leu Val Met Glu  Gln Glu Glu Ser Pro  Pro Glu Glu
    2480                2485                2490

Asp Thr  Glu Arg Thr Gln Ile  Asn Val Leu Ala Val  Gln Ala Ile
    2495                2500                2505

Thr Ser  Leu Val Leu Ser Ala  Met Thr Val Pro Val  Ala Gly Asn
    2510                2515                2520

Pro Ala  Val Ser Cys Leu Glu  Gln Gln Pro Arg Asn  Lys Pro Leu
    2525                2530                2535

Lys Ala  Leu Asp Thr Arg Phe  Gly Arg Lys Leu Ser  Ile Ile Arg
    2540                2545                2550

Gly Ile  Val Glu Gln Glu Ile  Gln Ala Met Val Ser  Lys Arg Glu
    2555                2560                2565

Asn Ile  Ala Thr His His Leu  Tyr Gln Ala Trp Asp  Pro Val Pro
    2570                2575                2580

Ser Leu  Ser Pro Ala Thr Thr  Gly Ala Leu Ile Ser  His Glu Lys
    2585                2590                2595

Leu Leu  Leu Gln Ile Asn Pro  Glu Arg Glu Leu Gly  Ser Met Ser
    2600                2605                2610
```

```
Tyr Lys  Leu Gly Gln Val Ser  Ile His Ser Val Trp  Leu Gly Asn
    2615                 2620                 2625

Ser Ile  Thr Pro Leu Arg Glu  Glu Glu Trp Asp Glu  Glu Glu Glu
    2630                 2635                 2640

Glu Glu  Ala Asp Ala Pro Ala  Pro Ser Ser Pro Pro  Thr Ser Pro
    2645                 2650                 2655

Val Asn  Ser Arg Lys His Arg  Ala Gly Val Asp Ile  His Ser Cys
    2660                 2665                 2670

Ser Gln  Phe Leu Leu Glu Leu  Tyr Ser Arg Trp Ile  Leu Pro Ser
    2675                 2680                 2685

Ser Ser  Ala Arg Arg Thr Pro  Ala Ile Leu Ile Ser  Glu Val Val
    2690                 2695                 2700

Arg Ser  Leu Leu Val Val Ser  Asp Leu Phe Thr Glu  Arg Asn Gln
    2705                 2710                 2715

Phe Glu  Leu Met Tyr Val Thr  Leu Thr Glu Leu Arg  Arg Val His
    2720                 2725                 2730

Pro Ser  Glu Asp Glu Ile Leu  Ala Gln Tyr Leu Val  Pro Ala Thr
    2735                 2740                 2745

Cys Lys  Ala Ala Ala Val Leu  Gly Met Asp Lys Ala  Val Ala Glu
    2750                 2755                 2760

Pro Val  Ser Arg Leu Leu Glu  Ser Thr Leu Arg Ser  Ser His Leu
    2765                 2770                 2775

Pro Ser  Arg Val Gly Ala Leu  His Gly Val Leu Tyr  Val Leu Glu
    2780                 2785                 2790

Cys Asp  Leu Leu Asp Asp Thr  Ala Lys Gln Leu Ile  Pro Val Ile
    2795                 2800                 2805

Ser Asp  Tyr Leu Leu Ser Asn  Leu Lys Gly Ile Ala  His Cys Val
    2810                 2815                 2820

Asn Ile  His Ser Gln Gln His  Val Leu Val Met Cys  Ala Thr Ala
    2825                 2830                 2835

Phe Tyr  Leu Ile Glu Asn Tyr  Pro Leu Asp Val Gly  Pro Glu Phe
    2840                 2845                 2850

Ser Ala  Ser Ile Ile Gln Met  Cys Gly Val Met Leu  Ser Gly Ser
    2855                 2860                 2865
```

```
Glu Glu  Ser Thr Pro Ser Ile  Ile Tyr His Cys Ala  Leu Arg Gly
    2870                 2875                 2880

Leu Glu  Arg Leu Leu Leu Ser  Glu Gln Leu Ser Arg  Leu Asp Ala
    2885                 2890                 2895

Glu Ser  Leu Val Lys Leu Ser  Val Asp Arg Val Asn  Val His Ser
    2900                 2905                 2910

Pro His  Arg Ala Met Ala Ala  Leu Gly Leu Met Leu  Thr Cys Met
    2915                 2920                 2925

Tyr Thr  Gly Lys Glu Lys Val  Ser Pro Gly Arg Thr  Ser Asp Pro
    2930                 2935                 2940

Asn Pro  Ala Ala Pro Asp Ser  Glu Ser Val Ile Val  Ala Met Glu
    2945                 2950                 2955

Arg Val  Ser Val Leu Phe Asp  Arg Ile Arg Lys Gly  Phe Pro Cys
    2960                 2965                 2970

Glu Ala  Arg Val Val Ala Arg  Ile Leu Pro Gln Phe  Leu Asp Asp
    2975                 2980                 2985

Phe Phe  Pro Pro Gln Asp Ile  Met Asn Lys Val Ile  Gly Glu Phe
    2990                 2995                 3000

Leu Ser  Asn Gln Gln Pro Tyr  Pro Gln Phe Met Ala  Thr Val Val
    3005                 3010                 3015

Tyr Lys  Val Phe Gln Thr Leu  His Ser Thr Gly Gln  Ser Ser Met
    3020                 3025                 3030

Val Arg  Asp Trp Val Met Leu  Ser Leu Ser Asn Phe  Thr Gln Arg
    3035                 3040                 3045

Ala Pro  Val Ala Met Ala Thr  Trp Ser Leu Ser Cys  Phe Phe Val
    3050                 3055                 3060

Ser Ala  Ser Thr Ser Pro Trp  Val Ala Ala Ile Leu  Pro His Val
    3065                 3070                 3075

Ile Ser  Arg Met Gly Lys Leu  Glu Gln Val Asp Val  Asn Leu Phe
    3080                 3085                 3090

Cys Leu  Val Ala Thr Asp Phe  Tyr Arg His Gln Ile  Glu Glu Glu
    3095                 3100                 3105

Leu Asp  Arg Arg Ala Phe Gln  Ser Val Leu Glu Val  Val Ala Ala
    3110                 3115                 3120
```

Pro Gly Ser Pro Tyr His Arg Leu Leu Thr Cys Leu Arg Asn Val
3125 3130 3135

His Lys Val Thr Thr Cys
3140

<210> 48
<211> 89
<212> PRT
<213> Homo sapiens

<400> 48

Met Gly Ile Leu Lys Leu Gln Val Phe Leu Ile Val Leu Ser Val Ala
1 5 10 15

Leu Asn His Leu Lys Ala Thr Pro Ile Glu Ser His Gln Val Glu Lys
20 25 30

Arg Lys Cys Asn Thr Ala Thr Cys Ala Thr Gln Arg Leu Ala Asn Phe
35 40 45

Leu Val His Ser Ser Asn Asn Phe Gly Ala Ile Leu Ser Ser Thr Asn
50 55 60

Val Gly Ser Asn Thr Tyr Gly Lys Arg Asn Ala Val Glu Val Leu Lys
65 70 75 80

Arg Glu Pro Leu Asn Tyr Leu Pro Leu
85

<210> 49
<211> 776
<212> PRT
<213> Homo sapiens

<400> 49

Met Ala Glu Pro Arg Gln Glu Phe Glu Val Met Glu Asp His Ala Gly
1 5 10 15

Thr Tyr Gly Leu Gly Asp Arg Lys Asp Gln Gly Gly Tyr Thr Met His
20 25 30

Gln Asp Gln Glu Gly Asp Thr Asp Ala Gly Leu Lys Glu Ser Pro Leu
35 40 45

Gln Thr Pro Thr Glu Asp Gly Ser Glu Glu Pro Gly Ser Glu Thr Ser
50 55 60

Asp Ala Lys Ser Thr Pro Thr Ala Glu Asp Val Thr Ala Pro Leu Val
65 70 75 80

Asp Glu Gly Ala Pro Gly Lys Gln Ala Ala Ala Gln Pro His Thr Glu

85 90 95

Ile Pro Glu Gly Thr Thr Ala Glu Glu Ala Gly Ile Gly Asp Thr Pro
100 105 110

Ser Leu Glu Asp Glu Ala Ala Gly His Val Thr Gln Glu Pro Glu Ser
115 120 125

Gly Lys Val Val Gln Glu Gly Phe Leu Arg Glu Pro Gly Pro Pro Gly
130 135 140

Leu Ser His Gln Leu Met Ser Gly Met Pro Gly Ala Pro Leu Leu Pro
145 150 155 160

Glu Gly Pro Arg Glu Ala Thr Arg Gln Pro Ser Gly Thr Gly Pro Glu
165 170 175

Asp Thr Glu Gly Gly Arg His Ala Pro Glu Leu Leu Lys His Gln Leu
180 185 190

Leu Gly Asp Leu His Gln Glu Gly Pro Pro Leu Lys Gly Ala Gly Gly
195 200 205

Lys Glu Arg Pro Gly Ser Lys Glu Glu Val Asp Glu Asp Arg Asp Val
210 215 220

Asp Glu Ser Ser Pro Gln Asp Ser Pro Pro Ser Lys Ala Ser Pro Ala
225 230 235 240

Gln Asp Gly Arg Pro Pro Gln Thr Ala Ala Arg Glu Ala Thr Ser Ile
245 250 255

Pro Gly Phe Pro Ala Glu Gly Ala Ile Pro Leu Pro Val Asp Phe Leu
260 265 270

Ser Lys Val Ser Thr Glu Ile Pro Ala Ser Glu Pro Asp Gly Pro Ser
275 280 285

Val Gly Arg Ala Lys Gly Gln Asp Ala Pro Leu Glu Phe Thr Phe His
290 295 300

Val Glu Ile Thr Pro Asn Val Gln Lys Glu Gln Ala His Ser Glu Glu
305 310 315 320

His Leu Gly Arg Ala Ala Phe Pro Gly Ala Pro Gly Glu Gly Pro Glu
325 330 335

Ala Arg Gly Pro Ser Leu Gly Glu Asp Thr Lys Glu Ala Asp Leu Pro
340 345 350

Glu Pro Ser Glu Lys Gln Pro Ala Ala Ala Pro Arg Gly Lys Pro Val

355 360 365

Ser Arg Val Pro Gln Leu Lys Ala Arg Met Val Ser Lys Ser Lys Asp
370 375 380

Gly Thr Gly Ser Asp Asp Lys Lys Ala Lys Thr Ser Thr Arg Ser Ser
385 390 395 400

Ala Lys Thr Leu Lys Asn Arg Pro Cys Leu Ser Pro Lys His Pro Thr
405 410 415

Pro Gly Ser Ser Asp Pro Leu Ile Gln Pro Ser Ser Pro Ala Val Cys
420 425 430

Pro Glu Pro Pro Ser Ser Pro Lys Tyr Val Ser Ser Val Thr Ser Arg
435 440 445

Thr Gly Ser Ser Gly Ala Lys Glu Met Lys Leu Lys Gly Ala Asp Gly
450 455 460

Lys Thr Lys Ile Ala Thr Pro Arg Gly Ala Ala Pro Pro Gly Gln Lys
465 470 475 480

Gly Gln Ala Asn Ala Thr Arg Ile Pro Ala Lys Thr Pro Pro Ala Pro
485 490 495

Lys Thr Pro Pro Ser Ser Ala Thr Lys Gln Val Gln Arg Arg Pro Pro
500 505 510

Pro Ala Gly Pro Arg Ser Glu Arg Gly Glu Pro Pro Lys Ser Gly Asp
515 520 525

Arg Ser Gly Tyr Ser Ser Pro Gly Ser Pro Gly Thr Pro Gly Ser Arg
530 535 540

Ser Arg Thr Pro Ser Leu Pro Thr Pro Pro Thr Arg Glu Pro Lys Lys
545 550 555 560

Val Ala Val Val Arg Thr Pro Pro Lys Ser Pro Ser Ser Ala Lys Ser
565 570 575

Arg Leu Gln Thr Ala Pro Val Pro Met Pro Asp Leu Lys Asn Val Lys
580 585 590

Ser Lys Ile Gly Ser Thr Glu Asn Leu Lys His Gln Pro Gly Gly Gly
595 600 605

Lys Val Gln Ile Ile Asn Lys Lys Leu Asp Leu Ser Asn Val Gln Ser
610 615 620

Lys Cys Gly Ser Lys Asp Asn Ile Lys His Val Pro Gly Gly Gly Ser

625 630 635 640

Val Gln Ile Val Tyr Lys Pro Val Asp Leu Ser Lys Val Thr Ser Lys
645 650 655

Cys Gly Ser Leu Gly Asn Ile His His Lys Pro Gly Gly Gly Gln Val
660 665 670

Glu Val Lys Ser Glu Lys Leu Asp Phe Lys Asp Arg Val Gln Ser Lys
675 680 685

Ile Gly Ser Leu Asp Asn Ile Thr His Val Pro Gly Gly Gly Asn Lys
690 695 700

Lys Ile Glu Thr His Lys Leu Thr Phe Arg Glu Asn Ala Lys Ala Lys
705 710 715 720

Thr Asp His Gly Ala Glu Ile Val Tyr Lys Ser Pro Val Val Ser Gly
725 730 735

Asp Thr Ser Pro Arg His Leu Ser Asn Val Ser Ser Thr Gly Ser Ile
740 745 750

Asp Met Val Asp Ser Pro Gln Leu Ala Thr Leu Ala Asp Glu Val Ser
755 760 765

Ala Ser Leu Ala Lys Gln Gly Leu
770 775

<210> 50
<211> 253
<212> PRT
<213> Homo sapiens

<400> 50

Met Ala Asn Leu Gly Cys Trp Met Leu Val Leu Phe Val Ala Thr Trp
1 5 10 15

Ser Asp Leu Gly Leu Cys Lys Lys Arg Pro Lys Pro Gly Gly Trp Asn
20 25 30

Thr Gly Gly Ser Arg Tyr Pro Gly Gln Gly Ser Pro Gly Gly Asn Arg
35 40 45

Tyr Pro Pro Gln Gly Gly Gly Gly Trp Gly Gln Pro His Gly Gly Gly
50 55 60

Trp Gly Gln Pro His Gly Gly Gly Trp Gly Gln Pro His Gly Gly Gly
65 70 75 80

Trp Gly Gln Pro His Gly Gly Gly Trp Gly Gln Gly Gly Gly Thr His
85 90 95

```
Ser Gln Trp Asn Lys Pro Ser Lys Pro Lys Thr Asn Met Lys His Met
            100                 105                 110

Ala Gly Ala Ala Ala Ala Gly Ala Val Val Gly Gly Leu Gly Gly Tyr
        115                 120                 125

Met Leu Gly Ser Ala Met Ser Arg Pro Ile Ile His Phe Gly Ser Asp
    130                 135                 140

Tyr Glu Asp Arg Tyr Tyr Arg Glu Asn Met His Arg Tyr Pro Asn Gln
145                 150                 155                 160

Val Tyr Tyr Arg Pro Met Asp Glu Tyr Ser Asn Gln Asn Asn Phe Val
                165                 170                 175

His Asp Cys Val Asn Ile Thr Ile Lys Gln His Thr Val Thr Thr Thr
            180                 185                 190

Thr Lys Gly Glu Asn Phe Thr Glu Thr Asp Val Lys Met Met Glu Arg
        195                 200                 205

Val Val Glu Gln Met Cys Ile Thr Gln Tyr Glu Arg Glu Ser Gln Ala
    210                 215                 220

Tyr Tyr Gln Arg Gly Ser Ser Met Val Leu Phe Ser Ser Pro Pro Val
225                 230                 235                 240

Ile Leu Leu Ile Ser Phe Leu Ile Phe Leu Ile Val Gly
                245                 250


<210>  51
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<212>  PRT
<213>  Homo sapiens

<400>  51

Met Asp Val Phe Met Lys Gly Leu Ser Lys Ala Lys Glu Gly Val Val
1               5                   10                  15

Ala Ala Ala Glu Lys Thr Lys Gln Gly Val Ala Glu Ala Ala Gly Lys
            20                  25                  30

Thr Lys Glu Gly Val Leu Tyr Val Gly Ser Lys Thr Lys Glu Gly Val
        35                  40                  45

Val His Gly Val Ala Thr Val Ala Glu Lys Thr Lys Glu Gln Val Thr
    50                  55                  60

Asn Val Gly Gly Ala Val Val Thr Gly Val Thr Ala Val Ala Gln Lys
65                  70                  75                  80
```

```
Thr Val Glu Gly Ala Gly Ser Ile Ala Ala Ala Thr Gly Phe Val Lys
                85                  90                  95


Lys Asp Gln Leu Gly Lys Asn Glu Glu Gly Ala Pro Gln Glu Gly Ile
            100                 105                 110


Leu Glu Asp Met Pro Val Asp Pro Asp Asn Glu Ala Tyr Glu Met Pro
        115                 120                 125


Ser Glu Glu Gly Tyr Gln Asp Tyr Glu Pro Glu Ala
    130                 135                 140


<210>  52
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<400>  52

Met Asp Val Phe Met Lys Gly Leu Ser Lys Ala Lys Glu Gly Val Val
1               5                   10                  15


Ala Ala Ala Glu Lys Thr Lys Gln Gly Val Ala Glu Ala Ala Gly Lys
            20                  25                  30


Thr Lys Glu Gly Val Leu Tyr Val Gly Ser Lys Thr Lys Glu Gly Val
        35                  40                  45


Val His Gly Val Ala Thr Val Ala Glu Lys Thr Lys Glu Gln Val Thr
    50                  55                  60


Asn Val Gly Gly Ala Val Val Thr Gly Val Thr Ala Val Ala Gln Lys
65                  70                  75                  80


Thr Val Glu Gly Ala Gly Ser Ile Ala Ala Ala Thr Gly Phe Val Lys
                85                  90                  95


Lys Asp Gln Leu Gly Lys Asn Glu Glu Gly Ala Pro Gln Glu Gly Ile
            100                 105                 110


Leu Glu Asp Met Pro Val Asp Pro Asp Asn Glu Ala Tyr Glu Met Pro
        115                 120                 125


Ser Glu Glu Gly Tyr Gln Asp Tyr Glu Pro Glu Ala
    130                 135                 140


<210>  53
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<213>  Homo sapiens

<400>  53

Gln Leu Val Lys Ser Glu Leu Glu Glu Lys Lys Ser Glu Leu Arg His
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1 5 10 15

Lys Leu Lys Tyr Val Pro His Glu Tyr Ile Glu Leu Ile Glu Ile Ala
20 25 30

Arg Asn Ser Thr Gln Asp Arg Ile Leu Glu Met Lys Val Met Glu Phe
35 40 45

Phe Met Lys Val Tyr Gly Tyr Arg Gly Lys His Leu Gly Gly Ser Arg
50 55 60

Lys Pro Asp Gly Ala Ile Tyr Thr Val Gly Ser Pro Ile Asp Tyr Gly
65 70 75 80

Val Ile Val Asp Thr Lys Ala Tyr Ser Gly Gly Tyr Asn Leu Pro Ile
85 90 95

Gly Gln Ala Asp Glu Met Gln Arg Tyr Val Glu Glu Asn Gln Thr Arg
100 105 110

Asn Lys His Ile Asn Pro Asn Glu Trp Trp Lys Val Tyr Pro Ser Ser
115 120 125

Val Thr Glu Phe Lys Phe Leu Phe Val Ser Gly His Phe Lys Gly Asn
130 135 140

Tyr Lys Ala Gln Leu Thr Arg Leu Asn His Ile Thr Asn Cys Asn Gly
145 150 155 160

Ala Val Leu Ser Val Glu Glu Leu Leu Ile Gly Gly Glu Met Ile Lys
165 170 175

Ala Gly Thr Leu Thr Leu Glu Glu Val Arg Arg Lys Phe Asn Asn Gly
180 185 190

Glu Ile Asn Phe
195

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Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
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Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
            20   25   30

His Gly Gly Gly
        35

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Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
1   5   10   15

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
            20   25   30

Gly His Gly Gly
        35

<210> 56
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Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
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Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
            20   25   30

His Gly Ser Gly
        35

<210> 57
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Tyr Lys Asp Asp Asp Asp Lys Met Ala Pro Lys Lys Lys Arg Lys Val
            20                  25                  30


Gly Ile His Gly Val Pro Ala Ala Val Asp Leu Arg Thr Leu Gly Tyr
        35                  40                  45


Ser Gln Gln Gln Gln Glu Lys Ile Lys Pro Lys Val Arg Ser Thr Val
    50                  55                  60


Ala Gln His His Glu Ala Leu Val Gly His Gly Phe Thr His Ala His
65                  70                  75                  80


Ile Val Ala Leu Ser Gln His Pro Ala Ala Leu Gly Thr Val Ala Val
                85                  90                  95


Lys Tyr Gln Asp Met Ile Ala Ala Leu Pro Glu Ala Thr His Glu Ala
            100                 105                 110


Ile Val Gly Val Gly Lys Gln Trp Ser Gly Ala Arg Ala Leu Glu Ala
        115                 120                 125


Leu Leu Thr Val Ala Gly Glu Leu Arg Gly Pro Pro Leu Gln Leu Asp
    130                 135                 140


Thr Gly Gln Leu Leu Lys Ile Ala Lys Arg Gly Gly Val Thr Ala Val
145                 150                 155                 160


Glu Ala Val His Ala Trp Arg Asn Ala Leu Thr Gly Ala Pro Leu Asn
                165                 170                 175
```

```
Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
            180                 185                 190

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
        195                 200                 205

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
    210                 215                 220

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
225                 230                 235                 240

Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala
                245                 250                 255

Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu
            260                 265                 270

Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val
        275                 280                 285

Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val
    290                 295                 300

Gln Arg Leu Leu Pro Val Leu Cys Gln Ala His Gly Leu Thr Pro Glu
305                 310                 315                 320

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
                325                 330                 335

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
            340                 345                 350

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
        355                 360                 365

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
    370                 375                 380

His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly
385                 390                 395                 400

Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys
                405                 410                 415

Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala
            420                 425                 430

Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu
        435                 440                 445
```

```
Pro Val Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala
    450                 455                 460

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
465                 470                 475                 480

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
                485                 490                 495

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
            500                 505                 510

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala His Gly Leu Thr
        515                 520                 525

Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala
    530                 535                 540

Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His
545                 550                 555                 560

Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly
                565                 570                 575

Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys
            580                 585                 590

Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
        595                 600                 605

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
    610                 615                 620

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
625                 630                 635                 640

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
                645                 650                 655

Leu Leu Pro Val Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val
            660                 665                 670

Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val
        675                 680                 685

Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr
    690                 695                 700

Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala
705                 710                 715                 720
```

```
Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala His Gly
                725                 730                 735

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
            740                 745                 750

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
        755                 760                 765

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
    770                 775                 780

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
785                 790                 795                 800

Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala
                805                 810                 815

Ser Xaa Xaa Gly Gly Arg Pro Ala Leu Glu Ser Ile Val Ala Gln Leu
            820                 825                 830

Ser Arg Pro Asp Pro Ala Leu Ala Ala Leu Thr Asn Asp His Leu Val
        835                 840                 845

Ala Leu Ala Cys Leu Gly Gly Arg Pro Ala Leu Asp Ala Val Lys Lys
    850                 855                 860

Gly Leu Pro His Ala Pro Ala Leu Ile Lys Arg Thr Asn Arg Arg Ile
865                 870                 875                 880

Pro Glu Arg Thr Ser His Arg Val Ala Gly Ser Gln Leu Val Lys Ser
                885                 890                 895

Glu Leu Glu Glu Lys Lys Ser Glu Leu Arg His Lys Leu Lys Tyr Val
            900                 905                 910

Pro His Glu Tyr Ile Glu Leu Ile Glu Ile Ala Arg Asn Ser Thr Gln
        915                 920                 925

Asp Arg Ile Leu Glu Met Lys Val Met Glu Phe Phe Met Lys Val Tyr
    930                 935                 940

Gly Tyr Arg Gly Lys His Leu Gly Gly Ser Arg Lys Pro Asp Gly Ala
945                 950                 955                 960

Ile Tyr Thr Val Gly Ser Pro Ile Asp Tyr Gly Val Ile Val Asp Thr
                965                 970                 975

Lys Ala Tyr Ser Gly Gly Tyr Asn Leu Pro Ile Gly Gln Ala Asp Glu
            980                 985                 990
```

```
Met Gln Arg Tyr Val Glu Glu Asn  Gln Thr Arg Asn Lys  His Ile Asn
        995                 1000                1005


Pro Asn  Glu Trp Trp Lys Val  Tyr Pro Ser Ser Val  Thr Glu Phe
    1010                1015                1020


Lys Phe  Leu Phe Val Ser Gly  His Phe Lys Gly Asn  Tyr Lys Ala
    1025                1030                1035


Gln Leu  Thr Arg Leu Asn His  Ile Thr Asn Cys Asn  Gly Ala Val
    1040                1045                1050


Leu Ser  Val Glu Glu Leu Leu  Ile Gly Gly Glu Met  Ile Lys Ala
    1055                1060                1065


Gly Thr  Leu Thr Leu Glu Glu  Val Arg Arg Lys Phe  Asn Asn Gly
    1070                1075                1080


Glu Ile  Asn Phe Arg Ser
    1085


<210>  58
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Met Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp His Asp Ile Asp
1 5 10 15

Tyr Lys Asp Asp Asp Asp Lys Met Ala Pro Lys Lys Lys Arg Lys Val
20 25 30

Gly Ile His Gly Val Pro Ala Ala Val Asp Leu Arg Thr Leu Gly Tyr
35 40 45

Ser Gln Gln Gln Gln Glu Lys Ile Lys Pro Lys Val Arg Ser Thr Val
50 55 60

Ala Gln His His Glu Ala Leu Val Gly His Gly Phe Thr His Ala His
65 70 75 80

Ile Val Ala Leu Ser Gln His Pro Ala Ala Leu Gly Thr Val Ala Val
85 90 95

Lys Tyr Gln Asp Met Ile Ala Ala Leu Pro Glu Ala Thr His Glu Ala
100 105 110

Ile Val Gly Val Gly Lys Gln Trp Ser Gly Ala Arg Ala Leu Glu Ala
115 120 125

Leu Leu Thr Val Ala Gly Glu Leu Arg Gly Pro Pro Leu Gln Leu Asp
130 135 140

Thr Gly Gln Leu Leu Lys Ile Ala Lys Arg Gly Gly Val Thr Ala Val
145 150 155 160

Glu Ala Val His Ala Trp Arg Asn Ala Leu Thr Gly Ala Pro Leu Asn
165 170 175

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
180 185 190

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
195 200 205

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
210 215 220

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
225 230 235 240

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
245 250 255

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
260 265 270

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
275 280 285

```
Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
    290                 295                 300

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
305                 310                 315                 320

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
                325                 330                 335

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
            340                 345                 350

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
        355                 360                 365

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
    370                 375                 380

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
385                 390                 395                 400

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
                405                 410                 415

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
            420                 425                 430

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
        435                 440                 445

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
    450                 455                 460

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
465                 470                 475                 480

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
                485                 490                 495

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
            500                 505                 510

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
        515                 520                 525

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
    530                 535                 540

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
545                 550                 555                 560
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Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
                565                 570                 575

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
            580                 585                 590

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
        595                 600                 605

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
    610                 615                 620

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
625                 630                 635                 640

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
                645                 650                 655

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
            660                 665                 670

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
        675                 680                 685

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
    690                 695                 700

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
705                 710                 715                 720

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
                725                 730                 735

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
            740                 745                 750

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
        755                 760                 765

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
    770                 775                 780

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
785                 790                 795                 800

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
                805                 810                 815

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
            820                 825                 830
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Ile Ala Ser Xaa Xaa Gly Gly Arg Pro Ala Leu Glu Ser Ile Val Ala
        835                 840                 845

Gln Leu Ser Arg Pro Asp Pro Ala Leu Ala Ala Leu Thr Asn Asp His
    850                 855                 860

Leu Val Ala Leu Ala Cys Leu Gly Gly Arg Pro Ala Leu Asp Ala Val
865                 870                 875                 880

Lys Lys Gly Leu Pro His Ala Pro Ala Leu Ile Lys Arg Thr Asn Arg
                885                 890                 895

Arg Ile Pro Glu Arg Thr Ser His Arg Val Ala Gly Ser Gln Leu Val
            900                 905                 910

Lys Ser Glu Leu Glu Glu Lys Lys Ser Glu Leu Arg His Lys Leu Lys
        915                 920                 925

Tyr Val Pro His Glu Tyr Ile Glu Leu Ile Glu Ile Ala Arg Asn Ser
    930                 935                 940

Thr Gln Asp Arg Ile Leu Glu Met Lys Val Met Glu Phe Phe Met Lys
945                 950                 955                 960

Val Tyr Gly Tyr Arg Gly Lys His Leu Gly Gly Ser Arg Lys Pro Asp
                965                 970                 975

Gly Ala Ile Tyr Thr Val Gly Ser Pro Ile Asp Tyr Gly Val Ile Val
            980                 985                 990

Asp Thr Lys Ala Tyr Ser Gly Gly  Tyr Asn Leu Pro Ile  Gly Gln Ala
        995                 1000                1005

Asp Glu  Met Gln Arg Tyr Val  Glu Glu Asn Gln Thr  Arg Asn Lys
    1010                1015                1020

His Ile  Asn Pro Asn Glu Trp  Trp Lys Val Tyr Pro  Ser Ser Val
    1025                1030                1035

Thr Glu  Phe Lys Phe Leu Phe  Val Ser Gly His Phe  Lys Gly Asn
    1040                1045                1050

Tyr Lys  Ala Gln Leu Thr Arg  Leu Asn His Ile Thr  Asn Cys Asn
    1055                1060                1065

Gly Ala  Val Leu Ser Val Glu  Glu Leu Leu Ile Gly  Gly Glu Met
    1070                1075                1080

Ile Lys  Ala Gly Thr Leu Thr  Leu Glu Glu Val Arg  Arg Lys Phe
    1085                1090                1095
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Asn Asn Gly Glu Ile Asn Phe Arg Ser
    1100   1105

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Met Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp His Asp Ile Asp
1 5 10 15

Tyr Lys Asp Asp Asp Asp Lys Met Ala Pro Lys Lys Lys Arg Lys Val
20 25 30

Gly Ile His Gly Val Pro Ala Ala Val Asp Leu Arg Thr Leu Gly Tyr
35 40 45

Ser Gln Gln Gln Gln Glu Lys Ile Lys Pro Lys Val Arg Ser Thr Val
50 55 60

Ala Gln His His Glu Ala Leu Val Gly His Gly Phe Thr His Ala His
65 70 75 80

Ile Val Ala Leu Ser Gln His Pro Ala Ala Leu Gly Thr Val Ala Val
85 90 95

Lys Tyr Gln Asp Met Ile Ala Ala Leu Pro Glu Ala Thr His Glu Ala
100 105 110

Ile Val Gly Val Gly Lys Gln Trp Ser Gly Ala Arg Ala Leu Glu Ala

```
        115                 120                 125

Leu Leu Thr Val Ala Gly Glu Leu Arg Gly Pro Pro Leu Gln Leu Asp
    130                 135                 140

Thr Gly Gln Leu Leu Lys Ile Ala Lys Arg Gly Gly Val Thr Ala Val
145                 150                 155                 160

Glu Ala Val His Ala Trp Arg Asn Ala Leu Thr Gly Ala Pro Leu Asn
                165                 170                 175

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
            180                 185                 190

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
        195                 200                 205

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
    210                 215                 220

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
225                 230                 235                 240

Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala
                245                 250                 255

Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu
            260                 265                 270

Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val
        275                 280                 285

Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val
    290                 295                 300

Gln Arg Leu Leu Pro Val Leu Cys Gln Ala His Gly Leu Thr Pro Glu
305                 310                 315                 320

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
                325                 330                 335

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
            340                 345                 350

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
        355                 360                 365

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
    370                 375                 380

His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly
```

385 390 395 400

Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys
405 410 415

Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala
420 425 430

Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu
435 440 445

Pro Val Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala
450 455 460

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
465 470 475 480

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
485 490 495

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
500 505 510

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala His Gly Leu Thr
515 520 525

Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala
530 535 540

Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His
545 550 555 560

Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly
565 570 575

Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys
580 585 590

Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
595 600 605

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
610 615 620

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
625 630 635 640

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
645 650 655

Leu Leu Pro Val Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val

660 665 670

Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val
675 680 685

Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr
690 695 700

Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala
705 710 715 720

Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala His Gly
725 730 735

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
740 745 750

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
755 760 765

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
770 775 780

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
785 790 795 800

Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala
805 810 815

Ser Xaa Xaa Gly Gly Arg Pro Ala Leu Glu Ser Ile Val Ala Gln Leu
820 825 830

Ser Arg Pro Asp Pro Ala Leu Ala Ala Leu Thr Asn Asp His Leu Val
835 840 845

Ala Leu Ala Cys Leu Gly Gly Arg Pro Ala Leu Asp Ala Val Lys Lys
850 855 860

Gly Leu Pro His Ala Pro Ala Leu Ile Lys Arg Thr Asn Arg Arg Ile
865 870 875 880

Pro Glu Arg Thr Ser His Arg Val Ala Gly Ser Val Leu Glu Lys Ser
885 890 895

Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr Glu Leu Thr Asn Ile
900 905 910

Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala Ser Lys Lys Lys Thr
915 920 925

Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile Ser Thr Lys Ile Phe

930 935 940

Thr Asp Glu Leu Gly Phe Ser Gly Lys His Leu Gly Gly Ser Asn Lys
945 950 955 960

Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala Ile Ile Leu Asp Ser
965 970 975

Lys Ala Tyr Ser Glu Gly Phe Pro Leu Thr Ala Ser His Thr Asp Ala
980 985 990

Met Gly Arg Tyr Leu Arg Gln Phe Thr Glu Arg Lys Glu Glu Ile Lys
995 1000 1005

Pro Thr Trp Trp Asp Ile Ala Pro Glu His Leu Asp Asn Thr Tyr
1010 1015 1020

Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asn Tyr Lys Glu Gln
1025 1030 1035

Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly Ala Leu
1040 1045 1050

Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr Gln
1055 1060 1065

Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu Asp Tyr Asn
1070 1075 1080

Ile Ser Tyr
1085

<210> 60
<211> 1104
<212> PRT
<213> Homo sapiens

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<223> Any naturally occurring amino acid

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<222> (836)..(837)
<223> Any naturally occurring amino acid

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Met Asp Tyr Lys Asp His Asp Gly Asp Tyr Lys Asp His Asp Ile Asp
1               5                  10                  15

Tyr Lys Asp Asp Asp Asp Lys Met Ala Pro Lys Lys Lys Arg Lys Val
            20                  25                  30

Gly Ile His Gly Val Pro Ala Ala Val Asp Leu Arg Thr Leu Gly Tyr
        35                  40                  45

Ser Gln Gln Gln Gln Glu Lys Ile Lys Pro Lys Val Arg Ser Thr Val
    50                  55                  60

Ala Gln His His Glu Ala Leu Val Gly His Gly Phe Thr His Ala His
65                  70                  75                  80

Ile Val Ala Leu Ser Gln His Pro Ala Ala Leu Gly Thr Val Ala Val
                85                  90                  95

Lys Tyr Gln Asp Met Ile Ala Ala Leu Pro Glu Ala Thr His Glu Ala
            100                 105                 110

Ile Val Gly Val Gly Lys Gln Trp Ser Gly Ala Arg Ala Leu Glu Ala
        115                 120                 125

Leu Leu Thr Val Ala Gly Glu Leu Arg Gly Pro Pro Leu Gln Leu Asp
    130                 135                 140

Thr Gly Gln Leu Leu Lys Ile Ala Lys Arg Gly Gly Val Thr Ala Val
145                 150                 155                 160

Glu Ala Val His Ala Trp Arg Asn Ala Leu Thr Gly Ala Pro Leu Asn
                165                 170                 175

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
            180                 185                 190

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
        195                 200                 205

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
    210                 215                 220

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
225                 230                 235                 240
```

```
Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
                245                 250                 255

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
            260                 265                 270

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
        275                 280                 285

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
    290                 295                 300

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
305                 310                 315                 320

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
                325                 330                 335

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
            340                 345                 350

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
        355                 360                 365

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
    370                 375                 380

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
385                 390                 395                 400

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
                405                 410                 415

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
            420                 425                 430

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
        435                 440                 445

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
    450                 455                 460

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
465                 470                 475                 480

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
                485                 490                 495

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
            500                 505                 510
```

```
Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
        515                 520                 525

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
    530                 535                 540

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
545                 550                 555                 560

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
                565                 570                 575

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
            580                 585                 590

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
        595                 600                 605

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
    610                 615                 620

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
625                 630                 635                 640

Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
                645                 650                 655

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
            660                 665                 670

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
        675                 680                 685

Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
    690                 695                 700

Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
705                 710                 715                 720

Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu
                725                 730                 735

Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly
            740                 745                 750

Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
        755                 760                 765

Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
    770                 775                 780
```

```
Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
785                 790                 795                 800

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
                805                 810                 815

Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
            820                 825                 830

Ile Ala Ser Xaa Xaa Gly Gly Arg Pro Ala Leu Glu Ser Ile Val Ala
        835                 840                 845

Gln Leu Ser Arg Pro Asp Pro Ala Leu Ala Ala Leu Thr Asn Asp His
    850                 855                 860

Leu Val Ala Leu Ala Cys Leu Gly Gly Arg Pro Ala Leu Asp Ala Val
865                 870                 875                 880

Lys Lys Gly Leu Pro His Ala Pro Ala Leu Ile Lys Arg Thr Asn Arg
                885                 890                 895

Arg Ile Pro Glu Arg Thr Ser His Arg Val Ala Gly Ser Val Leu Glu
            900                 905                 910

Lys Ser Asp Ile Glu Lys Phe Lys Asn Gln Leu Arg Thr Glu Leu Thr
        915                 920                 925

Asn Ile Asp His Ser Tyr Leu Lys Gly Ile Asp Ile Ala Ser Lys Lys
    930                 935                 940

Lys Thr Ser Asn Val Glu Asn Thr Glu Phe Glu Ala Ile Ser Thr Lys
945                 950                 955                 960

Ile Phe Thr Asp Glu Leu Gly Phe Ser Gly Lys His Leu Gly Gly Ser
                965                 970                 975

Asn Lys Pro Asp Gly Leu Leu Trp Asp Asp Asp Cys Ala Ile Ile Leu
            980                 985                 990

Asp Ser Lys Ala Tyr Ser Glu Gly  Phe Pro Leu Thr Ala  Ser His Thr
        995                 1000                1005

Asp Ala  Met Gly Arg Tyr Leu  Arg Gln Phe Thr Glu  Arg Lys Glu
    1010                1015                1020

Glu Ile  Lys Pro Thr Trp Trp  Asp Ile Ala Pro Glu  His Leu Asp
    1025                1030                1035

Asn Thr  Tyr Phe Ala Tyr Val  Ser Gly Ser Phe Ser  Gly Asn Tyr
    1040                1045                1050
```

Lys Glu Gln Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly
1055 1060 1065

Gly Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr
1070 1075 1080

Lys Thr Gln Lys Met Ser Lys Lys Glu Val Lys Lys Ser Ile Leu
1085 1090 1095

Asp Tyr Asn Ile Ser Tyr
1100

<210> 61
<211> 1464
<212> PRT
<213> Homo sapiens

<400> 61

Met Phe Ser Phe Val Asp Leu Arg Leu Leu Leu Leu Leu Ala Ala Thr
1 5 10 15

Ala Leu Leu Thr His Gly Gln Glu Glu Gly Gln Val Glu Gly Gln Asp
20 25 30

Glu Asp Ile Pro Pro Ile Thr Cys Val Gln Asn Gly Leu Arg Tyr His
35 40 45

Asp Arg Asp Val Trp Lys Pro Glu Pro Cys Arg Ile Cys Val Cys Asp
50 55 60

Asn Gly Lys Val Leu Cys Asp Asp Val Ile Cys Asp Glu Thr Lys Asn
65 70 75 80

Cys Pro Gly Ala Glu Val Pro Glu Gly Glu Cys Cys Pro Val Cys Pro
85 90 95

Asp Gly Ser Glu Ser Pro Thr Asp Gln Glu Thr Thr Gly Val Glu Gly
100 105 110

Pro Lys Gly Asp Thr Gly Pro Arg Gly Pro Arg Gly Pro Ala Gly Pro
115 120 125

Pro Gly Arg Asp Gly Ile Pro Gly Gln Pro Gly Leu Pro Gly Pro Pro
130 135 140

Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly Gly Asn Phe Ala
145 150 155 160

Pro Gln Leu Ser Tyr Gly Tyr Asp Glu Lys Ser Thr Gly Gly Ile Ser
165 170 175

```
Val Pro Gly Pro Met Gly Pro Ser Gly Pro Arg Gly Leu Pro Gly Pro
            180                 185                 190

Pro Gly Ala Pro Gly Pro Gln Gly Phe Gln Gly Pro Pro Gly Glu Pro
        195                 200                 205

Gly Glu Pro Gly Ala Ser Gly Pro Met Gly Pro Arg Gly Pro Pro Gly
    210                 215                 220

Pro Pro Gly Lys Asn Gly Asp Asp Gly Glu Ala Gly Lys Pro Gly Arg
225                 230                 235                 240

Pro Gly Glu Arg Gly Pro Pro Gly Pro Gln Gly Ala Arg Gly Leu Pro
                245                 250                 255

Gly Thr Ala Gly Leu Pro Gly Met Lys Gly His Arg Gly Phe Ser Gly
            260                 265                 270

Leu Asp Gly Ala Lys Gly Asp Ala Gly Pro Ala Gly Pro Lys Gly Glu
        275                 280                 285

Pro Gly Ser Pro Gly Glu Asn Gly Ala Pro Gly Gln Met Gly Pro Arg
    290                 295                 300

Gly Leu Pro Gly Glu Arg Gly Arg Pro Gly Ala Pro Gly Pro Ala Gly
305                 310                 315                 320

Ala Arg Gly Asn Asp Gly Ala Thr Gly Ala Ala Gly Pro Pro Gly Pro
                325                 330                 335

Thr Gly Pro Ala Gly Pro Pro Gly Phe Pro Gly Ala Val Gly Ala Lys
            340                 345                 350

Gly Glu Ala Gly Pro Gln Gly Pro Arg Gly Ser Glu Gly Pro Gln Gly
        355                 360                 365

Val Arg Gly Glu Pro Gly Pro Pro Gly Pro Ala Gly Ala Ala Gly Pro
    370                 375                 380

Ala Gly Asn Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys Gly Ala Asn
385                 390                 395                 400

Gly Ala Pro Gly Ile Ala Gly Ala Pro Gly Phe Pro Gly Ala Arg Gly
                405                 410                 415

Pro Ser Gly Pro Gln Gly Pro Gly Gly Pro Pro Gly Pro Lys Gly Asn
            420                 425                 430

Ser Gly Glu Pro Gly Ala Pro Gly Ser Lys Gly Asp Thr Gly Ala Lys
        435                 440                 445
```

```
Gly Glu Pro Gly Pro Val Gly Val Gln Gly Pro Pro Gly Pro Ala Gly
    450                 455                 460

Glu Glu Gly Lys Arg Gly Ala Arg Gly Glu Pro Gly Pro Thr Gly Leu
465                 470                 475                 480

Pro Gly Pro Pro Gly Glu Arg Gly Gly Pro Gly Ser Arg Gly Phe Pro
                485                 490                 495

Gly Ala Asp Gly Val Ala Gly Pro Lys Gly Pro Ala Gly Glu Arg Gly
            500                 505                 510

Ser Pro Gly Pro Ala Gly Pro Lys Gly Ser Pro Gly Glu Ala Gly Arg
        515                 520                 525

Pro Gly Glu Ala Gly Leu Pro Gly Ala Lys Gly Leu Thr Gly Ser Pro
    530                 535                 540

Gly Ser Pro Gly Pro Asp Gly Lys Thr Gly Pro Pro Gly Pro Ala Gly
545                 550                 555                 560

Gln Asp Gly Arg Pro Gly Pro Pro Gly Pro Pro Gly Ala Arg Gly Gln
                565                 570                 575

Ala Gly Val Met Gly Phe Pro Gly Pro Lys Gly Ala Ala Gly Glu Pro
            580                 585                 590

Gly Lys Ala Gly Glu Arg Gly Val Pro Gly Pro Pro Gly Ala Val Gly
        595                 600                 605

Pro Ala Gly Lys Asp Gly Glu Ala Gly Ala Gln Gly Pro Pro Gly Pro
    610                 615                 620

Ala Gly Pro Ala Gly Glu Arg Gly Glu Gln Gly Pro Ala Gly Ser Pro
625                 630                 635                 640

Gly Phe Gln Gly Leu Pro Gly Pro Ala Gly Pro Pro Gly Glu Ala Gly
                645                 650                 655

Lys Pro Gly Glu Gln Gly Val Pro Gly Asp Leu Gly Ala Pro Gly Pro
            660                 665                 670

Ser Gly Ala Arg Gly Glu Arg Gly Phe Pro Gly Glu Arg Gly Val Gln
        675                 680                 685

Gly Pro Pro Gly Pro Ala Gly Pro Arg Gly Ala Asn Gly Ala Pro Gly
    690                 695                 700

Asn Asp Gly Ala Lys Gly Asp Ala Gly Ala Pro Gly Ala Pro Gly Ser
705                 710                 715                 720
```

```
Gln Gly Ala Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Ala Ala
                725                 730                 735

Gly Leu Pro Gly Pro Lys Gly Asp Arg Gly Asp Ala Gly Pro Lys Gly
            740                 745                 750

Ala Asp Gly Ser Pro Gly Lys Asp Gly Val Arg Gly Leu Thr Gly Pro
        755                 760                 765

Ile Gly Pro Pro Gly Pro Ala Gly Ala Pro Gly Asp Lys Gly Glu Ser
    770                 775                 780

Gly Pro Ser Gly Pro Ala Gly Pro Thr Gly Ala Arg Gly Ala Pro Gly
785                 790                 795                 800

Asp Arg Gly Glu Pro Gly Pro Pro Gly Pro Ala Gly Phe Ala Gly Pro
                805                 810                 815

Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys Gly Glu Pro Gly Asp Ala
            820                 825                 830

Gly Ala Lys Gly Asp Ala Gly Pro Pro Gly Pro Ala Gly Pro Ala Gly
        835                 840                 845

Pro Pro Gly Pro Ile Gly Asn Val Gly Ala Pro Gly Ala Lys Gly Ala
    850                 855                 860

Arg Gly Ser Ala Gly Pro Pro Gly Ala Thr Gly Phe Pro Gly Ala Ala
865                 870                 875                 880

Gly Arg Val Gly Pro Pro Gly Pro Ser Gly Asn Ala Gly Pro Pro Gly
                885                 890                 895

Pro Pro Gly Pro Ala Gly Lys Glu Gly Gly Lys Gly Pro Arg Gly Glu
            900                 905                 910

Thr Gly Pro Ala Gly Arg Pro Gly Glu Val Gly Pro Pro Gly Pro Pro
        915                 920                 925

Gly Pro Ala Gly Glu Lys Gly Ser Pro Gly Ala Asp Gly Pro Ala Gly
    930                 935                 940

Ala Pro Gly Thr Pro Gly Pro Gln Gly Ile Ala Gly Gln Arg Gly Val
945                 950                 955                 960

Val Gly Leu Pro Gly Gln Arg Gly Glu Arg Gly Phe Pro Gly Leu Pro
                965                 970                 975

Gly Pro Ser Gly Glu Pro Gly Lys Gln Gly Pro Ser Gly Ala Ser Gly
            980                 985                 990
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```
Glu Arg Gly Pro Pro Gly Pro Met  Gly Pro Pro Gly Leu  Ala Gly Pro
        995                 1000                1005


Pro Gly  Glu Ser Gly Arg Glu  Gly Ala Pro Gly Ala  Glu Gly Ser
    1010                1015                1020


Pro Gly  Arg Asp Gly Ser Pro  Gly Ala Lys Gly Asp  Arg Gly Glu
    1025                1030                1035


Thr Gly  Pro Ala Gly Pro Pro  Gly Ala Pro Gly Ala  Pro Gly Ala
    1040                1045                1050


Pro Gly  Pro Val Gly Pro Ala  Gly Lys Ser Gly Asp  Arg Gly Glu
    1055                1060                1065


Thr Gly  Pro Ala Gly Pro Ala  Gly Pro Val Gly Pro  Val Gly Ala
    1070                1075                1080


Arg Gly  Pro Ala Gly Pro Gln  Gly Pro Arg Gly Asp  Lys Gly Glu
    1085                1090                1095


Thr Gly  Glu Gln Gly Asp Arg  Gly Ile Lys Gly His  Arg Gly Phe
    1100                1105                1110


Ser Gly  Leu Gln Gly Pro Pro  Gly Pro Pro Gly Ser  Pro Gly Glu
    1115                1120                1125


Gln Gly  Pro Ser Gly Ala Ser  Gly Pro Ala Gly Pro  Arg Gly Pro
    1130                1135                1140


Pro Gly  Ser Ala Gly Ala Pro  Gly Lys Asp Gly Leu  Asn Gly Leu
    1145                1150                1155


Pro Gly  Pro Ile Gly Pro Pro  Gly Pro Arg Gly Arg  Thr Gly Asp
    1160                1165                1170


Ala Gly  Pro Val Gly Pro Pro  Gly Pro Pro Gly Pro  Pro Gly Pro
    1175                1180                1185


Pro Gly  Pro Pro Ser Ala Gly  Phe Asp Phe Ser Phe  Leu Pro Gln
    1190                1195                1200


Pro Pro  Gln Glu Lys Ala His  Asp Gly Gly Arg Tyr  Tyr Arg Ala
    1205                1210                1215


Asp Asp  Ala Asn Val Val Arg  Asp Arg Asp Leu Glu  Val Asp Thr
    1220                1225                1230


Thr Leu  Lys Ser Leu Ser Gln  Gln Ile Glu Asn Ile  Arg Ser Pro
    1235                1240                1245
```

```
Glu Gly  Ser Arg Lys Asn Pro  Ala Arg Thr Cys Arg  Asp Leu Lys
    1250                 1255                 1260

Met Cys  His Ser Asp Trp Lys  Ser Gly Glu Tyr Trp  Ile Asp Pro
    1265                 1270                 1275

Asn Gln  Gly Cys Asn Leu Asp  Ala Ile Lys Val Phe  Cys Asn Met
    1280                 1285                 1290

Glu Thr  Gly Glu Thr Cys Val  Tyr Pro Thr Gln Pro  Ser Val Ala
    1295                 1300                 1305

Gln Lys  Asn Trp Tyr Ile Ser  Lys Asn Pro Lys Asp  Lys Arg His
    1310                 1315                 1320

Val Trp  Phe Gly Glu Ser Met  Thr Asp Gly Phe Gln  Phe Glu Tyr
    1325                 1330                 1335

Gly Gly  Gln Gly Ser Asp Pro  Ala Asp Val Ala Ile  Gln Leu Thr
    1340                 1345                 1350

Phe Leu  Arg Leu Met Ser Thr  Glu Ala Ser Gln Asn  Ile Thr Tyr
    1355                 1360                 1365

His Cys  Lys Asn Ser Val Ala  Tyr Met Asp Gln Gln  Thr Gly Asn
    1370                 1375                 1380

Leu Lys  Lys Ala Leu Leu Leu  Gln Gly Ser Asn Glu  Ile Glu Ile
    1385                 1390                 1395

Arg Ala  Glu Gly Asn Ser Arg  Phe Thr Tyr Ser Val  Thr Val Asp
    1400                 1405                 1410

Gly Cys  Thr Ser His Thr Gly  Ala Trp Gly Lys Thr  Val Ile Glu
    1415                 1420                 1425

Tyr Lys  Thr Thr Lys Thr Ser  Arg Leu Pro Ile Ile  Asp Val Ala
    1430                 1435                 1440

Pro Leu  Asp Val Gly Ala Pro  Asp Gln Glu Phe Gly  Phe Asp Val
    1445                 1450                 1455

Gly Pro  Val Cys Phe Leu
    1460
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<210> 62
<211> 1366
<212> PRT
<213> Homo sapiens

<400> 62

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Met Leu Ser Phe Val Asp Thr Arg Thr Leu Leu Leu Leu Ala Val Thr
1               5                  10                  15

Leu Cys Leu Ala Thr Cys Gln Ser Leu Gln Glu Glu Thr Val Arg Lys
            20                  25                  30

Gly Pro Ala Gly Asp Arg Gly Pro Arg Gly Glu Arg Gly Pro Pro Gly
        35                  40                  45

Pro Pro Gly Arg Asp Gly Glu Asp Gly Pro Thr Gly Pro Pro Gly Pro
    50                  55                  60

Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly Gly Asn Phe Ala Ala Gln
65                  70                  75                  80

Tyr Asp Gly Lys Gly Val Gly Leu Gly Pro Gly Pro Met Gly Leu Met
                85                  90                  95

Gly Pro Arg Gly Pro Pro Gly Ala Ala Gly Ala Pro Gly Pro Gln Gly
            100                 105                 110

Phe Gln Gly Pro Ala Gly Glu Pro Gly Glu Pro Gly Gln Thr Gly Pro
        115                 120                 125

Ala Gly Ala Arg Gly Pro Ala Gly Pro Pro Gly Lys Ala Gly Glu Asp
    130                 135                 140

Gly His Pro Gly Lys Pro Gly Arg Pro Gly Glu Arg Gly Val Val Gly
145                 150                 155                 160

Pro Gln Gly Ala Arg Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Phe
                165                 170                 175

Lys Gly Ile Arg Gly His Asn Gly Leu Asp Gly Leu Lys Gly Gln Pro
            180                 185                 190

Gly Ala Pro Gly Val Lys Gly Glu Pro Gly Ala Pro Gly Glu Asn Gly
        195                 200                 205

Thr Pro Gly Gln Thr Gly Ala Arg Gly Leu Pro Gly Glu Arg Gly Arg
    210                 215                 220

Val Gly Ala Pro Gly Pro Ala Gly Ala Arg Gly Ser Asp Gly Ser Val
225                 230                 235                 240

Gly Pro Val Gly Pro Ala Gly Pro Ile Gly Ser Ala Gly Pro Pro Gly
                245                 250                 255

Phe Pro Gly Ala Pro Gly Pro Lys Gly Glu Ile Gly Ala Val Gly Asn
            260                 265                 270
```

```
Ala Gly Pro Ala Gly Pro Ala Gly Pro Arg Gly Glu Val Gly Leu Pro
        275                 280                 285

Gly Leu Ser Gly Pro Val Gly Pro Pro Gly Asn Pro Gly Ala Asn Gly
    290                 295                 300

Leu Thr Gly Ala Lys Gly Ala Ala Gly Leu Pro Gly Val Ala Gly Ala
305                 310                 315                 320

Pro Gly Leu Pro Gly Pro Arg Gly Ile Pro Gly Pro Val Gly Ala Ala
                325                 330                 335

Gly Ala Thr Gly Ala Arg Gly Leu Val Gly Glu Pro Gly Pro Ala Gly
            340                 345                 350

Ser Lys Gly Glu Ser Gly Asn Lys Gly Glu Pro Gly Ser Ala Gly Pro
        355                 360                 365

Gln Gly Pro Pro Gly Pro Ser Gly Glu Glu Gly Lys Arg Gly Pro Asn
    370                 375                 380

Gly Glu Ala Gly Ser Ala Gly Pro Pro Gly Pro Pro Gly Leu Arg Gly
385                 390                 395                 400

Ser Pro Gly Ser Arg Gly Leu Pro Gly Ala Asp Gly Arg Ala Gly Val
                405                 410                 415

Met Gly Pro Pro Gly Ser Arg Gly Ala Ser Gly Pro Ala Gly Val Arg
            420                 425                 430

Gly Pro Asn Gly Asp Ala Gly Arg Pro Gly Glu Pro Gly Leu Met Gly
        435                 440                 445

Pro Arg Gly Leu Pro Gly Ser Pro Gly Asn Ile Gly Pro Ala Gly Lys
    450                 455                 460

Glu Gly Pro Val Gly Leu Pro Gly Ile Asp Gly Arg Pro Gly Pro Ile
465                 470                 475                 480

Gly Pro Ala Gly Ala Arg Gly Glu Pro Gly Asn Ile Gly Phe Pro Gly
                485                 490                 495

Pro Lys Gly Pro Thr Gly Asp Pro Gly Lys Asn Gly Asp Lys Gly His
            500                 505                 510

Ala Gly Leu Ala Gly Ala Arg Gly Ala Pro Gly Pro Asp Gly Asn Asn
        515                 520                 525

Gly Ala Gln Gly Pro Pro Gly Pro Gln Gly Val Gln Gly Gly Lys Gly
    530                 535                 540
```

```
Glu Gln Gly Pro Pro Gly Pro Pro Gly Phe Gln Gly Leu Pro Gly Pro
545                 550                 555                 560

Ser Gly Pro Ala Gly Glu Val Gly Lys Pro Gly Glu Arg Gly Leu His
                565                 570                 575

Gly Glu Phe Gly Leu Pro Gly Pro Ala Gly Pro Arg Gly Glu Arg Gly
            580                 585                 590

Pro Pro Gly Glu Ser Gly Ala Ala Gly Pro Thr Gly Pro Ile Gly Ser
        595                 600                 605

Arg Gly Pro Ser Gly Pro Pro Gly Pro Asp Gly Asn Lys Gly Glu Pro
    610                 615                 620

Gly Val Val Gly Ala Val Gly Thr Ala Gly Pro Ser Gly Pro Ser Gly
625                 630                 635                 640

Leu Pro Gly Glu Arg Gly Ala Ala Gly Ile Pro Gly Gly Lys Gly Glu
                645                 650                 655

Lys Gly Glu Pro Gly Leu Arg Gly Glu Ile Gly Asn Pro Gly Arg Asp
            660                 665                 670

Gly Ala Arg Gly Ala Pro Gly Ala Val Gly Ala Pro Gly Pro Ala Gly
        675                 680                 685

Ala Thr Gly Asp Arg Gly Glu Ala Gly Ala Ala Gly Pro Ala Gly Pro
    690                 695                 700

Ala Gly Pro Arg Gly Ser Pro Gly Glu Arg Gly Glu Val Gly Pro Ala
705                 710                 715                 720

Gly Pro Asn Gly Phe Ala Gly Pro Ala Gly Ala Ala Gly Gln Pro Gly
                725                 730                 735

Ala Lys Gly Glu Arg Gly Ala Lys Gly Pro Lys Gly Glu Asn Gly Val
            740                 745                 750

Val Gly Pro Thr Gly Pro Val Gly Ala Ala Gly Pro Ala Gly Pro Asn
        755                 760                 765

Gly Pro Pro Gly Pro Ala Gly Ser Arg Gly Asp Gly Gly Pro Pro Gly
    770                 775                 780

Met Thr Gly Phe Pro Gly Ala Ala Gly Arg Thr Gly Pro Pro Gly Pro
785                 790                 795                 800

Ser Gly Ile Ser Gly Pro Pro Gly Pro Pro Gly Pro Ala Gly Lys Glu
                805                 810                 815
```

```
Gly Leu Arg Gly Pro Arg Gly Asp Gln Gly Pro Val Gly Arg Thr Gly
            820                 825                 830

Glu Val Gly Ala Val Gly Pro Pro Gly Phe Ala Gly Glu Lys Gly Pro
        835                 840                 845

Ser Gly Glu Ala Gly Thr Ala Gly Pro Pro Gly Thr Pro Gly Pro Gln
    850                 855                 860

Gly Leu Leu Gly Ala Pro Gly Ile Leu Gly Leu Pro Gly Ser Arg Gly
865                 870                 875                 880

Glu Arg Gly Leu Pro Gly Val Ala Gly Ala Val Gly Glu Pro Gly Pro
                885                 890                 895

Leu Gly Ile Ala Gly Pro Pro Gly Ala Arg Gly Pro Pro Gly Ala Val
            900                 905                 910

Gly Ser Pro Gly Val Asn Gly Ala Pro Gly Glu Ala Gly Arg Asp Gly
        915                 920                 925

Asn Pro Gly Asn Asp Gly Pro Pro Gly Arg Asp Gly Gln Pro Gly His
    930                 935                 940

Lys Gly Glu Arg Gly Tyr Pro Gly Asn Ile Gly Pro Val Gly Ala Ala
945                 950                 955                 960

Gly Ala Pro Gly Pro His Gly Pro Val Gly Pro Ala Gly Lys His Gly
                965                 970                 975

Asn Arg Gly Glu Thr Gly Pro Ser Gly Pro Val Gly Pro Ala Gly Ala
            980                 985                 990

Val Gly Pro Arg Gly Pro Ser Gly  Pro Gln Gly Ile Arg  Gly Asp Lys
        995                 1000                1005

Gly Glu  Pro Gly Glu Lys Gly  Pro Arg Gly Leu Pro  Gly Leu Lys
    1010                1015                1020

Gly His  Asn Gly Leu Gln Gly  Leu Pro Gly Ile Ala  Gly His His
    1025                1030                1035

Gly Asp  Gln Gly Ala Pro Gly  Ser Val Gly Pro Ala  Gly Pro Arg
    1040                1045                1050

Gly Pro  Ala Gly Pro Ser Gly  Pro Ala Gly Lys Asp  Gly Arg Thr
    1055                1060                1065

Gly His  Pro Gly Thr Val Gly  Pro Ala Gly Ile Arg  Gly Pro Gln
    1070                1075                1080
```

```
Gly His  Gln Gly Pro Ala Gly  Pro Pro Gly Pro Pro  Gly Pro Pro
    1085                1090                1095

Gly Pro  Pro Gly Val Ser Gly  Gly Gly Tyr Asp Phe  Gly Tyr Asp
    1100                1105                1110

Gly Asp  Phe Tyr Arg Ala Asp  Gln Pro Arg Ser Ala  Pro Ser Leu
    1115                1120                1125

Arg Pro  Lys Asp Tyr Glu Val  Asp Ala Thr Leu Lys  Ser Leu Asn
    1130                1135                1140

Asn Gln  Ile Glu Thr Leu Leu  Thr Pro Glu Gly Ser  Arg Lys Asn
    1145                1150                1155

Pro Ala  Arg Thr Cys Arg Asp  Leu Arg Leu Ser His  Pro Glu Trp
    1160                1165                1170

Ser Ser  Gly Tyr Tyr Trp Ile  Asp Pro Asn Gln Gly  Cys Thr Met
    1175                1180                1185

Asp Ala  Ile Lys Val Tyr Cys  Asp Phe Ser Thr Gly  Glu Thr Cys
    1190                1195                1200

Ile Arg  Ala Gln Pro Glu Asn  Ile Pro Ala Lys Asn  Trp Tyr Arg
    1205                1210                1215

Ser Ser  Lys Asp Lys Lys His  Val Trp Leu Gly Glu  Thr Ile Asn
    1220                1225                1230

Ala Gly  Ser Gln Phe Glu Tyr  Asn Val Glu Gly Val  Thr Ser Lys
    1235                1240                1245

Glu Met  Ala Thr Gln Leu Ala  Phe Met Arg Leu Leu  Ala Asn Tyr
    1250                1255                1260

Ala Ser  Gln Asn Ile Thr Tyr  His Cys Lys Asn Ser  Ile Ala Tyr
    1265                1270                1275

Met Asp  Glu Glu Thr Gly Asn  Leu Lys Lys Ala Val  Ile Leu Gln
    1280                1285                1290

Gly Ser  Asn Asp Val Glu Leu  Val Ala Glu Gly Asn  Ser Arg Phe
    1295                1300                1305

Thr Tyr  Thr Val Leu Val Asp  Gly Cys Ser Lys Lys  Thr Asn Glu
    1310                1315                1320

Trp Gly  Lys Thr Ile Ile Glu  Tyr Lys Thr Asn Lys  Pro Ser Arg
    1325                1330                1335
```

Leu Pro Phe Leu Asp Ile Ala Pro Leu Asp Ile Gly Gly Ala Asp
1340 1345 1350

Gln Glu Phe Phe Val Asp Ile Gly Pro Val Cys Phe Lys
1355 1360 1365

<210> 63
<211> 1487
<212> PRT
<213> Homo sapiens

<400> 63

Met Ile Arg Leu Gly Ala Pro Gln Thr Leu Val Leu Leu Thr Leu Leu
1 5 10 15

Val Ala Ala Val Leu Arg Cys Gln Gly Gln Asp Val Gln Glu Ala Gly
20 25 30

Ser Cys Val Gln Asp Gly Gln Arg Tyr Asn Asp Lys Asp Val Trp Lys
35 40 45

Pro Glu Pro Cys Arg Ile Cys Val Cys Asp Thr Gly Thr Val Leu Cys
50 55 60

Asp Asp Ile Ile Cys Glu Asp Val Lys Asp Cys Leu Ser Pro Glu Ile
65 70 75 80

Pro Phe Gly Glu Cys Cys Pro Ile Cys Pro Thr Asp Leu Ala Thr Ala
85 90 95

Ser Gly Gln Pro Gly Pro Lys Gly Gln Lys Gly Glu Pro Gly Asp Ile
100 105 110

Lys Asp Ile Val Gly Pro Lys Gly Pro Pro Gly Pro Gln Gly Pro Ala
115 120 125

Gly Glu Gln Gly Pro Arg Gly Asp Arg Gly Asp Lys Gly Glu Lys Gly
130 135 140

Ala Pro Gly Pro Arg Gly Arg Asp Gly Glu Pro Gly Thr Pro Gly Asn
145 150 155 160

Pro Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly
165 170 175

Gly Asn Phe Ala Ala Gln Met Ala Gly Gly Phe Asp Glu Lys Ala Gly
180 185 190

Gly Ala Gln Leu Gly Val Met Gln Gly Pro Met Gly Pro Met Gly Pro
195 200 205

Arg Gly Pro Pro Gly Pro Ala Gly Ala Pro Gly Pro Gln Gly Phe Gln

```
    210                 215                 220

Gly Asn Pro Gly Glu Pro Gly Glu Pro Gly Val Ser Gly Pro Met Gly
225                 230                 235                 240

Pro Arg Gly Pro Pro Gly Pro Pro Gly Lys Pro Gly Asp Asp Gly Glu
                245                 250                 255

Ala Gly Lys Pro Gly Lys Ala Gly Glu Arg Gly Pro Pro Gly Pro Gln
            260                 265                 270

Gly Ala Arg Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Val Lys Gly
        275                 280                 285

His Arg Gly Tyr Pro Gly Leu Asp Gly Ala Lys Gly Glu Ala Gly Ala
    290                 295                 300

Pro Gly Val Lys Gly Glu Ser Gly Ser Pro Gly Glu Asn Gly Ser Pro
305                 310                 315                 320

Gly Pro Met Gly Pro Arg Gly Leu Pro Gly Glu Arg Gly Arg Thr Gly
                325                 330                 335

Pro Ala Gly Ala Ala Gly Ala Arg Gly Asn Asp Gly Gln Pro Gly Pro
            340                 345                 350

Ala Gly Pro Pro Gly Pro Val Gly Pro Ala Gly Gly Pro Gly Phe Pro
        355                 360                 365

Gly Ala Pro Gly Ala Lys Gly Glu Ala Gly Pro Thr Gly Ala Arg Gly
    370                 375                 380

Pro Glu Gly Ala Gln Gly Pro Arg Gly Glu Pro Gly Thr Pro Gly Ser
385                 390                 395                 400

Pro Gly Pro Ala Gly Ala Ser Gly Asn Pro Gly Thr Asp Gly Ile Pro
                405                 410                 415

Gly Ala Lys Gly Ser Ala Gly Ala Pro Gly Ile Ala Gly Ala Pro Gly
            420                 425                 430

Phe Pro Gly Pro Arg Gly Pro Pro Gly Pro Gln Gly Ala Thr Gly Pro
        435                 440                 445

Leu Gly Pro Lys Gly Gln Thr Gly Glu Pro Gly Ile Ala Gly Phe Lys
    450                 455                 460

Gly Glu Gln Gly Pro Lys Gly Glu Pro Gly Pro Ala Gly Pro Gln Gly
465                 470                 475                 480

Ala Pro Gly Pro Ala Gly Glu Glu Gly Lys Arg Gly Ala Arg Gly Glu
```

485 490 495

Pro Gly Gly Val Gly Pro Ile Gly Pro Pro Gly Glu Arg Gly Ala Pro
500 505 510

Gly Asn Arg Gly Phe Pro Gly Gln Asp Gly Leu Ala Gly Pro Lys Gly
515 520 525

Ala Pro Gly Glu Arg Gly Pro Ser Gly Leu Ala Gly Pro Lys Gly Ala
530 535 540

Asn Gly Asp Pro Gly Arg Pro Gly Glu Pro Gly Leu Pro Gly Ala Arg
545 550 555 560

Gly Leu Thr Gly Arg Pro Gly Asp Ala Gly Pro Gln Gly Lys Val Gly
565 570 575

Pro Ser Gly Ala Pro Gly Glu Asp Gly Arg Pro Gly Pro Pro Gly Pro
580 585 590

Gln Gly Ala Arg Gly Gln Pro Gly Val Met Gly Phe Pro Gly Pro Lys
595 600 605

Gly Ala Asn Gly Glu Pro Gly Lys Ala Gly Glu Lys Gly Leu Pro Gly
610 615 620

Ala Pro Gly Leu Arg Gly Leu Pro Gly Lys Asp Gly Glu Thr Gly Ala
625 630 635 640

Ala Gly Pro Pro Gly Pro Ala Gly Pro Ala Gly Glu Arg Gly Glu Gln
645 650 655

Gly Ala Pro Gly Pro Ser Gly Phe Gln Gly Leu Pro Gly Pro Pro Gly
660 665 670

Pro Pro Gly Glu Gly Gly Lys Pro Gly Asp Gln Gly Val Pro Gly Glu
675 680 685

Ala Gly Ala Pro Gly Leu Val Gly Pro Arg Gly Glu Arg Gly Phe Pro
690 695 700

Gly Glu Arg Gly Ser Pro Gly Ala Gln Gly Leu Gln Gly Pro Arg Gly
705 710 715 720

Leu Pro Gly Thr Pro Gly Thr Asp Gly Pro Lys Gly Ala Ser Gly Pro
725 730 735

Ala Gly Pro Pro Gly Ala Gln Gly Pro Pro Gly Leu Gln Gly Met Pro
740 745 750

Gly Glu Arg Gly Ala Ala Gly Ile Ala Gly Pro Lys Gly Asp Arg Gly

```
        755                 760                 765

Asp Val Gly Glu Lys Gly Pro Glu Gly Ala Pro Gly Lys Asp Gly Gly
    770                 775                 780

Arg Gly Leu Thr Gly Pro Ile Gly Pro Pro Gly Pro Ala Gly Ala Asn
785                 790                 795                 800

Gly Glu Lys Gly Glu Val Gly Pro Pro Gly Pro Ala Gly Ser Ala Gly
                805                 810                 815

Ala Arg Gly Ala Pro Gly Glu Arg Gly Glu Thr Gly Pro Pro Gly Pro
            820                 825                 830

Ala Gly Phe Ala Gly Pro Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys
        835                 840                 845

Gly Glu Gln Gly Glu Ala Gly Gln Lys Gly Asp Ala Gly Ala Pro Gly
    850                 855                 860

Pro Gln Gly Pro Ser Gly Ala Pro Gly Pro Gln Gly Pro Thr Gly Val
865                 870                 875                 880

Thr Gly Pro Lys Gly Ala Arg Gly Ala Gln Gly Pro Pro Gly Ala Thr
                885                 890                 895

Gly Phe Pro Gly Ala Ala Gly Arg Val Gly Pro Pro Gly Ser Asn Gly
            900                 905                 910

Asn Pro Gly Pro Pro Gly Pro Pro Gly Pro Ser Gly Lys Asp Gly Pro
        915                 920                 925

Lys Gly Ala Arg Gly Asp Ser Gly Pro Pro Gly Arg Ala Gly Glu Pro
    930                 935                 940

Gly Leu Gln Gly Pro Ala Gly Pro Pro Gly Glu Lys Gly Glu Pro Gly
945                 950                 955                 960

Asp Asp Gly Pro Ser Gly Ala Glu Gly Pro Pro Gly Pro Gln Gly Leu
                965                 970                 975

Ala Gly Gln Arg Gly Ile Val Gly Leu Pro Gly Gln Arg Gly Glu Arg
            980                 985                 990

Gly Phe Pro Gly Leu Pro Gly Pro  Ser Gly Glu Pro Gly  Lys Gln Gly
        995                 1000                1005

Ala Pro  Gly Ala Ser Gly Asp  Arg Gly Pro Pro Gly  Pro Val Gly
    1010                1015                1020

Pro Pro  Gly Leu Thr Gly Pro  Ala Gly Glu Pro Gly  Arg Glu Gly
```

```
    1025                1030                1035

Ser Pro  Gly Ala Asp Gly Pro  Pro Gly Arg Asp Gly  Ala Ala Gly
    1040                1045                1050

Val Lys  Gly Asp Arg Gly Glu  Thr Gly Ala Val Gly  Ala Pro Gly
    1055                1060                1065

Ala Pro  Gly Pro Pro Gly Ser  Pro Gly Pro Ala Gly  Pro Thr Gly
    1070                1075                1080

Lys Gln  Gly Asp Arg Gly Glu  Ala Gly Ala Gln Gly  Pro Met Gly
    1085                1090                1095

Pro Ser  Gly Pro Ala Gly Ala  Arg Gly Ile Gln Gly  Pro Gln Gly
    1100                1105                1110

Pro Arg  Gly Asp Lys Gly Glu  Ala Gly Glu Pro Gly  Glu Arg Gly
    1115                1120                1125

Leu Lys  Gly His Arg Gly Phe  Thr Gly Leu Gln Gly  Leu Pro Gly
    1130                1135                1140

Pro Pro  Gly Pro Ser Gly Asp  Gln Gly Ala Ser Gly  Pro Ala Gly
    1145                1150                1155

Pro Ser  Gly Pro Arg Gly Pro  Pro Gly Pro Val Gly  Pro Ser Gly
    1160                1165                1170

Lys Asp  Gly Ala Asn Gly Ile  Pro Gly Pro Ile Gly  Pro Pro Gly
    1175                1180                1185

Pro Arg  Gly Arg Ser Gly Glu  Thr Gly Pro Ala Gly  Pro Pro Gly
    1190                1195                1200

Asn Pro  Gly Pro Pro Gly Pro  Pro Gly Pro Pro Gly  Pro Gly Ile
    1205                1210                1215

Asp Met  Ser Ala Phe Ala Gly  Leu Gly Pro Arg Glu  Lys Gly Pro
    1220                1225                1230

Asp Pro  Leu Gln Tyr Met Arg  Ala Asp Gln Ala Ala  Gly Gly Leu
    1235                1240                1245

Arg Gln  His Asp Ala Glu Val  Asp Ala Thr Leu Lys  Ser Leu Asn
    1250                1255                1260

Asn Gln  Ile Glu Ser Ile Arg  Ser Pro Glu Gly Ser  Arg Lys Asn
    1265                1270                1275

Pro Ala  Arg Thr Cys Arg Asp  Leu Lys Leu Cys His  Pro Glu Trp
```

1280 1285 1290

Lys Ser Gly Asp Tyr Trp Ile Asp Pro Asn Gln Gly Cys Thr Leu
1295 1300 1305

Asp Ala Met Lys Val Phe Cys Asn Met Glu Thr Gly Glu Thr Cys
1310 1315 1320

Val Tyr Pro Asn Pro Ala Asn Val Pro Lys Lys Asn Trp Trp Ser
1325 1330 1335

Ser Lys Ser Lys Glu Lys Lys His Ile Trp Phe Gly Glu Thr Ile
1340 1345 1350

Asn Gly Gly Phe His Phe Ser Tyr Gly Asp Asp Asn Leu Ala Pro
1355 1360 1365

Asn Thr Ala Asn Val Gln Met Thr Phe Leu Arg Leu Leu Ser Thr
1370 1375 1380

Glu Gly Ser Gln Asn Ile Thr Tyr His Cys Lys Asn Ser Ile Ala
1385 1390 1395

Tyr Leu Asp Glu Ala Ala Gly Asn Leu Lys Lys Ala Leu Leu Ile
1400 1405 1410

Gln Gly Ser Asn Asp Val Glu Ile Arg Ala Glu Gly Asn Ser Arg
1415 1420 1425

Phe Thr Tyr Thr Ala Leu Lys Asp Gly Cys Thr Lys His Thr Gly
1430 1435 1440

Lys Trp Gly Lys Thr Val Ile Glu Tyr Arg Ser Gln Lys Thr Ser
1445 1450 1455

Arg Leu Pro Ile Ile Asp Ile Ala Pro Met Asp Ile Gly Gly Pro
1460 1465 1470

Glu Gln Glu Phe Gly Val Asp Ile Gly Pro Val Cys Phe Leu
1475 1480 1485

<210> 64
<211> 1418
<212> PRT
<213> Homo sapiens

<400> 64

Met Ile Arg Leu Gly Ala Pro Gln Thr Leu Val Leu Leu Thr Leu Leu
1 5 10 15

Val Ala Ala Val Leu Arg Cys Gln Gly Gln Asp Val Arg Gln Pro Gly
20 25 30

```
Pro Lys Gly Gln Lys Gly Glu Pro Gly Asp Ile Lys Asp Ile Val Gly
        35                  40                  45

Pro Lys Gly Pro Pro Gly Pro Gln Gly Pro Ala Gly Glu Gln Gly Pro
    50                  55                  60

Arg Gly Asp Arg Gly Asp Lys Gly Glu Lys Gly Ala Pro Gly Pro Arg
65                  70                  75                  80

Gly Arg Asp Gly Glu Pro Gly Thr Pro Gly Asn Pro Gly Pro Pro Gly
                85                  90                  95

Pro Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly Gly Asn Phe Ala Ala
            100                 105                 110

Gln Met Ala Gly Gly Phe Asp Glu Lys Ala Gly Gly Ala Gln Leu Gly
        115                 120                 125

Val Met Gln Gly Pro Met Gly Pro Met Gly Pro Arg Gly Pro Pro Gly
    130                 135                 140

Pro Ala Gly Ala Pro Gly Pro Gln Gly Phe Gln Gly Asn Pro Gly Glu
145                 150                 155                 160

Pro Gly Glu Pro Gly Val Ser Gly Pro Met Gly Pro Arg Gly Pro Pro
                165                 170                 175

Gly Pro Pro Gly Lys Pro Gly Asp Asp Gly Glu Ala Gly Lys Pro Gly
            180                 185                 190

Lys Ala Gly Glu Arg Gly Pro Pro Gly Pro Gln Gly Ala Arg Gly Phe
        195                 200                 205

Pro Gly Thr Pro Gly Leu Pro Gly Val Lys Gly His Arg Gly Tyr Pro
    210                 215                 220

Gly Leu Asp Gly Ala Lys Gly Glu Ala Gly Ala Pro Gly Val Lys Gly
225                 230                 235                 240

Glu Ser Gly Ser Pro Gly Glu Asn Gly Ser Pro Gly Pro Met Gly Pro
                245                 250                 255

Arg Gly Leu Pro Gly Glu Arg Gly Arg Thr Gly Pro Ala Gly Ala Ala
            260                 265                 270

Gly Ala Arg Gly Asn Asp Gly Gln Pro Gly Pro Ala Gly Pro Pro Gly
        275                 280                 285

Pro Val Gly Pro Ala Gly Gly Pro Gly Phe Pro Gly Ala Pro Gly Ala
    290                 295                 300
```

```
Lys Gly Glu Ala Gly Pro Thr Gly Ala Arg Gly Pro Glu Gly Ala Gln
305                 310                 315                 320

Gly Pro Arg Gly Glu Pro Gly Thr Pro Gly Ser Pro Gly Pro Ala Gly
                325                 330                 335

Ala Ser Gly Asn Pro Gly Thr Asp Gly Ile Pro Gly Ala Lys Gly Ser
            340                 345                 350

Ala Gly Ala Pro Gly Ile Ala Gly Ala Pro Gly Phe Pro Gly Pro Arg
        355                 360                 365

Gly Pro Pro Gly Pro Gln Gly Ala Thr Gly Pro Leu Gly Pro Lys Gly
    370                 375                 380

Gln Thr Gly Glu Pro Gly Ile Ala Gly Phe Lys Gly Glu Gln Gly Pro
385                 390                 395                 400

Lys Gly Glu Pro Gly Pro Ala Gly Pro Gln Gly Ala Pro Gly Pro Ala
                405                 410                 415

Gly Glu Glu Gly Lys Arg Gly Ala Arg Gly Glu Pro Gly Gly Val Gly
            420                 425                 430

Pro Ile Gly Pro Pro Gly Glu Arg Gly Ala Pro Gly Asn Arg Gly Phe
        435                 440                 445

Pro Gly Gln Asp Gly Leu Ala Gly Pro Lys Gly Ala Pro Gly Glu Arg
    450                 455                 460

Gly Pro Ser Gly Leu Ala Gly Pro Lys Gly Ala Asn Gly Asp Pro Gly
465                 470                 475                 480

Arg Pro Gly Glu Pro Gly Leu Pro Gly Ala Arg Gly Leu Thr Gly Arg
                485                 490                 495

Pro Gly Asp Ala Gly Pro Gln Gly Lys Val Gly Pro Ser Gly Ala Pro
            500                 505                 510

Gly Glu Asp Gly Arg Pro Gly Pro Pro Gly Pro Gln Gly Ala Arg Gly
        515                 520                 525

Gln Pro Gly Val Met Gly Phe Pro Gly Pro Lys Gly Ala Asn Gly Glu
    530                 535                 540

Pro Gly Lys Ala Gly Glu Lys Gly Leu Pro Gly Ala Pro Gly Leu Arg
545                 550                 555                 560

Gly Leu Pro Gly Lys Asp Gly Glu Thr Gly Ala Ala Gly Pro Pro Gly
                565                 570                 575
```

```
Pro Ala Gly Pro Ala Gly Glu Arg Gly Glu Gln Gly Ala Pro Gly Pro
            580                 585                 590

Ser Gly Phe Gln Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Glu Gly
        595                 600                 605

Gly Lys Pro Gly Asp Gln Gly Val Pro Gly Glu Ala Gly Ala Pro Gly
    610                 615                 620

Leu Val Gly Pro Arg Gly Glu Arg Gly Phe Pro Gly Glu Arg Gly Ser
625                 630                 635                 640

Pro Gly Ala Gln Gly Leu Gln Gly Pro Arg Gly Leu Pro Gly Thr Pro
                645                 650                 655

Gly Thr Asp Gly Pro Lys Gly Ala Ser Gly Pro Ala Gly Pro Pro Gly
            660                 665                 670

Ala Gln Gly Pro Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Ala
        675                 680                 685

Ala Gly Ile Ala Gly Pro Lys Gly Asp Arg Gly Asp Val Gly Glu Lys
    690                 695                 700

Gly Pro Glu Gly Ala Pro Gly Lys Asp Gly Gly Arg Gly Leu Thr Gly
705                 710                 715                 720

Pro Ile Gly Pro Pro Gly Pro Ala Gly Ala Asn Gly Glu Lys Gly Glu
                725                 730                 735

Val Gly Pro Pro Gly Pro Ala Gly Ser Ala Gly Ala Arg Gly Ala Pro
            740                 745                 750

Gly Glu Arg Gly Glu Thr Gly Pro Pro Gly Pro Ala Gly Phe Ala Gly
        755                 760                 765

Pro Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys Gly Glu Gln Gly Glu
    770                 775                 780

Ala Gly Gln Lys Gly Asp Ala Gly Ala Pro Gly Pro Gln Gly Pro Ser
785                 790                 795                 800

Gly Ala Pro Gly Pro Gln Gly Pro Thr Gly Val Thr Gly Pro Lys Gly
                805                 810                 815

Ala Arg Gly Ala Gln Gly Pro Pro Gly Ala Thr Gly Phe Pro Gly Ala
            820                 825                 830

Ala Gly Arg Val Gly Pro Pro Gly Ser Asn Gly Asn Pro Gly Pro Pro
        835                 840                 845
```

```
Gly Pro Pro Gly Pro Ser Gly Lys Asp Gly Pro Lys Gly Ala Arg Gly
    850                 855                 860

Asp Ser Gly Pro Pro Gly Arg Ala Gly Glu Pro Gly Leu Gln Gly Pro
865                 870                 875                 880

Ala Gly Pro Pro Gly Glu Lys Gly Glu Pro Gly Asp Asp Gly Pro Ser
                885                 890                 895

Gly Ala Glu Gly Pro Pro Gly Pro Gln Gly Leu Ala Gly Gln Arg Gly
            900                 905                 910

Ile Val Gly Leu Pro Gly Gln Arg Gly Glu Arg Gly Phe Pro Gly Leu
        915                 920                 925

Pro Gly Pro Ser Gly Glu Pro Gly Lys Gln Gly Ala Pro Gly Ala Ser
    930                 935                 940

Gly Asp Arg Gly Pro Pro Gly Pro Val Gly Pro Pro Gly Leu Thr Gly
945                 950                 955                 960

Pro Ala Gly Glu Pro Gly Arg Glu Gly Ser Pro Gly Ala Asp Gly Pro
                965                 970                 975

Pro Gly Arg Asp Gly Ala Ala Gly Val Lys Gly Asp Arg Gly Glu Thr
            980                 985                 990

Gly Ala Val Gly Ala Pro Gly Ala  Pro Gly Pro Pro Gly  Ser Pro Gly
        995                 1000                1005

Pro Ala  Gly Pro Thr Gly Lys  Gln Gly Asp Arg Gly  Glu Ala Gly
    1010                1015                1020

Ala Gln  Gly Pro Met Gly Pro  Ser Gly Pro Ala Gly  Ala Arg Gly
    1025                1030                1035

Ile Gln  Gly Pro Gln Gly Pro  Arg Gly Asp Lys Gly  Glu Ala Gly
    1040                1045                1050

Glu Pro  Gly Glu Arg Gly Leu  Lys Gly His Arg Gly  Phe Thr Gly
    1055                1060                1065

Leu Gln  Gly Leu Pro Gly Pro  Pro Gly Pro Ser Gly  Asp Gln Gly
    1070                1075                1080

Ala Ser  Gly Pro Ala Gly Pro  Ser Gly Pro Arg Gly  Pro Pro Gly
    1085                1090                1095

Pro Val  Gly Pro Ser Gly Lys  Asp Gly Ala Asn Gly  Ile Pro Gly
    1100                1105                1110
```

```
Pro Ile  Gly Pro Pro Gly Pro  Arg Gly Arg Ser Gly  Glu Thr Gly
    1115                 1120                 1125

Pro Ala  Gly Pro Pro Gly Asn  Pro Gly Pro Pro Gly  Pro Pro Gly
    1130                 1135                 1140

Pro Pro  Gly Pro Gly Ile Asp  Met Ser Ala Phe Ala  Gly Leu Gly
    1145                 1150                 1155

Pro Arg  Glu Lys Gly Pro Asp  Pro Leu Gln Tyr Met  Arg Ala Asp
    1160                 1165                 1170

Gln Ala  Ala Gly Gly Leu Arg  Gln His Asp Ala Glu  Val Asp Ala
    1175                 1180                 1185

Thr Leu  Lys Ser Leu Asn Asn  Gln Ile Glu Ser Ile  Arg Ser Pro
    1190                 1195                 1200

Glu Gly  Ser Arg Lys Asn Pro  Ala Arg Thr Cys Arg  Asp Leu Lys
    1205                 1210                 1215

Leu Cys  His Pro Glu Trp Lys  Ser Gly Asp Tyr Trp  Ile Asp Pro
    1220                 1225                 1230

Asn Gln  Gly Cys Thr Leu Asp  Ala Met Lys Val Phe  Cys Asn Met
    1235                 1240                 1245

Glu Thr  Gly Glu Thr Cys Val  Tyr Pro Asn Pro Ala  Asn Val Pro
    1250                 1255                 1260

Lys Lys  Asn Trp Trp Ser Ser  Lys Ser Lys Glu Lys  Lys His Ile
    1265                 1270                 1275

Trp Phe  Gly Glu Thr Ile Asn  Gly Gly Phe His Phe  Ser Tyr Gly
    1280                 1285                 1290

Asp Asp  Asn Leu Ala Pro Asn  Thr Ala Asn Val Gln  Met Thr Phe
    1295                 1300                 1305

Leu Arg  Leu Leu Ser Thr Glu  Gly Ser Gln Asn Ile  Thr Tyr His
    1310                 1315                 1320

Cys Lys  Asn Ser Ile Ala Tyr  Leu Asp Glu Ala Ala  Gly Asn Leu
    1325                 1330                 1335

Lys Lys  Ala Leu Leu Ile Gln  Gly Ser Asn Asp Val  Glu Ile Arg
    1340                 1345                 1350

Ala Glu  Gly Asn Ser Arg Phe  Thr Tyr Thr Ala Leu  Lys Asp Gly
    1355                 1360                 1365
```

Cys Thr Lys His Thr Gly Lys Trp Gly Lys Thr Val Ile Glu Tyr
1370 1375 1380

Arg Ser Gln Lys Thr Ser Arg Leu Pro Ile Ile Asp Ile Ala Pro
1385 1390 1395

Met Asp Ile Gly Gly Pro Glu Gln Glu Phe Gly Val Asp Ile Gly
1400 1405 1410

Pro Val Cys Phe Leu
1415

<210> 65
<211> 1466
<212> PRT
<213> Homo sapiens

<400> 65

Met Met Ser Phe Val Gln Lys Gly Ser Trp Leu Leu Leu Ala Leu Leu
1 5 10 15

His Pro Thr Ile Ile Leu Ala Gln Gln Glu Ala Val Glu Gly Gly Cys
20 25 30

Ser His Leu Gly Gln Ser Tyr Ala Asp Arg Asp Val Trp Lys Pro Glu
35 40 45

Pro Cys Gln Ile Cys Val Cys Asp Ser Gly Ser Val Leu Cys Asp Asp
50 55 60

Ile Ile Cys Asp Asp Gln Glu Leu Asp Cys Pro Asn Pro Glu Ile Pro
65 70 75 80

Phe Gly Glu Cys Cys Ala Val Cys Pro Gln Pro Pro Thr Ala Pro Thr
85 90 95

Arg Pro Pro Asn Gly Gln Gly Pro Gln Gly Pro Lys Gly Asp Pro Gly
100 105 110

Pro Pro Gly Ile Pro Gly Arg Asn Gly Asp Pro Gly Ile Pro Gly Gln
115 120 125

Pro Gly Ser Pro Gly Ser Pro Gly Pro Pro Gly Ile Cys Glu Ser Cys
130 135 140

Pro Thr Gly Pro Gln Asn Tyr Ser Pro Gln Tyr Asp Ser Tyr Asp Val
145 150 155 160

Lys Ser Gly Val Ala Val Gly Gly Leu Ala Gly Tyr Pro Gly Pro Ala
165 170 175

```
Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Thr Ser Gly His Pro Gly
            180                 185                 190

Ser Pro Gly Ser Pro Gly Tyr Gln Gly Pro Pro Gly Glu Pro Gly Gln
        195                 200                 205

Ala Gly Pro Ser Gly Pro Pro Gly Pro Pro Gly Ala Ile Gly Pro Ser
    210                 215                 220

Gly Pro Ala Gly Lys Asp Gly Glu Ser Gly Arg Pro Gly Arg Pro Gly
225                 230                 235                 240

Glu Arg Gly Leu Pro Gly Pro Pro Gly Ile Lys Gly Pro Ala Gly Ile
                245                 250                 255

Pro Gly Phe Pro Gly Met Lys Gly His Arg Gly Phe Asp Gly Arg Asn
            260                 265                 270

Gly Glu Lys Gly Glu Thr Gly Ala Pro Gly Leu Lys Gly Glu Asn Gly
        275                 280                 285

Leu Pro Gly Glu Asn Gly Ala Pro Gly Pro Met Gly Pro Arg Gly Ala
    290                 295                 300

Pro Gly Glu Arg Gly Arg Pro Gly Leu Pro Gly Ala Ala Gly Ala Arg
305                 310                 315                 320

Gly Asn Asp Gly Ala Arg Gly Ser Asp Gly Gln Pro Gly Pro Pro Gly
                325                 330                 335

Pro Pro Gly Thr Ala Gly Phe Pro Gly Ser Pro Gly Ala Lys Gly Glu
            340                 345                 350

Val Gly Pro Ala Gly Ser Pro Gly Ser Asn Gly Ala Pro Gly Gln Arg
        355                 360                 365

Gly Glu Pro Gly Pro Gln Gly His Ala Gly Ala Gln Gly Pro Pro Gly
    370                 375                 380

Pro Pro Gly Ile Asn Gly Ser Pro Gly Gly Lys Gly Glu Met Gly Pro
385                 390                 395                 400

Ala Gly Ile Pro Gly Ala Pro Gly Leu Met Gly Ala Arg Gly Pro Pro
                405                 410                 415

Gly Pro Ala Gly Ala Asn Gly Ala Pro Gly Leu Arg Gly Gly Ala Gly
            420                 425                 430

Glu Pro Gly Lys Asn Gly Ala Lys Gly Glu Pro Gly Pro Arg Gly Glu
        435                 440                 445
```

```
Arg Gly Glu Ala Gly Ile Pro Gly Val Pro Gly Ala Lys Gly Glu Asp
    450                 455                 460

Gly Lys Asp Gly Ser Pro Gly Glu Pro Gly Ala Asn Gly Leu Pro Gly
465                 470                 475                 480

Ala Ala Gly Glu Arg Gly Ala Pro Gly Phe Arg Gly Pro Ala Gly Pro
                485                 490                 495

Asn Gly Ile Pro Gly Glu Lys Gly Pro Ala Gly Glu Arg Gly Ala Pro
            500                 505                 510

Gly Pro Ala Gly Pro Arg Gly Ala Ala Gly Glu Pro Gly Arg Asp Gly
        515                 520                 525

Val Pro Gly Gly Pro Gly Met Arg Gly Met Pro Gly Ser Pro Gly Gly
    530                 535                 540

Pro Gly Ser Asp Gly Lys Pro Gly Pro Pro Gly Ser Gln Gly Glu Ser
545                 550                 555                 560

Gly Arg Pro Gly Pro Pro Gly Pro Ser Gly Pro Arg Gly Gln Pro Gly
                565                 570                 575

Val Met Gly Phe Pro Gly Pro Lys Gly Asn Asp Gly Ala Pro Gly Lys
            580                 585                 590

Asn Gly Glu Arg Gly Gly Pro Gly Gly Pro Gly Pro Gln Gly Pro Pro
        595                 600                 605

Gly Lys Asn Gly Glu Thr Gly Pro Gln Gly Pro Pro Gly Pro Thr Gly
    610                 615                 620

Pro Gly Gly Asp Lys Gly Asp Thr Gly Pro Pro Gly Pro Gln Gly Leu
625                 630                 635                 640

Gln Gly Leu Pro Gly Thr Gly Gly Pro Pro Gly Glu Asn Gly Lys Pro
                645                 650                 655

Gly Glu Pro Gly Pro Lys Gly Asp Ala Gly Ala Pro Gly Ala Pro Gly
            660                 665                 670

Gly Lys Gly Asp Ala Gly Ala Pro Gly Glu Arg Gly Pro Pro Gly Leu
        675                 680                 685

Ala Gly Ala Pro Gly Leu Arg Gly Gly Ala Gly Pro Pro Gly Pro Glu
    690                 695                 700

Gly Gly Lys Gly Ala Ala Gly Pro Pro Gly Pro Pro Gly Ala Ala Gly
705                 710                 715                 720
```

```
Thr Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Gly Leu Gly Ser
                725                 730                 735

Pro Gly Pro Lys Gly Asp Lys Gly Glu Pro Gly Gly Pro Gly Ala Asp
            740                 745                 750

Gly Val Pro Gly Lys Asp Gly Pro Arg Gly Pro Thr Gly Pro Ile Gly
        755                 760                 765

Pro Pro Gly Pro Ala Gly Gln Pro Gly Asp Lys Gly Glu Gly Gly Ala
    770                 775                 780

Pro Gly Leu Pro Gly Ile Ala Gly Pro Arg Gly Ser Pro Gly Glu Arg
785                 790                 795                 800

Gly Glu Thr Gly Pro Pro Gly Pro Ala Gly Phe Pro Gly Ala Pro Gly
                805                 810                 815

Gln Asn Gly Glu Pro Gly Gly Lys Gly Glu Arg Gly Ala Pro Gly Glu
            820                 825                 830

Lys Gly Glu Gly Gly Pro Pro Gly Val Ala Gly Pro Pro Gly Gly Ser
        835                 840                 845

Gly Pro Ala Gly Pro Pro Gly Pro Gln Gly Val Lys Gly Glu Arg Gly
    850                 855                 860

Ser Pro Gly Gly Pro Gly Ala Ala Gly Phe Pro Gly Ala Arg Gly Leu
865                 870                 875                 880

Pro Gly Pro Pro Gly Ser Asn Gly Asn Pro Gly Pro Pro Gly Pro Ser
                885                 890                 895

Gly Ser Pro Gly Lys Asp Gly Pro Pro Gly Pro Ala Gly Asn Thr Gly
            900                 905                 910

Ala Pro Gly Ser Pro Gly Val Ser Gly Pro Lys Gly Asp Ala Gly Gln
        915                 920                 925

Pro Gly Glu Lys Gly Ser Pro Gly Ala Gln Gly Pro Pro Gly Ala Pro
    930                 935                 940

Gly Pro Leu Gly Ile Ala Gly Ile Thr Gly Ala Arg Gly Leu Ala Gly
945                 950                 955                 960

Pro Pro Gly Met Pro Gly Pro Arg Gly Ser Pro Gly Pro Gln Gly Val
                965                 970                 975

Lys Gly Glu Ser Gly Lys Pro Gly Ala Asn Gly Leu Ser Gly Glu Arg
            980                 985                 990
```

```
Gly Pro Pro Gly Pro Gln Gly Leu  Pro Gly Leu Ala Gly  Thr Ala Gly
        995                 1000                1005


Glu Pro  Gly Arg Asp Gly Asn  Pro Gly Ser Asp Gly  Leu Pro Gly
    1010                1015                1020


Arg Asp  Gly Ser Pro Gly Gly  Lys Gly Asp Arg Gly  Glu Asn Gly
    1025                1030                1035


Ser Pro  Gly Ala Pro Gly Ala  Pro Gly His Pro Gly  Pro Pro Gly
    1040                1045                1050


Pro Val  Gly Pro Ala Gly Lys  Ser Gly Asp Arg Gly  Glu Ser Gly
    1055                1060                1065


Pro Ala  Gly Pro Ala Gly Ala  Pro Gly Pro Ala Gly  Ser Arg Gly
    1070                1075                1080


Ala Pro  Gly Pro Gln Gly Pro  Arg Gly Asp Lys Gly  Glu Thr Gly
    1085                1090                1095


Glu Arg  Gly Ala Ala Gly Ile  Lys Gly His Arg Gly  Phe Pro Gly
    1100                1105                1110


Asn Pro  Gly Ala Pro Gly Ser  Pro Gly Pro Ala Gly  Gln Gln Gly
    1115                1120                1125


Ala Ile  Gly Ser Pro Gly Pro  Ala Gly Pro Arg Gly  Pro Val Gly
    1130                1135                1140


Pro Ser  Gly Pro Pro Gly Lys  Asp Gly Thr Ser Gly  His Pro Gly
    1145                1150                1155


Pro Ile  Gly Pro Pro Gly Pro  Arg Gly Asn Arg Gly  Glu Arg Gly
    1160                1165                1170


Ser Glu  Gly Ser Pro Gly His  Pro Gly Gln Pro Gly  Pro Pro Gly
    1175                1180                1185


Pro Pro  Gly Ala Pro Gly Pro  Cys Cys Gly Gly Val  Gly Ala Ala
    1190                1195                1200


Ala Ile  Ala Gly Ile Gly Gly  Glu Lys Ala Gly Gly  Phe Ala Pro
    1205                1210                1215


Tyr Tyr  Gly Asp Glu Pro Met  Asp Phe Lys Ile Asn  Thr Asp Glu
    1220                1225                1230


Ile Met  Thr Ser Leu Lys Ser  Val Asn Gly Gln Ile  Glu Ser Leu
    1235                1240                1245
```

```
Ile Ser  Pro Asp Gly Ser Arg  Lys Asn Pro Ala Arg  Asn Cys Arg
    1250                 1255                 1260

Asp Leu  Lys Phe Cys His Pro  Glu Leu Lys Ser Gly  Glu Tyr Trp
    1265                 1270                 1275

Val Asp  Pro Asn Gln Gly Cys  Lys Leu Asp Ala Ile  Lys Val Phe
    1280                 1285                 1290

Cys Asn  Met Glu Thr Gly Glu  Thr Cys Ile Ser Ala  Asn Pro Leu
    1295                 1300                 1305

Asn Val  Pro Arg Lys His Trp  Trp Thr Asp Ser Ser  Ala Glu Lys
    1310                 1315                 1320

Lys His  Val Trp Phe Gly Glu  Ser Met Asp Gly Gly  Phe Gln Phe
    1325                 1330                 1335

Ser Tyr  Gly Asn Pro Glu Leu  Pro Glu Asp Val Leu  Asp Val Gln
    1340                 1345                 1350

Leu Ala  Phe Leu Arg Leu Leu  Ser Ser Arg Ala Ser  Gln Asn Ile
    1355                 1360                 1365

Thr Tyr  His Cys Lys Asn Ser  Ile Ala Tyr Met Asp  Gln Ala Ser
    1370                 1375                 1380

Gly Asn  Val Lys Lys Ala Leu  Lys Leu Met Gly Ser  Asn Glu Gly
    1385                 1390                 1395

Glu Phe  Lys Ala Glu Gly Asn  Ser Lys Phe Thr Tyr  Thr Val Leu
    1400                 1405                 1410

Glu Asp  Gly Cys Thr Lys His  Thr Gly Glu Trp Ser  Lys Thr Val
    1415                 1420                 1425

Phe Glu  Tyr Arg Thr Arg Lys  Ala Val Arg Leu Pro  Ile Val Asp
    1430                 1435                 1440

Ile Ala  Pro Tyr Asp Ile Gly  Gly Pro Asp Gln Glu  Phe Gly Val
    1445                 1450                 1455

Asp Val  Gly Pro Val Cys Phe  Leu
    1460                 1465
```

<210> 66
<211> 1669
<212> PRT
<213> Homo sapiens

<400> 66

```
Met Gly Pro Arg Leu Ser Val Trp Leu Leu Leu Leu Pro Ala Ala Leu
1               5                  10                  15

Leu Leu His Glu Glu His Ser Arg Ala Ala Ala Lys Gly Gly Cys Ala
            20                  25                  30

Gly Ser Gly Cys Gly Lys Cys Asp Cys His Gly Val Lys Gly Gln Lys
        35                  40                  45

Gly Glu Arg Gly Leu Pro Gly Leu Gln Gly Val Ile Gly Phe Pro Gly
    50                  55                  60

Met Gln Gly Pro Glu Gly Pro Gln Gly Pro Pro Gly Gln Lys Gly Asp
65                  70                  75                  80

Thr Gly Glu Pro Gly Leu Pro Gly Thr Lys Gly Thr Arg Gly Pro Pro
                85                  90                  95

Gly Ala Ser Gly Tyr Pro Gly Asn Pro Gly Leu Pro Gly Ile Pro Gly
            100                 105                 110

Gln Asp Gly Pro Pro Gly Pro Pro Gly Ile Pro Gly Cys Asn Gly Thr
        115                 120                 125

Lys Gly Glu Arg Gly Pro Leu Gly Pro Pro Gly Leu Pro Gly Phe Ala
    130                 135                 140

Gly Asn Pro Gly Pro Pro Gly Leu Pro Gly Met Lys Gly Asp Pro Gly
145                 150                 155                 160

Glu Ile Leu Gly His Val Pro Gly Met Leu Leu Lys Gly Glu Arg Gly
                165                 170                 175

Phe Pro Gly Ile Pro Gly Thr Pro Gly Pro Pro Gly Leu Pro Gly Leu
            180                 185                 190

Gln Gly Pro Val Gly Pro Pro Gly Phe Thr Gly Pro Pro Gly Pro Pro
        195                 200                 205

Gly Pro Pro Gly Pro Pro Gly Glu Lys Gly Gln Met Gly Leu Ser Phe
    210                 215                 220

Gln Gly Pro Lys Gly Asp Lys Gly Asp Gln Gly Val Ser Gly Pro Pro
225                 230                 235                 240

Gly Val Pro Gly Gln Ala Gln Val Gln Glu Lys Gly Asp Phe Ala Thr
                245                 250                 255

Lys Gly Glu Lys Gly Gln Lys Gly Glu Pro Gly Phe Gln Gly Met Pro
            260                 265                 270
```

```
Gly Val Gly Glu Lys Gly Glu Pro Gly Lys Pro Gly Pro Arg Gly Lys
        275                 280                 285

Pro Gly Lys Asp Gly Asp Lys Gly Glu Lys Gly Ser Pro Gly Phe Pro
    290                 295                 300

Gly Glu Pro Gly Tyr Pro Gly Leu Ile Gly Arg Gln Gly Pro Gln Gly
305                 310                 315                 320

Glu Lys Gly Glu Ala Gly Pro Pro Gly Pro Pro Gly Ile Val Ile Gly
                325                 330                 335

Thr Gly Pro Leu Gly Glu Lys Gly Glu Arg Gly Tyr Pro Gly Thr Pro
            340                 345                 350

Gly Pro Arg Gly Glu Pro Gly Pro Lys Gly Phe Pro Gly Leu Pro Gly
        355                 360                 365

Gln Pro Gly Pro Pro Gly Leu Pro Val Pro Gly Gln Ala Gly Ala Pro
    370                 375                 380

Gly Phe Pro Gly Glu Arg Gly Glu Lys Gly Asp Arg Gly Phe Pro Gly
385                 390                 395                 400

Thr Ser Leu Pro Gly Pro Ser Gly Arg Asp Gly Leu Pro Gly Pro Pro
                405                 410                 415

Gly Ser Pro Gly Pro Pro Gly Gln Pro Gly Tyr Thr Asn Gly Ile Val
            420                 425                 430

Glu Cys Gln Pro Gly Pro Pro Gly Asp Gln Gly Pro Pro Gly Ile Pro
        435                 440                 445

Gly Gln Pro Gly Phe Ile Gly Glu Ile Gly Glu Lys Gly Gln Lys Gly
    450                 455                 460

Glu Ser Cys Leu Ile Cys Asp Ile Asp Gly Tyr Arg Gly Pro Pro Gly
465                 470                 475                 480

Pro Gln Gly Pro Pro Gly Glu Ile Gly Phe Pro Gly Gln Pro Gly Ala
                485                 490                 495

Lys Gly Asp Arg Gly Leu Pro Gly Arg Asp Gly Val Ala Gly Val Pro
            500                 505                 510

Gly Pro Gln Gly Thr Pro Gly Leu Ile Gly Gln Pro Gly Ala Lys Gly
        515                 520                 525

Glu Pro Gly Glu Phe Tyr Phe Asp Leu Arg Leu Lys Gly Asp Lys Gly
    530                 535                 540
```

```
Asp Pro Gly Phe Pro Gly Gln Pro Gly Met Thr Gly Arg Ala Gly Ser
545                 550                 555                 560

Pro Gly Arg Asp Gly His Pro Gly Leu Pro Gly Pro Lys Gly Ser Pro
                565                 570                 575

Gly Ser Val Gly Leu Lys Gly Glu Arg Gly Pro Pro Gly Gly Val Gly
            580                 585                 590

Phe Pro Gly Ser Arg Gly Asp Thr Gly Pro Pro Gly Pro Pro Gly Tyr
        595                 600                 605

Gly Pro Ala Gly Pro Ile Gly Asp Lys Gly Gln Ala Gly Phe Pro Gly
    610                 615                 620

Gly Pro Gly Ser Pro Gly Leu Pro Gly Pro Lys Gly Glu Pro Gly Lys
625                 630                 635                 640

Ile Val Pro Leu Pro Gly Pro Pro Gly Ala Glu Gly Leu Pro Gly Ser
                645                 650                 655

Pro Gly Phe Pro Gly Pro Gln Gly Asp Arg Gly Phe Pro Gly Thr Pro
            660                 665                 670

Gly Arg Pro Gly Leu Pro Gly Glu Lys Gly Ala Val Gly Gln Pro Gly
        675                 680                 685

Ile Gly Phe Pro Gly Pro Pro Gly Pro Lys Gly Val Asp Gly Leu Pro
    690                 695                 700

Gly Asp Met Gly Pro Pro Gly Thr Pro Gly Arg Pro Gly Phe Asn Gly
705                 710                 715                 720

Leu Pro Gly Asn Pro Gly Val Gln Gly Gln Lys Gly Glu Pro Gly Val
                725                 730                 735

Gly Leu Pro Gly Leu Lys Gly Leu Pro Gly Leu Pro Gly Ile Pro Gly
            740                 745                 750

Thr Pro Gly Glu Lys Gly Ser Ile Gly Val Pro Gly Val Pro Gly Glu
        755                 760                 765

His Gly Ala Ile Gly Pro Pro Gly Leu Gln Gly Ile Arg Gly Glu Pro
    770                 775                 780

Gly Pro Pro Gly Leu Pro Gly Ser Val Gly Ser Pro Gly Val Pro Gly
785                 790                 795                 800

Ile Gly Pro Pro Gly Ala Arg Gly Pro Pro Gly Gly Gln Gly Pro Pro
                805                 810                 815
```

```
Gly Leu Ser Gly Pro Pro Gly Ile Lys Gly Glu Lys Gly Phe Pro Gly
            820                 825                 830

Phe Pro Gly Leu Asp Met Pro Gly Pro Lys Gly Asp Lys Gly Ala Gln
        835                 840                 845

Gly Leu Pro Gly Ile Thr Gly Gln Ser Gly Leu Pro Gly Leu Pro Gly
    850                 855                 860

Gln Gln Gly Ala Pro Gly Ile Pro Gly Phe Pro Gly Ser Lys Gly Glu
865                 870                 875                 880

Met Gly Val Met Gly Thr Pro Gly Gln Pro Gly Ser Pro Gly Pro Val
                885                 890                 895

Gly Ala Pro Gly Leu Pro Gly Glu Lys Gly Asp His Gly Phe Pro Gly
            900                 905                 910

Ser Ser Gly Pro Arg Gly Asp Pro Gly Leu Lys Gly Asp Lys Gly Asp
        915                 920                 925

Val Gly Leu Pro Gly Lys Pro Gly Ser Met Asp Lys Val Asp Met Gly
    930                 935                 940

Ser Met Lys Gly Gln Lys Gly Asp Gln Gly Glu Lys Gly Gln Ile Gly
945                 950                 955                 960

Pro Ile Gly Glu Lys Gly Ser Arg Gly Asp Pro Gly Thr Pro Gly Val
                965                 970                 975

Pro Gly Lys Asp Gly Gln Ala Gly Gln Pro Gly Gln Pro Gly Pro Lys
            980                 985                 990

Gly Asp Pro Gly Ile Ser Gly Thr  Pro Gly Ala Pro Gly  Leu Pro Gly
        995                 1000                1005

Pro Lys  Gly Ser Val Gly Gly  Met Gly Leu Pro Gly  Thr Pro Gly
    1010                1015                1020

Glu Lys  Gly Val Pro Gly Ile  Pro Gly Pro Gln Gly  Ser Pro Gly
    1025                1030                1035

Leu Pro  Gly Asp Lys Gly Ala  Lys Gly Glu Lys Gly  Gln Ala Gly
    1040                1045                1050

Pro Pro  Gly Ile Gly Ile Pro  Gly Leu Arg Gly Glu  Lys Gly Asp
    1055                1060                1065

Gln Gly  Ile Ala Gly Phe Pro  Gly Ser Pro Gly Glu  Lys Gly Glu
    1070                1075                1080
```

```
Lys Gly  Ser Ile Gly Ile Pro  Gly Met Pro Gly Ser  Pro Gly Leu
    1085                1090                1095

Lys Gly  Ser Pro Gly Ser Val  Gly Tyr Pro Gly Ser  Pro Gly Leu
    1100                1105                1110

Pro Gly  Glu Lys Gly Asp Lys  Gly Leu Pro Gly Leu  Asp Gly Ile
    1115                1120                1125

Pro Gly  Val Lys Gly Glu Ala  Gly Leu Pro Gly Thr  Pro Gly Pro
    1130                1135                1140

Thr Gly  Pro Ala Gly Gln Lys  Gly Glu Pro Gly Ser  Asp Gly Ile
    1145                1150                1155

Pro Gly  Ser Ala Gly Glu Lys  Gly Glu Pro Gly Leu  Pro Gly Arg
    1160                1165                1170

Gly Phe  Pro Gly Phe Pro Gly  Ala Lys Gly Asp Lys  Gly Ser Lys
    1175                1180                1185

Gly Glu  Val Gly Phe Pro Gly  Leu Ala Gly Ser Pro  Gly Ile Pro
    1190                1195                1200

Gly Ser  Lys Gly Glu Gln Gly  Phe Met Gly Pro Pro  Gly Pro Gln
    1205                1210                1215

Gly Gln  Pro Gly Leu Pro Gly  Ser Pro Gly His Ala  Thr Glu Gly
    1220                1225                1230

Pro Lys  Gly Asp Arg Gly Pro  Gln Gly Gln Pro Gly  Leu Pro Gly
    1235                1240                1245

Leu Pro  Gly Pro Met Gly Pro  Pro Gly Leu Pro Gly  Ile Asp Gly
    1250                1255                1260

Val Lys  Gly Asp Lys Gly Asn  Pro Gly Trp Pro Gly  Ala Pro Gly
    1265                1270                1275

Val Pro  Gly Pro Lys Gly Asp  Pro Gly Phe Gln Gly  Met Pro Gly
    1280                1285                1290

Ile Gly  Gly Ser Pro Gly Ile  Thr Gly Ser Lys Gly  Asp Met Gly
    1295                1300                1305

Pro Pro  Gly Val Pro Gly Phe  Gln Gly Pro Lys Gly  Leu Pro Gly
    1310                1315                1320

Leu Gln  Gly Ile Lys Gly Asp  Gln Gly Asp Gln Gly  Val Pro Gly
    1325                1330                1335
```

```
Ala Lys  Gly Leu Pro Gly Pro  Pro Gly Pro Pro Gly  Pro Tyr Asp
    1340                 1345                 1350

Ile Ile  Lys Gly Glu Pro Gly  Leu Pro Gly Pro Glu  Gly Pro Pro
    1355                 1360                 1365

Gly Leu  Lys Gly Leu Gln Gly  Leu Pro Gly Pro Lys  Gly Gln Gln
    1370                 1375                 1380

Gly Val  Thr Gly Leu Val Gly  Ile Pro Gly Pro Pro  Gly Ile Pro
    1385                 1390                 1395

Gly Phe  Asp Gly Ala Pro Gly  Gln Lys Gly Glu Met  Gly Pro Ala
    1400                 1405                 1410

Gly Pro  Thr Gly Pro Arg Gly  Phe Pro Gly Pro Pro  Gly Pro Asp
    1415                 1420                 1425

Gly Leu  Pro Gly Ser Met Gly  Pro Pro Gly Thr Pro  Ser Val Asp
    1430                 1435                 1440

His Gly  Phe Leu Val Thr Arg  His Ser Gln Thr Ile  Asp Asp Pro
    1445                 1450                 1455

Gln Cys  Pro Ser Gly Thr Lys  Ile Leu Tyr His Gly  Tyr Ser Leu
    1460                 1465                 1470

Leu Tyr  Val Gln Gly Asn Glu  Arg Ala His Gly Gln  Asp Leu Gly
    1475                 1480                 1485

Thr Ala  Gly Ser Cys Leu Arg  Lys Phe Ser Thr Met  Pro Phe Leu
    1490                 1495                 1500

Phe Cys  Asn Ile Asn Asn Val  Cys Asn Phe Ala Ser  Arg Asn Asp
    1505                 1510                 1515

Tyr Ser  Tyr Trp Leu Ser Thr  Pro Glu Pro Met Pro  Met Ser Met
    1520                 1525                 1530

Ala Pro  Ile Thr Gly Glu Asn  Ile Arg Pro Phe Ile  Ser Arg Cys
    1535                 1540                 1545

Ala Val  Cys Glu Ala Pro Ala  Met Val Met Ala Val  His Ser Gln
    1550                 1555                 1560

Thr Ile  Gln Ile Pro Pro Cys  Pro Ser Gly Trp Ser  Ser Leu Trp
    1565                 1570                 1575

Ile Gly  Tyr Ser Phe Val Met  His Thr Ser Ala Gly  Ala Glu Gly
    1580                 1585                 1590
```

Ser Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu Glu Glu Phe
1595 1600 1605

Arg Ser Ala Pro Phe Ile Glu Cys His Gly Arg Gly Thr Cys Asn
1610 1615 1620

Tyr Tyr Ala Asn Ala Tyr Ser Phe Trp Leu Ala Thr Ile Glu Arg
1625 1630 1635

Ser Glu Met Phe Lys Lys Pro Thr Pro Ser Thr Leu Lys Ala Gly
1640 1645 1650

Glu Leu Arg Thr His Val Ser Arg Cys Gln Val Cys Met Arg Arg
1655 1660 1665

Thr

<210> 67
<211> 1712
<212> PRT
<213> Homo sapiens

<400> 67

Met Gly Arg Asp Gln Arg Ala Val Ala Gly Pro Ala Leu Arg Arg Trp
1 5 10 15

Leu Leu Leu Gly Thr Val Thr Val Gly Phe Leu Ala Gln Ser Val Leu
20 25 30

Ala Gly Val Lys Lys Phe Asp Val Pro Cys Gly Gly Arg Asp Cys Ser
35 40 45

Gly Gly Cys Gln Cys Tyr Pro Glu Lys Gly Gly Arg Gly Gln Pro Gly
50 55 60

Pro Val Gly Pro Gln Gly Tyr Asn Gly Pro Pro Gly Leu Gln Gly Phe
65 70 75 80

Pro Gly Leu Gln Gly Arg Lys Gly Asp Lys Gly Glu Arg Gly Ala Pro
85 90 95

Gly Val Thr Gly Pro Lys Gly Asp Val Gly Ala Arg Gly Val Ser Gly
100 105 110

Phe Pro Gly Ala Asp Gly Ile Pro Gly His Pro Gly Gln Gly Gly Pro
115 120 125

Arg Gly Arg Pro Gly Tyr Asp Gly Cys Asn Gly Thr Gln Gly Asp Ser
130 135 140

Gly Pro Gln Gly Pro Pro Gly Ser Glu Gly Phe Thr Gly Pro Pro Gly

```
145                 150                 155                 160

Pro Gln Gly Pro Lys Gly Gln Lys Gly Glu Pro Tyr Ala Leu Pro Lys
                165                 170                 175

Glu Glu Arg Asp Arg Tyr Arg Gly Glu Pro Gly Glu Pro Gly Leu Val
            180                 185                 190

Gly Phe Gln Gly Pro Pro Gly Arg Pro Gly His Val Gly Gln Met Gly
        195                 200                 205

Pro Val Gly Ala Pro Gly Arg Pro Gly Pro Pro Gly Pro Pro Gly Pro
    210                 215                 220

Lys Gly Gln Gln Gly Asn Arg Gly Leu Gly Phe Tyr Gly Val Lys Gly
225                 230                 235                 240

Glu Lys Gly Asp Val Gly Gln Pro Gly Pro Asn Gly Ile Pro Ser Asp
                245                 250                 255

Thr Leu His Pro Ile Ile Ala Pro Thr Gly Val Thr Phe His Pro Asp
            260                 265                 270

Gln Tyr Lys Gly Glu Lys Gly Ser Glu Gly Glu Pro Gly Ile Arg Gly
        275                 280                 285

Ile Ser Leu Lys Gly Glu Glu Gly Ile Met Gly Phe Pro Gly Leu Arg
    290                 295                 300

Gly Tyr Pro Gly Leu Ser Gly Glu Lys Gly Ser Pro Gly Gln Lys Gly
305                 310                 315                 320

Ser Arg Gly Leu Asp Gly Tyr Gln Gly Pro Asp Gly Pro Arg Gly Pro
                325                 330                 335

Lys Gly Glu Ala Gly Asp Pro Gly Pro Pro Gly Leu Pro Ala Tyr Ser
            340                 345                 350

Pro His Pro Ser Leu Ala Lys Gly Ala Arg Gly Asp Pro Gly Phe Pro
        355                 360                 365

Gly Ala Gln Gly Glu Pro Gly Ser Gln Gly Glu Pro Gly Asp Pro Gly
    370                 375                 380

Leu Pro Gly Pro Pro Gly Leu Ser Ile Gly Asp Gly Asp Gln Arg Arg
385                 390                 395                 400

Gly Leu Pro Gly Glu Met Gly Pro Lys Gly Phe Ile Gly Asp Pro Gly
                405                 410                 415

Ile Pro Ala Leu Tyr Gly Gly Pro Pro Gly Pro Asp Gly Lys Arg Gly
```

```
            420                 425                 430

Pro Pro Gly Pro Pro Gly Leu Pro Gly Pro Pro Gly Pro Asp Gly Phe
        435                 440                 445

Leu Phe Gly Leu Lys Gly Ala Lys Gly Arg Ala Gly Phe Pro Gly Leu
    450                 455                 460

Pro Gly Ser Pro Gly Ala Arg Gly Pro Lys Gly Trp Lys Gly Asp Ala
465                 470                 475                 480

Gly Glu Cys Arg Cys Thr Glu Gly Asp Glu Ala Ile Lys Gly Leu Pro
                485                 490                 495

Gly Leu Pro Gly Pro Lys Gly Phe Ala Gly Ile Asn Gly Glu Pro Gly
            500                 505                 510

Arg Lys Gly Asp Arg Gly Asp Pro Gly Gln His Gly Leu Pro Gly Phe
        515                 520                 525

Pro Gly Leu Lys Gly Val Pro Gly Asn Ile Gly Ala Pro Gly Pro Lys
    530                 535                 540

Gly Ala Lys Gly Asp Ser Arg Thr Ile Thr Thr Lys Gly Glu Arg Gly
545                 550                 555                 560

Gln Pro Gly Val Pro Gly Val Pro Gly Met Lys Gly Asp Asp Gly Ser
                565                 570                 575

Pro Gly Arg Asp Gly Leu Asp Gly Phe Pro Gly Leu Pro Gly Pro Pro
            580                 585                 590

Gly Asp Gly Ile Lys Gly Pro Pro Gly Asp Pro Gly Tyr Pro Gly Ile
        595                 600                 605

Pro Gly Thr Lys Gly Thr Pro Gly Glu Met Gly Pro Pro Gly Leu Gly
    610                 615                 620

Leu Pro Gly Leu Lys Gly Gln Arg Gly Phe Pro Gly Asp Ala Gly Leu
625                 630                 635                 640

Pro Gly Pro Pro Gly Phe Leu Gly Pro Pro Gly Pro Ala Gly Thr Pro
                645                 650                 655

Gly Gln Ile Asp Cys Asp Thr Asp Val Lys Arg Ala Val Gly Gly Asp
            660                 665                 670

Arg Gln Glu Ala Ile Gln Pro Gly Cys Ile Gly Gly Pro Lys Gly Leu
        675                 680                 685

Pro Gly Leu Pro Gly Pro Pro Gly Pro Thr Gly Ala Lys Gly Leu Arg
```

690 695 700

Gly Ile Pro Gly Phe Ala Gly Ala Asp Gly Gly Pro Gly Pro Arg Gly
705 710 715 720

Leu Pro Gly Asp Ala Gly Arg Glu Gly Phe Pro Gly Pro Pro Gly Phe
725 730 735

Ile Gly Pro Arg Gly Ser Lys Gly Ala Val Gly Leu Pro Gly Pro Asp
740 745 750

Gly Ser Pro Gly Pro Ile Gly Leu Pro Gly Pro Asp Gly Pro Pro Gly
755 760 765

Glu Arg Gly Leu Pro Gly Glu Val Leu Gly Ala Gln Pro Gly Pro Arg
770 775 780

Gly Asp Ala Gly Val Pro Gly Gln Pro Gly Leu Lys Gly Leu Pro Gly
785 790 795 800

Asp Arg Gly Pro Pro Gly Phe Arg Gly Ser Gln Gly Met Pro Gly Met
805 810 815

Pro Gly Leu Lys Gly Gln Pro Gly Leu Pro Gly Pro Ser Gly Gln Pro
820 825 830

Gly Leu Tyr Gly Pro Pro Gly Leu His Gly Phe Pro Gly Ala Pro Gly
835 840 845

Gln Glu Gly Pro Leu Gly Leu Pro Gly Ile Pro Gly Arg Glu Gly Leu
850 855 860

Pro Gly Asp Arg Gly Asp Pro Gly Asp Thr Gly Ala Pro Gly Pro Val
865 870 875 880

Gly Met Lys Gly Leu Ser Gly Asp Arg Gly Asp Ala Gly Phe Thr Gly
885 890 895

Glu Gln Gly His Pro Gly Ser Pro Gly Phe Lys Gly Ile Asp Gly Met
900 905 910

Pro Gly Thr Pro Gly Leu Lys Gly Asp Arg Gly Ser Pro Gly Met Asp
915 920 925

Gly Phe Gln Gly Met Pro Gly Leu Lys Gly Arg Pro Gly Phe Pro Gly
930 935 940

Ser Lys Gly Glu Ala Gly Phe Phe Gly Ile Pro Gly Leu Lys Gly Leu
945 950 955 960

Ala Gly Glu Pro Gly Phe Lys Gly Ser Arg Gly Asp Pro Gly Pro Pro

965 970 975

Gly Pro Pro Pro Val Ile Leu Pro Gly Met Lys Asp Ile Lys Gly Glu
980 985 990

Lys Gly Asp Glu Gly Pro Met Gly Leu Lys Gly Tyr Leu Gly Ala Lys
995 1000 1005

Gly Ile Gln Gly Met Pro Gly Ile Pro Gly Leu Ser Gly Ile Pro
1010 1015 1020

Gly Leu Pro Gly Arg Pro Gly His Ile Lys Gly Val Lys Gly Asp
1025 1030 1035

Ile Gly Val Pro Gly Ile Pro Gly Leu Pro Gly Phe Pro Gly Val
1040 1045 1050

Ala Gly Pro Pro Gly Ile Thr Gly Phe Pro Gly Phe Ile Gly Ser
1055 1060 1065

Arg Gly Asp Lys Gly Ala Pro Gly Arg Ala Gly Leu Tyr Gly Glu
1070 1075 1080

Ile Gly Ala Thr Gly Asp Phe Gly Asp Ile Gly Asp Thr Ile Asn
1085 1090 1095

Leu Pro Gly Arg Pro Gly Leu Lys Gly Glu Arg Gly Thr Thr Gly
1100 1105 1110

Ile Pro Gly Leu Lys Gly Phe Phe Gly Glu Lys Gly Thr Glu Gly
1115 1120 1125

Asp Ile Gly Phe Pro Gly Ile Thr Gly Val Thr Gly Val Gln Gly
1130 1135 1140

Pro Pro Gly Leu Lys Gly Gln Thr Gly Phe Pro Gly Leu Thr Gly
1145 1150 1155

Pro Pro Gly Ser Gln Gly Glu Leu Gly Arg Ile Gly Leu Pro Gly
1160 1165 1170

Gly Lys Gly Asp Asp Gly Trp Pro Gly Ala Pro Gly Leu Pro Gly
1175 1180 1185

Phe Pro Gly Leu Arg Gly Ile Arg Gly Leu His Gly Leu Pro Gly
1190 1195 1200

Thr Lys Gly Phe Pro Gly Ser Pro Gly Ser Asp Ile His Gly Asp
1205 1210 1215

Pro Gly Phe Pro Gly Pro Pro Gly Glu Arg Gly Asp Pro Gly Glu

1220 1225 1230

Ala Asn Thr Leu Pro Gly Pro Val Gly Val Pro Gly Gln Lys Gly
1235 1240 1245

Asp Gln Gly Ala Pro Gly Glu Arg Gly Pro Pro Gly Ser Pro Gly
1250 1255 1260

Leu Gln Gly Phe Pro Gly Ile Thr Pro Pro Ser Asn Ile Ser Gly
1265 1270 1275

Ala Pro Gly Asp Lys Gly Ala Pro Gly Ile Phe Gly Leu Lys Gly
1280 1285 1290

Tyr Arg Gly Pro Pro Gly Pro Pro Gly Ser Ala Ala Leu Pro Gly
1295 1300 1305

Ser Lys Gly Asp Thr Gly Asn Pro Gly Ala Pro Gly Thr Pro Gly
1310 1315 1320

Thr Lys Gly Trp Ala Gly Asp Ser Gly Pro Gln Gly Arg Pro Gly
1325 1330 1335

Val Phe Gly Leu Pro Gly Glu Lys Gly Pro Arg Gly Glu Gln Gly
1340 1345 1350

Phe Met Gly Asn Thr Gly Pro Thr Gly Ala Val Gly Asp Arg Gly
1355 1360 1365

Pro Lys Gly Pro Lys Gly Asp Pro Gly Phe Pro Gly Ala Pro Gly
1370 1375 1380

Thr Val Gly Ala Pro Gly Ile Ala Gly Ile Pro Gln Lys Ile Ala
1385 1390 1395

Val Gln Pro Gly Thr Val Gly Pro Gln Gly Arg Arg Gly Pro Pro
1400 1405 1410

Gly Ala Pro Gly Glu Met Gly Pro Gln Gly Pro Pro Gly Glu Pro
1415 1420 1425

Gly Phe Arg Gly Ala Pro Gly Lys Ala Gly Pro Gln Gly Arg Gly
1430 1435 1440

Gly Val Ser Ala Val Pro Gly Phe Arg Gly Asp Glu Gly Pro Ile
1445 1450 1455

Gly His Gln Gly Pro Ile Gly Gln Glu Gly Ala Pro Gly Arg Pro
1460 1465 1470

Gly Ser Pro Gly Leu Pro Gly Met Pro Gly Arg Ser Val Ser Ile

1475 1480 1485

Gly Tyr Leu Leu Val Lys His Ser Gln Thr Asp Gln Glu Pro Met
1490 1495 1500

Cys Pro Val Gly Met Asn Lys Leu Trp Ser Gly Tyr Ser Leu Leu
1505 1510 1515

Tyr Phe Glu Gly Gln Glu Lys Ala His Asn Gln Asp Leu Gly Leu
1520 1525 1530

Ala Gly Ser Cys Leu Ala Arg Phe Ser Thr Met Pro Phe Leu Tyr
1535 1540 1545

Cys Asn Pro Gly Asp Val Cys Tyr Tyr Ala Ser Arg Asn Asp Lys
1550 1555 1560

Ser Tyr Trp Leu Ser Thr Thr Ala Pro Leu Pro Met Met Pro Val
1565 1570 1575

Ala Glu Asp Glu Ile Lys Pro Tyr Ile Ser Arg Cys Ser Val Cys
1580 1585 1590

Glu Ala Pro Ala Ile Ala Ile Ala Val His Ser Gln Asp Val Ser
1595 1600 1605

Ile Pro His Cys Pro Ala Gly Trp Arg Ser Leu Trp Ile Gly Tyr
1610 1615 1620

Ser Phe Leu Met His Thr Ala Ala Gly Asp Glu Gly Gly Gly Gln
1625 1630 1635

Ser Leu Val Ser Pro Gly Ser Cys Leu Glu Asp Phe Arg Ala Thr
1640 1645 1650

Pro Phe Ile Glu Cys Asn Gly Gly Arg Gly Thr Cys His Tyr Tyr
1655 1660 1665

Ala Asn Lys Tyr Ser Phe Trp Leu Thr Thr Ile Pro Glu Gln Ser
1670 1675 1680

Phe Gln Gly Ser Pro Ser Ala Asp Thr Leu Lys Ala Gly Leu Ile
1685 1690 1695

Arg Thr His Ile Ser Arg Cys Gln Val Cys Met Lys Asn Leu
1700 1705 1710

<210> 68
<211> 1670
<212> PRT
<213> Homo sapiens

<400> 68

```
Met Ser Ala Arg Thr Ala Pro Arg Pro Gln Val Leu Leu Leu Pro Leu
1               5                  10                  15

Leu Leu Val Leu Leu Ala Ala Ala Pro Ala Ala Ser Lys Gly Cys Val
            20                  25                  30

Cys Lys Asp Lys Gly Gln Cys Phe Cys Asp Gly Ala Lys Gly Glu Lys
        35                  40                  45

Gly Glu Lys Gly Phe Pro Gly Pro Pro Gly Ser Pro Gly Gln Lys Gly
    50                  55                  60

Phe Thr Gly Pro Glu Gly Leu Pro Gly Pro Gln Gly Pro Lys Gly Phe
65                  70                  75                  80

Pro Gly Leu Pro Gly Leu Thr Gly Ser Lys Gly Val Arg Gly Ile Ser
                85                  90                  95

Gly Leu Pro Gly Phe Ser Gly Ser Pro Gly Leu Pro Gly Thr Pro Gly
            100                 105                 110

Asn Thr Gly Pro Tyr Gly Leu Val Gly Val Pro Gly Cys Ser Gly Ser
        115                 120                 125

Lys Gly Glu Gln Gly Phe Pro Gly Leu Pro Gly Thr Leu Gly Tyr Pro
    130                 135                 140

Gly Ile Pro Gly Ala Ala Gly Leu Lys Gly Gln Lys Gly Ala Pro Ala
145                 150                 155                 160

Lys Glu Glu Asp Ile Glu Leu Asp Ala Lys Gly Asp Pro Gly Leu Pro
                165                 170                 175

Gly Ala Pro Gly Pro Gln Gly Leu Pro Gly Pro Pro Gly Phe Pro Gly
            180                 185                 190

Pro Val Gly Pro Pro Gly Pro Pro Gly Phe Phe Gly Phe Pro Gly Ala
        195                 200                 205

Met Gly Pro Arg Gly Pro Lys Gly His Met Gly Glu Arg Val Ile Gly
    210                 215                 220

His Lys Gly Glu Arg Gly Val Lys Gly Leu Thr Gly Pro Pro Gly Pro
225                 230                 235                 240

Pro Gly Thr Val Ile Val Thr Leu Thr Gly Pro Asp Asn Arg Thr Asp
                245                 250                 255

Leu Lys Gly Glu Lys Gly Asp Lys Gly Ala Met Gly Glu Pro Gly Pro
            260                 265                 270
```

```
Pro Gly Pro Ser Gly Leu Pro Gly Glu Ser Tyr Gly Ser Glu Lys Gly
        275                 280                 285

Ala Pro Gly Asp Pro Gly Leu Gln Gly Lys Pro Gly Lys Asp Gly Val
    290                 295                 300

Pro Gly Phe Pro Gly Ser Glu Gly Val Lys Gly Asn Arg Gly Phe Pro
305                 310                 315                 320

Gly Leu Met Gly Glu Asp Gly Ile Lys Gly Gln Lys Gly Asp Ile Gly
                325                 330                 335

Pro Pro Gly Phe Arg Gly Pro Thr Glu Tyr Tyr Asp Thr Tyr Gln Glu
            340                 345                 350

Lys Gly Asp Glu Gly Thr Pro Gly Pro Pro Gly Pro Arg Gly Ala Arg
        355                 360                 365

Gly Pro Gln Gly Pro Ser Gly Pro Pro Gly Val Pro Gly Ser Pro Gly
    370                 375                 380

Ser Ser Arg Pro Gly Leu Arg Gly Ala Pro Gly Trp Pro Gly Leu Lys
385                 390                 395                 400

Gly Ser Lys Gly Glu Arg Gly Arg Pro Gly Lys Asp Ala Met Gly Thr
                405                 410                 415

Pro Gly Ser Pro Gly Cys Ala Gly Ser Pro Gly Leu Pro Gly Ser Pro
            420                 425                 430

Gly Pro Pro Gly Pro Pro Gly Asp Ile Val Phe Arg Lys Gly Pro Pro
        435                 440                 445

Gly Asp His Gly Leu Pro Gly Tyr Leu Gly Ser Pro Gly Ile Pro Gly
    450                 455                 460

Val Asp Gly Pro Lys Gly Glu Pro Gly Leu Leu Cys Thr Gln Cys Pro
465                 470                 475                 480

Tyr Ile Pro Gly Pro Pro Gly Leu Pro Gly Leu Pro Gly Leu His Gly
                485                 490                 495

Val Lys Gly Ile Pro Gly Arg Gln Gly Ala Ala Gly Leu Lys Gly Ser
            500                 505                 510

Pro Gly Ser Pro Gly Asn Thr Gly Leu Pro Gly Phe Pro Gly Phe Pro
        515                 520                 525

Gly Ala Gln Gly Asp Pro Gly Leu Lys Gly Glu Lys Gly Glu Thr Leu
    530                 535                 540
```

```
Gln Pro Glu Gly Gln Val Gly Val Pro Gly Asp Pro Gly Leu Arg Gly
545                 550                 555                 560

Gln Pro Gly Arg Lys Gly Leu Asp Gly Ile Pro Gly Thr Pro Gly Val
                565                 570                 575

Lys Gly Leu Pro Gly Pro Lys Gly Glu Leu Ala Leu Ser Gly Glu Lys
            580                 585                 590

Gly Asp Gln Gly Pro Pro Gly Asp Pro Gly Ser Pro Gly Ser Pro Gly
        595                 600                 605

Pro Ala Gly Pro Ala Gly Pro Pro Gly Tyr Gly Pro Gln Gly Glu Pro
    610                 615                 620

Gly Leu Gln Gly Thr Gln Gly Val Pro Gly Ala Pro Gly Pro Pro Gly
625                 630                 635                 640

Glu Ala Gly Pro Arg Gly Glu Leu Ser Val Ser Thr Pro Val Pro Gly
                645                 650                 655

Pro Pro Gly Pro Pro Gly Pro Pro Gly His Pro Gly Pro Gln Gly Pro
            660                 665                 670

Pro Gly Ile Pro Gly Ser Leu Gly Lys Cys Gly Asp Pro Gly Leu Pro
        675                 680                 685

Gly Pro Asp Gly Glu Pro Gly Ile Pro Gly Ile Gly Phe Pro Gly Pro
    690                 695                 700

Pro Gly Pro Lys Gly Asp Gln Gly Phe Pro Gly Thr Lys Gly Ser Leu
705                 710                 715                 720

Gly Cys Pro Gly Lys Met Gly Glu Pro Gly Leu Pro Gly Lys Pro Gly
                725                 730                 735

Leu Pro Gly Ala Lys Gly Glu Pro Ala Val Ala Met Pro Gly Gly Pro
            740                 745                 750

Gly Thr Pro Gly Phe Pro Gly Glu Arg Gly Asn Ser Gly Glu His Gly
        755                 760                 765

Glu Ile Gly Leu Pro Gly Leu Pro Gly Leu Pro Gly Thr Pro Gly Asn
    770                 775                 780

Glu Gly Leu Asp Gly Pro Arg Gly Asp Pro Gly Gln Pro Gly Pro Pro
785                 790                 795                 800

Gly Glu Gln Gly Pro Pro Gly Arg Cys Ile Glu Gly Pro Arg Gly Ala
                805                 810                 815
```

```
Gln Gly Leu Pro Gly Leu Asn Gly Leu Lys Gly Gln Gln Gly Arg Arg
            820                 825                 830

Gly Lys Thr Gly Pro Lys Gly Asp Pro Gly Ile Pro Gly Leu Asp Arg
        835                 840                 845

Ser Gly Phe Pro Gly Glu Thr Gly Ser Pro Gly Ile Pro Gly His Gln
    850                 855                 860

Gly Glu Met Gly Pro Leu Gly Gln Arg Gly Tyr Pro Gly Asn Pro Gly
865                 870                 875                 880

Ile Leu Gly Pro Pro Gly Glu Asp Gly Val Ile Gly Met Met Gly Phe
                885                 890                 895

Pro Gly Ala Ile Gly Pro Pro Gly Pro Pro Gly Asn Pro Gly Thr Pro
            900                 905                 910

Gly Gln Arg Gly Ser Pro Gly Ile Pro Gly Val Lys Gly Gln Arg Gly
        915                 920                 925

Thr Pro Gly Ala Lys Gly Glu Gln Gly Asp Lys Gly Asn Pro Gly Pro
    930                 935                 940

Ser Glu Ile Ser His Val Ile Gly Asp Lys Gly Glu Pro Gly Leu Lys
945                 950                 955                 960

Gly Phe Ala Gly Asn Pro Gly Glu Lys Gly Asn Arg Gly Val Pro Gly
                965                 970                 975

Met Pro Gly Leu Lys Gly Leu Lys Gly Leu Pro Gly Pro Ala Gly Pro
            980                 985                 990

Pro Gly Pro Arg Gly Asp Leu Gly  Ser Thr Gly Asn Pro  Gly Glu Pro
        995                 1000                1005

Gly Leu  Arg Gly Ile Pro Gly  Ser Met Gly Asn Met  Gly Met Pro
    1010                1015                1020

Gly Ser  Lys Gly Lys Arg Gly  Thr Leu Gly Phe Pro  Gly Arg Ala
    1025                1030                1035

Gly Arg  Pro Gly Leu Pro Gly  Ile His Gly Leu Gln  Gly Asp Lys
    1040                1045                1050

Gly Glu  Pro Gly Tyr Ser Glu  Gly Thr Arg Pro Gly  Pro Pro Gly
    1055                1060                1065

Pro Thr  Gly Asp Pro Gly Leu  Pro Gly Asp Met Gly  Lys Lys Gly
    1070                1075                1080
```

```
Glu Met  Gly Gln Pro Gly Pro  Pro Gly His Leu Gly  Pro Ala Gly
    1085                 1090                 1095

Pro Glu  Gly Ala Pro Gly Ser  Pro Gly Ser Pro Gly  Leu Pro Gly
    1100                 1105                 1110

Lys Pro  Gly Pro His Gly Asp  Leu Gly Phe Lys Gly  Ile Lys Gly
    1115                 1120                 1125

Leu Leu  Gly Pro Pro Gly Ile  Arg Gly Pro Pro Gly  Leu Pro Gly
    1130                 1135                 1140

Phe Pro  Gly Ser Pro Gly Pro  Met Gly Ile Arg Gly  Asp Gln Gly
    1145                 1150                 1155

Arg Asp  Gly Ile Pro Gly Pro  Ala Gly Glu Lys Gly  Glu Thr Gly
    1160                 1165                 1170

Leu Leu  Arg Ala Pro Pro Gly  Pro Arg Gly Asn Pro  Gly Ala Gln
    1175                 1180                 1185

Gly Ala  Lys Gly Asp Arg Gly  Ala Pro Gly Phe Pro  Gly Leu Pro
    1190                 1195                 1200

Gly Arg  Lys Gly Ala Met Gly  Asp Ala Gly Pro Arg  Gly Pro Thr
    1205                 1210                 1215

Gly Ile  Glu Gly Phe Pro Gly  Pro Pro Gly Leu Pro  Gly Ala Ile
    1220                 1225                 1230

Ile Pro  Gly Gln Thr Gly Asn  Arg Gly Pro Pro Gly  Ser Arg Gly
    1235                 1240                 1245

Ser Pro  Gly Ala Pro Gly Pro  Pro Gly Pro Pro Gly  Ser His Val
    1250                 1255                 1260

Ile Gly  Ile Lys Gly Asp Lys  Gly Ser Met Gly His  Pro Gly Pro
    1265                 1270                 1275

Lys Gly  Pro Pro Gly Thr Ala  Gly Asp Met Gly Pro  Pro Gly Arg
    1280                 1285                 1290

Leu Gly  Ala Pro Gly Thr Pro  Gly Leu Pro Gly Pro  Arg Gly Asp
    1295                 1300                 1305

Pro Gly  Phe Gln Gly Phe Pro  Gly Val Lys Gly Glu  Lys Gly Asn
    1310                 1315                 1320

Pro Gly  Phe Leu Gly Ser Ile  Gly Pro Pro Gly Pro  Ile Gly Pro
    1325                 1330                 1335
```

```
Lys Gly  Pro Pro Gly Val Arg  Gly Asp Pro Gly Thr  Leu Lys Ile
    1340                1345                1350

Ile Ser  Leu Pro Gly Ser Pro  Gly Pro Pro Gly Thr  Pro Gly Glu
    1355                1360                1365

Pro Gly  Met Gln Gly Glu Pro  Gly Pro Pro Gly Pro  Pro Gly Asn
    1370                1375                1380

Leu Gly  Pro Cys Gly Pro Arg  Gly Lys Pro Gly Lys  Asp Gly Lys
    1385                1390                1395

Pro Gly  Thr Pro Gly Pro Ala  Gly Glu Lys Gly Asn  Lys Gly Ser
    1400                1405                1410

Lys Gly  Glu Pro Gly Pro Ala  Gly Ser Asp Gly Leu  Pro Gly Leu
    1415                1420                1425

Lys Gly  Lys Arg Gly Asp Ser  Gly Ser Pro Ala Thr  Trp Thr Thr
    1430                1435                1440

Arg Gly  Phe Val Phe Thr Arg  His Ser Gln Thr Thr  Ala Ile Pro
    1445                1450                1455

Ser Cys  Pro Glu Gly Thr Val  Pro Leu Tyr Ser Gly  Phe Ser Phe
    1460                1465                1470

Leu Phe  Val Gln Gly Asn Gln  Arg Ala His Gly Gln  Asp Leu Gly
    1475                1480                1485

Thr Leu  Gly Ser Cys Leu Gln  Arg Phe Thr Thr Met  Pro Phe Leu
    1490                1495                1500

Phe Cys  Asn Val Asn Asp Val  Cys Asn Phe Ala Ser  Arg Asn Asp
    1505                1510                1515

Tyr Ser  Tyr Trp Leu Ser Thr  Pro Ala Leu Met Pro  Met Asn Met
    1520                1525                1530

Ala Pro  Ile Thr Gly Arg Ala  Leu Glu Pro Tyr Ile  Ser Arg Cys
    1535                1540                1545

Thr Val  Cys Glu Gly Pro Ala  Ile Ala Ile Ala Val  His Ser Gln
    1550                1555                1560

Thr Thr  Asp Ile Pro Pro Cys  Pro His Gly Trp Ile  Ser Leu Trp
    1565                1570                1575

Lys Gly  Phe Ser Phe Ile Met  Phe Thr Ser Ala Gly  Ser Glu Gly
    1580                1585                1590
```

```
Thr Gly  Gln Ala Leu Ala Ser  Pro Gly Ser Cys Leu  Glu Glu Phe
    1595                 1600                 1605


Arg Ala  Ser Pro Phe Leu Glu  Cys His Gly Arg Gly  Thr Cys Asn
    1610                 1615                 1620


Tyr Tyr  Ser Asn Ser Tyr Ser  Phe Trp Leu Ala Ser  Leu Asn Pro
    1625                 1630                 1635


Glu Arg  Met Phe Arg Lys Pro  Ile Pro Ser Thr Val  Lys Ala Gly
    1640                 1645                 1650


Glu Leu  Glu Lys Ile Ile Ser  Arg Cys Gln Val Cys  Met Lys Lys
    1655                 1660                 1665


Arg His
    1670
```

<210> 69
<211> 1690
<212> PRT
<213> Homo sapiens

<400> 69

```
Met Trp Ser Leu His Ile Val Leu Met Arg Cys Ser Phe Arg Leu Thr
1               5                  10                  15


Lys Ser Leu Ala Thr Gly Pro Trp Ser Leu Ile Leu Ile Leu Phe Ser
            20                  25                  30


Val Gln Tyr Val Tyr Gly Ser Gly Lys Lys Tyr Ile Gly Pro Cys Gly
        35                  40                  45


Gly Arg Asp Cys Ser Val Cys His Cys Val Pro Glu Lys Gly Ser Arg
    50                  55                  60


Gly Pro Pro Gly Pro Pro Gly Pro Gln Gly Pro Ile Gly Pro Leu Gly
65                  70                  75                  80


Ala Pro Gly Pro Ile Gly Leu Ser Gly Glu Lys Gly Met Arg Gly Asp
                85                  90                  95


Arg Gly Pro Pro Gly Ala Ala Gly Asp Lys Gly Asp Lys Gly Pro Thr
            100                 105                 110


Gly Val Pro Gly Phe Pro Gly Leu Asp Gly Ile Pro Gly His Pro Gly
        115                 120                 125


Pro Pro Gly Pro Arg Gly Lys Pro Gly Met Ser Gly His Asn Gly Ser
    130                 135                 140
```

```
Arg Gly Asp Pro Gly Phe Pro Gly Gly Arg Gly Ala Leu Gly Pro Gly
145                 150                 155                 160

Gly Pro Leu Gly His Pro Gly Glu Lys Gly Glu Lys Gly Asn Ser Val
                165                 170                 175

Phe Ile Leu Gly Ala Val Lys Gly Ile Gln Gly Asp Arg Gly Asp Pro
            180                 185                 190

Gly Leu Pro Gly Leu Pro Gly Ser Trp Gly Ala Gly Gly Pro Ala Gly
        195                 200                 205

Pro Thr Gly Tyr Pro Gly Glu Pro Gly Leu Val Gly Pro Pro Gly Gln
    210                 215                 220

Pro Gly Arg Pro Gly Leu Lys Gly Asn Pro Gly Val Gly Val Lys Gly
225                 230                 235                 240

Gln Met Gly Asp Pro Gly Glu Val Gly Gln Gln Gly Ser Pro Gly Pro
                245                 250                 255

Thr Leu Leu Val Glu Pro Pro Asp Phe Cys Leu Tyr Lys Gly Glu Lys
            260                 265                 270

Gly Ile Lys Gly Ile Pro Gly Met Val Gly Leu Pro Gly Pro Pro Gly
        275                 280                 285

Arg Lys Gly Glu Ser Gly Ile Gly Ala Lys Gly Glu Lys Gly Ile Pro
    290                 295                 300

Gly Phe Pro Gly Pro Arg Gly Asp Pro Gly Ser Tyr Gly Ser Pro Gly
305                 310                 315                 320

Phe Pro Gly Leu Lys Gly Glu Leu Gly Leu Val Gly Asp Pro Gly Leu
                325                 330                 335

Phe Gly Leu Ile Gly Pro Lys Gly Asp Pro Gly Asn Arg Gly His Pro
            340                 345                 350

Gly Pro Pro Gly Val Leu Val Thr Pro Pro Leu Pro Leu Lys Gly Pro
        355                 360                 365

Pro Gly Asp Pro Gly Phe Pro Gly Arg Tyr Gly Glu Thr Gly Asp Val
    370                 375                 380

Gly Pro Pro Gly Pro Pro Gly Leu Leu Gly Arg Pro Gly Glu Ala Cys
385                 390                 395                 400

Ala Gly Met Ile Gly Pro Pro Gly Pro Gln Gly Phe Pro Gly Leu Pro
                405                 410                 415
```

```
Gly Leu Pro Gly Glu Ala Gly Ile Pro Gly Arg Pro Asp Ser Ala Pro
            420                 425                 430

Gly Lys Pro Gly Lys Pro Gly Ser Pro Gly Leu Pro Gly Ala Pro Gly
        435                 440                 445

Leu Gln Gly Leu Pro Gly Ser Ser Val Ile Tyr Cys Ser Val Gly Asn
    450                 455                 460

Pro Gly Pro Gln Gly Ile Lys Gly Lys Val Gly Pro Pro Gly Gly Arg
465                 470                 475                 480

Gly Pro Lys Gly Glu Lys Gly Asn Glu Gly Leu Cys Ala Cys Glu Pro
                485                 490                 495

Gly Pro Met Gly Pro Pro Gly Pro Pro Gly Leu Pro Gly Arg Gln Gly
            500                 505                 510

Ser Lys Gly Asp Leu Gly Leu Pro Gly Trp Leu Gly Thr Lys Gly Asp
        515                 520                 525

Pro Gly Pro Pro Gly Ala Glu Gly Pro Pro Gly Leu Pro Gly Lys His
    530                 535                 540

Gly Ala Ser Gly Pro Pro Gly Asn Lys Gly Ala Lys Gly Asp Met Val
545                 550                 555                 560

Val Ser Arg Val Lys Gly His Lys Gly Glu Arg Gly Pro Asp Gly Pro
                565                 570                 575

Pro Gly Phe Pro Gly Gln Pro Gly Ser His Gly Arg Asp Gly His Ala
            580                 585                 590

Gly Glu Lys Gly Asp Pro Gly Pro Pro Gly Asp His Glu Asp Ala Thr
        595                 600                 605

Pro Gly Gly Lys Gly Phe Pro Gly Pro Leu Gly Pro Pro Gly Lys Ala
    610                 615                 620

Gly Pro Val Gly Pro Pro Gly Leu Gly Phe Pro Gly Pro Pro Gly Glu
625                 630                 635                 640

Arg Gly His Pro Gly Val Pro Gly His Pro Gly Val Arg Gly Pro Asp
                645                 650                 655

Gly Leu Lys Gly Gln Lys Gly Asp Thr Ile Ser Cys Asn Val Thr Tyr
            660                 665                 670

Pro Gly Arg His Gly Pro Pro Gly Phe Asp Gly Pro Pro Gly Pro Lys
        675                 680                 685
```

```
Gly Phe Pro Gly Pro Gln Gly Ala Pro Gly Leu Ser Gly Ser Asp Gly
    690                 695                 700

His Lys Gly Arg Pro Gly Thr Pro Gly Thr Ala Glu Ile Pro Gly Pro
705                 710                 715                 720

Pro Gly Phe Arg Gly Asp Met Gly Asp Pro Gly Phe Gly Gly Glu Lys
                725                 730                 735

Gly Ser Ser Pro Val Gly Pro Pro Gly Pro Pro Gly Ser Pro Gly Val
            740                 745                 750

Asn Gly Gln Lys Gly Ile Pro Gly Asp Pro Ala Phe Gly His Leu Gly
        755                 760                 765

Pro Pro Gly Lys Arg Gly Leu Ser Gly Val Pro Gly Ile Lys Gly Pro
    770                 775                 780

Arg Gly Asp Pro Gly Cys Pro Gly Ala Glu Gly Pro Ala Gly Ile Pro
785                 790                 795                 800

Gly Phe Leu Gly Leu Lys Gly Pro Lys Gly Arg Glu Gly His Ala Gly
                805                 810                 815

Phe Pro Gly Val Pro Gly Pro Pro Gly His Ser Cys Glu Arg Gly Ala
            820                 825                 830

Pro Gly Ile Pro Gly Gln Pro Gly Leu Pro Gly Tyr Pro Gly Ser Pro
        835                 840                 845

Gly Ala Pro Gly Gly Lys Gly Gln Pro Gly Asp Val Gly Pro Pro Gly
    850                 855                 860

Pro Ala Gly Met Lys Gly Leu Pro Gly Leu Pro Gly Arg Pro Gly Ala
865                 870                 875                 880

His Gly Pro Pro Gly Leu Pro Gly Ile Pro Gly Pro Phe Gly Asp Asp
                885                 890                 895

Gly Leu Pro Gly Pro Pro Gly Pro Lys Gly Pro Arg Gly Leu Pro Gly
            900                 905                 910

Phe Pro Gly Phe Pro Gly Glu Arg Gly Lys Pro Gly Ala Glu Gly Cys
        915                 920                 925

Pro Gly Ala Lys Gly Glu Pro Gly Glu Lys Gly Met Ser Gly Leu Pro
    930                 935                 940

Gly Asp Arg Gly Leu Arg Gly Ala Lys Gly Ala Ile Gly Pro Pro Gly
945                 950                 955                 960
```

```
Asp Glu Gly Glu Met Ala Ile Ile Ser Gln Lys Gly Thr Pro Gly Glu
               965                 970                 975

Pro Gly Pro Pro Gly Asp Asp Gly Phe Pro Gly Glu Arg Gly Asp Lys
           980                 985                 990

Gly Thr Pro Gly Met Gln Gly Arg  Arg Gly Glu Pro Gly  Arg Tyr Gly
       995                1000                1005

Pro Pro  Gly Phe His Arg Gly  Glu Pro Gly Glu Lys  Gly Gln Pro
    1010                1015                1020

Gly Pro  Pro Gly Pro Pro Gly  Pro Pro Gly Ser Thr  Gly Leu Arg
    1025                1030                1035

Gly Phe  Ile Gly Phe Pro Gly  Leu Pro Gly Asp Gln  Gly Glu Pro
    1040                1045                1050

Gly Ser  Pro Gly Pro Pro Gly  Phe Ser Gly Ile Asp  Gly Ala Arg
    1055                1060                1065

Gly Pro  Lys Gly Asn Lys Gly  Asp Pro Ala Ser His  Phe Gly Pro
    1070                1075                1080

Pro Gly  Pro Lys Gly Glu Pro  Gly Ser Pro Gly Cys  Pro Gly His
    1085                1090                1095

Phe Gly  Ala Ser Gly Glu Gln  Gly Leu Pro Gly Ile  Gln Gly Pro
    1100                1105                1110

Arg Gly  Ser Pro Gly Arg Pro  Gly Pro Pro Gly Ser  Ser Gly Pro
    1115                1120                1125

Pro Gly  Cys Pro Gly Asp His  Gly Met Pro Gly Leu  Arg Gly Gln
    1130                1135                1140

Pro Gly  Glu Met Gly Asp Pro  Gly Pro Arg Gly Leu  Gln Gly Asp
    1145                1150                1155

Pro Gly  Ile Pro Gly Pro Pro  Gly Ile Lys Gly Pro  Ser Gly Ser
    1160                1165                1170

Pro Gly  Leu Asn Gly Leu His  Gly Leu Lys Gly Gln  Lys Gly Thr
    1175                1180                1185

Lys Gly  Ala Ser Gly Leu His  Asp Val Gly Pro Pro  Gly Pro Val
    1190                1195                1200

Gly Ile  Pro Gly Leu Lys Gly  Glu Arg Gly Asp Pro  Gly Ser Pro
    1205                1210                1215
```

```
Gly Ile  Ser Pro Pro Gly Pro  Arg Gly Lys Lys Gly  Pro Pro Gly
    1220                 1225                 1230

Pro Pro  Gly Ser Ser Gly Pro  Pro Gly Pro Ala Gly  Ala Thr Gly
    1235                 1240                 1245

Arg Ala  Pro Lys Asp Ile Pro  Asp Pro Gly Pro Pro  Gly Asp Gln
    1250                 1255                 1260

Gly Pro  Pro Gly Pro Asp Gly  Pro Arg Gly Ala Pro  Gly Pro Pro
    1265                 1270                 1275

Gly Leu  Pro Gly Ser Val Asp  Leu Leu Arg Gly Glu  Pro Gly Asp
    1280                 1285                 1290

Cys Gly  Leu Pro Gly Pro Pro  Gly Pro Pro Gly Pro  Pro Gly Pro
    1295                 1300                 1305

Pro Gly  Tyr Lys Gly Phe Pro  Gly Cys Asp Gly Lys  Asp Gly Gln
    1310                 1315                 1320

Lys Gly  Pro Val Gly Phe Pro  Gly Pro Gln Gly Pro  His Gly Phe
    1325                 1330                 1335

Pro Gly  Pro Pro Gly Glu Lys  Gly Leu Pro Gly Pro  Pro Gly Arg
    1340                 1345                 1350

Lys Gly  Pro Thr Gly Leu Pro  Gly Pro Arg Gly Glu  Pro Gly Pro
    1355                 1360                 1365

Pro Ala  Asp Val Asp Asp Cys  Pro Arg Ile Pro Gly  Leu Pro Gly
    1370                 1375                 1380

Ala Pro  Gly Met Arg Gly Pro  Glu Gly Ala Met Gly  Leu Pro Gly
    1385                 1390                 1395

Met Arg  Gly Pro Ser Gly Pro  Gly Cys Lys Gly Glu  Pro Gly Leu
    1400                 1405                 1410

Asp Gly  Arg Arg Gly Val Asp  Gly Val Pro Gly Ser  Pro Gly Pro
    1415                 1420                 1425

Pro Gly  Arg Lys Gly Asp Thr  Gly Glu Asp Gly Tyr  Pro Gly Gly
    1430                 1435                 1440

Pro Gly  Pro Pro Gly Pro Ile  Gly Asp Pro Gly Pro  Lys Gly Phe
    1445                 1450                 1455

Gly Pro  Gly Tyr Leu Gly Gly  Phe Leu Leu Val Leu  His Ser Gln
    1460                 1465                 1470
```

```
Thr Asp  Gln Glu Pro Thr Cys  Pro Leu Gly Met Pro  Arg Leu Trp
    1475                 1480                 1485

Thr Gly  Tyr Ser Leu Leu Tyr  Leu Glu Gly Gln Glu  Lys Ala His
    1490                 1495                 1500

Asn Gln  Asp Leu Gly Leu Ala  Gly Ser Cys Leu Pro  Val Phe Ser
    1505                 1510                 1515

Thr Leu  Pro Phe Ala Tyr Cys  Asn Ile His Gln Val  Cys His Tyr
    1520                 1525                 1530

Ala Gln  Arg Asn Asp Arg Ser  Tyr Trp Leu Ala Ser  Ala Ala Pro
    1535                 1540                 1545

Leu Pro  Met Met Pro Leu Ser  Glu Glu Ala Ile Arg  Pro Tyr Val
    1550                 1555                 1560

Ser Arg  Cys Ala Val Cys Glu  Ala Pro Ala Gln Ala  Val Ala Val
    1565                 1570                 1575

His Ser  Gln Asp Gln Ser Ile  Pro Pro Cys Pro Gln  Thr Trp Arg
    1580                 1585                 1590

Ser Leu  Trp Ile Gly Tyr Ser  Phe Leu Met His Thr  Gly Ala Gly
    1595                 1600                 1605

Asp Gln  Gly Gly Gly Gln Ala  Leu Met Ser Pro Gly  Ser Cys Leu
    1610                 1615                 1620

Glu Asp  Phe Arg Ala Ala Pro  Phe Leu Glu Cys Gln  Gly Arg Gln
    1625                 1630                 1635

Gly Thr  Cys His Phe Phe Ala  Asn Lys Tyr Ser Phe  Trp Leu Thr
    1640                 1645                 1650

Thr Val  Lys Ala Asp Leu Gln  Phe Ser Ser Ala Pro  Ala Pro Asp
    1655                 1660                 1665

Thr Leu  Lys Glu Ser Gln Ala  Gln Arg Gln Lys Ile  Ser Arg Cys
    1670                 1675                 1680

Gln Val  Cys Val Lys Tyr Ser
    1685                 1690
```

<210> 70
<211> 1685
<212> PRT
<213> Homo sapiens

<400> 70

```
Met Lys Leu Arg Gly Val Ser Leu Ala Ala Gly Leu Phe Leu Leu Ala
1               5                  10                  15

Leu Ser Leu Trp Gly Gln Pro Ala Glu Ala Ala Ala Cys Tyr Gly Cys
            20                  25                  30

Ser Pro Gly Ser Lys Cys Asp Cys Ser Gly Ile Lys Gly Glu Lys Gly
        35                  40                  45

Glu Arg Gly Phe Pro Gly Leu Glu Gly His Pro Gly Leu Pro Gly Phe
    50                  55                  60

Pro Gly Pro Glu Gly Pro Pro Gly Pro Arg Gly Gln Lys Gly Asp Asp
65                  70                  75                  80

Gly Ile Pro Gly Pro Pro Gly Pro Lys Gly Ile Arg Gly Pro Pro Gly
                85                  90                  95

Leu Pro Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Met Pro Gly His
            100                 105                 110

Asp Gly Ala Pro Gly Pro Gln Gly Ile Pro Gly Cys Asn Gly Thr Lys
        115                 120                 125

Gly Glu Arg Gly Phe Pro Gly Ser Pro Gly Phe Pro Gly Leu Gln Gly
    130                 135                 140

Pro Pro Gly Pro Pro Gly Ile Pro Gly Met Lys Gly Glu Pro Gly Ser
145                 150                 155                 160

Ile Ile Met Ser Ser Leu Pro Gly Pro Lys Gly Asn Pro Gly Tyr Pro
                165                 170                 175

Gly Pro Pro Gly Ile Gln Gly Leu Pro Gly Pro Thr Gly Ile Pro Gly
            180                 185                 190

Pro Ile Gly Pro Pro Gly Pro Pro Gly Leu Met Gly Pro Pro Gly Pro
        195                 200                 205

Pro Gly Leu Pro Gly Pro Lys Gly Asn Met Gly Leu Asn Phe Gln Gly
    210                 215                 220

Pro Lys Gly Glu Lys Gly Glu Gln Gly Leu Gln Gly Pro Pro Gly Pro
225                 230                 235                 240

Pro Gly Gln Ile Ser Glu Gln Lys Arg Pro Ile Asp Val Glu Phe Gln
                245                 250                 255

Lys Gly Asp Gln Gly Leu Pro Gly Asp Arg Gly Pro Pro Gly Pro Pro
            260                 265                 270
```

```
Gly Ile Arg Gly Pro Pro Gly Pro Pro Gly Gly Glu Lys Gly Glu Lys
        275                 280                 285

Gly Glu Gln Gly Glu Pro Gly Lys Arg Gly Lys Pro Gly Lys Asp Gly
    290                 295                 300

Glu Asn Gly Gln Pro Gly Ile Pro Gly Leu Pro Gly Asp Pro Gly Tyr
305                 310                 315                 320

Pro Gly Glu Pro Gly Arg Asp Gly Glu Lys Gly Gln Lys Gly Asp Thr
                325                 330                 335

Gly Pro Pro Gly Pro Pro Gly Leu Val Ile Pro Arg Pro Gly Thr Gly
            340                 345                 350

Ile Thr Ile Gly Glu Lys Gly Asn Ile Gly Leu Pro Gly Leu Pro Gly
        355                 360                 365

Glu Lys Gly Glu Arg Gly Phe Pro Gly Ile Gln Gly Pro Pro Gly Leu
    370                 375                 380

Pro Gly Pro Pro Gly Ala Ala Val Met Gly Pro Pro Gly Pro Pro Gly
385                 390                 395                 400

Phe Pro Gly Glu Arg Gly Gln Lys Gly Asp Glu Gly Pro Pro Gly Ile
                405                 410                 415

Ser Ile Pro Gly Pro Pro Gly Leu Asp Gly Gln Pro Gly Ala Pro Gly
            420                 425                 430

Leu Pro Gly Pro Pro Gly Pro Ala Gly Pro His Ile Pro Pro Ser Asp
        435                 440                 445

Glu Ile Cys Glu Pro Gly Pro Pro Gly Pro Pro Gly Ser Pro Gly Asp
    450                 455                 460

Lys Gly Leu Gln Gly Glu Gln Gly Val Lys Gly Asp Lys Gly Asp Thr
465                 470                 475                 480

Cys Phe Asn Cys Ile Gly Thr Gly Ile Ser Gly Pro Pro Gly Gln Pro
                485                 490                 495

Gly Leu Pro Gly Leu Pro Gly Pro Pro Gly Ser Leu Gly Phe Pro Gly
            500                 505                 510

Gln Lys Gly Glu Lys Gly Gln Ala Gly Ala Thr Gly Pro Lys Gly Leu
        515                 520                 525

Pro Gly Ile Pro Gly Ala Pro Gly Ala Pro Gly Phe Pro Gly Ser Lys
    530                 535                 540
```

```
Gly Glu Pro Gly Asp Ile Leu Thr Phe Pro Gly Met Lys Gly Asp Lys
545                 550                 555                 560

Gly Glu Leu Gly Ser Pro Gly Ala Pro Gly Leu Pro Gly Leu Pro Gly
                565                 570                 575

Thr Pro Gly Gln Asp Gly Leu Pro Gly Leu Pro Gly Pro Lys Gly Glu
            580                 585                 590

Pro Gly Gly Ile Thr Phe Lys Gly Glu Arg Gly Pro Pro Gly Asn Pro
        595                 600                 605

Gly Leu Pro Gly Leu Pro Gly Asn Ile Gly Pro Met Gly Pro Pro Gly
    610                 615                 620

Phe Gly Pro Pro Gly Pro Val Gly Glu Lys Gly Ile Gln Gly Val Ala
625                 630                 635                 640

Gly Asn Pro Gly Gln Pro Gly Ile Pro Gly Pro Lys Gly Asp Pro Gly
                645                 650                 655

Gln Thr Ile Thr Gln Pro Gly Lys Pro Gly Leu Pro Gly Asn Pro Gly
            660                 665                 670

Arg Asp Gly Asp Val Gly Leu Pro Gly Asp Pro Gly Leu Pro Gly Gln
        675                 680                 685

Pro Gly Leu Pro Gly Ile Pro Gly Ser Lys Gly Glu Pro Gly Ile Pro
    690                 695                 700

Gly Ile Gly Leu Pro Gly Pro Pro Gly Pro Lys Gly Phe Pro Gly Ile
705                 710                 715                 720

Pro Gly Pro Pro Gly Ala Pro Gly Thr Pro Gly Arg Ile Gly Leu Glu
                725                 730                 735

Gly Pro Pro Gly Pro Pro Gly Phe Pro Gly Pro Lys Gly Glu Pro Gly
            740                 745                 750

Phe Ala Leu Pro Gly Pro Pro Gly Pro Pro Gly Leu Pro Gly Phe Lys
        755                 760                 765

Gly Ala Leu Gly Pro Lys Gly Asp Arg Gly Phe Pro Gly Pro Pro Gly
    770                 775                 780

Pro Pro Gly Arg Thr Gly Leu Asp Gly Leu Pro Gly Pro Lys Gly Asp
785                 790                 795                 800

Val Gly Pro Asn Gly Gln Pro Gly Pro Met Gly Pro Pro Gly Leu Pro
                805                 810                 815
```

```
Gly Ile Gly Val Gln Gly Pro Pro Gly Pro Pro Gly Ile Pro Gly Pro
            820                 825                 830

Ile Gly Gln Pro Gly Leu His Gly Ile Pro Gly Glu Lys Gly Asp Pro
        835                 840                 845

Gly Pro Pro Gly Leu Asp Val Pro Gly Pro Pro Gly Glu Arg Gly Ser
    850                 855                 860

Pro Gly Ile Pro Gly Ala Pro Gly Pro Ile Gly Pro Pro Gly Ser Pro
865                 870                 875                 880

Gly Leu Pro Gly Lys Ala Gly Ala Ser Gly Phe Pro Gly Thr Lys Gly
                885                 890                 895

Glu Met Gly Met Met Gly Pro Pro Gly Pro Pro Gly Pro Leu Gly Ile
            900                 905                 910

Pro Gly Arg Ser Gly Val Pro Gly Leu Lys Gly Asp Asp Gly Leu Gln
        915                 920                 925

Gly Gln Pro Gly Leu Pro Gly Pro Thr Gly Glu Lys Gly Ser Lys Gly
    930                 935                 940

Glu Pro Gly Leu Pro Gly Pro Pro Gly Pro Met Asp Pro Asn Leu Leu
945                 950                 955                 960

Gly Ser Lys Gly Glu Lys Gly Glu Pro Gly Leu Pro Gly Ile Pro Gly
                965                 970                 975

Val Ser Gly Pro Lys Gly Tyr Gln Gly Leu Pro Gly Asp Pro Gly Gln
            980                 985                 990

Pro Gly Leu Ser Gly Gln Pro Gly  Leu Pro Gly Pro Pro  Gly Pro Lys
        995                 1000                1005

Gly Asn  Pro Gly Leu Pro Gly  Gln Pro Gly Leu Ile  Gly Pro Pro
    1010                1015                1020

Gly Leu  Lys Gly Thr Ile Gly  Asp Met Gly Phe Pro  Gly Pro Gln
    1025                1030                1035

Gly Val  Glu Gly Pro Pro Gly  Pro Ser Gly Val Pro  Gly Gln Pro
    1040                1045                1050

Gly Ser  Pro Gly Leu Pro Gly  Gln Lys Gly Asp Lys  Gly Asp Pro
    1055                1060                1065

Gly Ile  Ser Ser Ile Gly Leu  Pro Gly Leu Pro Gly  Pro Lys Gly
    1070                1075                1080
```

```
Glu Pro  Gly Leu Pro Gly Tyr  Pro Gly Asn Pro Gly  Ile Lys Gly
    1085                 1090                 1095

Ser Val  Gly Asp Pro Gly Leu  Pro Gly Leu Pro Gly  Thr Pro Gly
    1100                 1105                 1110

Ala Lys  Gly Gln Pro Gly Leu  Pro Gly Phe Pro Gly  Thr Pro Gly
    1115                 1120                 1125

Pro Pro  Gly Pro Lys Gly Ile  Ser Gly Pro Pro Gly  Asn Pro Gly
    1130                 1135                 1140

Leu Pro  Gly Glu Pro Gly Pro  Val Gly Gly Gly Gly  His Pro Gly
    1145                 1150                 1155

Gln Pro  Gly Pro Pro Gly Glu  Lys Gly Lys Pro Gly  Gln Asp Gly
    1160                 1165                 1170

Ile Pro  Gly Pro Ala Gly Gln  Lys Gly Glu Pro Gly  Gln Pro Gly
    1175                 1180                 1185

Phe Gly  Asn Pro Gly Pro Pro  Gly Leu Pro Gly Leu  Ser Gly Gln
    1190                 1195                 1200

Lys Gly  Asp Gly Gly Leu Pro  Gly Ile Pro Gly Asn  Pro Gly Leu
    1205                 1210                 1215

Pro Gly  Pro Lys Gly Glu Pro  Gly Phe His Gly Phe  Pro Gly Val
    1220                 1225                 1230

Gln Gly  Pro Pro Gly Pro Pro  Gly Ser Pro Gly Pro  Ala Leu Glu
    1235                 1240                 1245

Gly Pro  Lys Gly Asn Pro Gly  Pro Gln Gly Pro Pro  Gly Arg Pro
    1250                 1255                 1260

Gly Leu  Pro Gly Pro Glu Gly  Pro Pro Gly Leu Pro  Gly Asn Gly
    1265                 1270                 1275

Gly Ile  Lys Gly Glu Lys Gly  Asn Pro Gly Gln Pro  Gly Leu Pro
    1280                 1285                 1290

Gly Leu  Pro Gly Leu Lys Gly  Asp Gln Gly Pro Pro  Gly Leu Gln
    1295                 1300                 1305

Gly Asn  Pro Gly Arg Pro Gly  Leu Asn Gly Met Lys  Gly Asp Pro
    1310                 1315                 1320

Gly Leu  Pro Gly Val Pro Gly  Phe Pro Gly Met Lys  Gly Pro Ser
    1325                 1330                 1335
```

```
Gly Val  Pro Gly Ser Ala Gly  Pro Glu Gly Glu Pro  Gly Leu Ile
    1340                1345                1350

Gly Pro  Pro Gly Pro Pro Gly  Leu Pro Gly Pro Ser  Gly Gln Ser
    1355                1360                1365

Ile Ile  Ile Lys Gly Asp Ala  Gly Pro Pro Gly Ile  Pro Gly Gln
    1370                1375                1380

Pro Gly  Leu Lys Gly Leu Pro  Gly Pro Gln Gly Pro  Gln Gly Leu
    1385                1390                1395

Pro Gly  Pro Thr Gly Pro Pro  Gly Asp Pro Gly Arg  Asn Gly Leu
    1400                1405                1410

Pro Gly  Phe Asp Gly Ala Gly  Gly Arg Lys Gly Asp  Pro Gly Leu
    1415                1420                1425

Pro Gly  Gln Pro Gly Thr Arg  Gly Leu Asp Gly Pro  Pro Gly Pro
    1430                1435                1440

Asp Gly  Leu Gln Gly Pro Pro  Gly Pro Pro Gly Thr  Ser Ser Val
    1445                1450                1455

Ala His  Gly Phe Leu Ile Thr  Arg His Ser Gln Thr  Thr Asp Ala
    1460                1465                1470

Pro Gln  Cys Pro Gln Gly Thr  Leu Gln Val Tyr Glu  Gly Phe Ser
    1475                1480                1485

Leu Leu  Tyr Val Gln Gly Asn  Lys Arg Ala His Gly  Gln Asp Leu
    1490                1495                1500

Gly Thr  Ala Gly Ser Cys Leu  Arg Arg Phe Ser Thr  Met Pro Phe
    1505                1510                1515

Met Phe  Cys Asn Ile Asn Asn  Val Cys Asn Phe Ala  Ser Arg Asn
    1520                1525                1530

Asp Tyr  Ser Tyr Trp Leu Ser  Thr Pro Glu Pro Met  Pro Met Ser
    1535                1540                1545

Met Gln  Pro Leu Lys Gly Gln  Ser Ile Gln Pro Phe  Ile Ser Arg
    1550                1555                1560

Cys Ala  Val Cys Glu Ala Pro  Ala Val Val Ile Ala  Val His Ser
    1565                1570                1575

Gln Thr  Ile Gln Ile Pro His  Cys Pro Gln Gly Trp  Asp Ser Leu
    1580                1585                1590
```

Trp Ile Gly Tyr Ser Phe Met Met His Thr Ser Ala Gly Ala Glu
1595 1600 1605

Gly Ser Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu Glu Glu
1610 1615 1620

Phe Arg Ser Ala Pro Phe Ile Glu Cys His Gly Arg Gly Thr Cys
1625 1630 1635

Asn Tyr Tyr Ala Asn Ser Tyr Ser Phe Trp Leu Ala Thr Val Asp
1640 1645 1650

Val Ser Asp Met Phe Ser Lys Pro Gln Ser Glu Thr Leu Lys Ala
1655 1660 1665

Gly Asp Leu Arg Thr Arg Ile Ser Arg Cys Gln Val Cys Met Lys
1670 1675 1680

Arg Thr
1685

<210> 71
<211> 1691
<212> PRT
<213> Homo sapiens

<400> 71

Met Leu Ile Asn Lys Leu Trp Leu Leu Leu Val Thr Leu Cys Leu Thr
1 5 10 15

Glu Glu Leu Ala Ala Ala Gly Glu Lys Ser Tyr Gly Lys Pro Cys Gly
20 25 30

Gly Gln Asp Cys Ser Gly Ser Cys Gln Cys Phe Pro Glu Lys Gly Ala
35 40 45

Arg Gly Arg Pro Gly Pro Ile Gly Ile Gln Gly Pro Thr Gly Pro Gln
50 55 60

Gly Phe Thr Gly Ser Thr Gly Leu Ser Gly Leu Lys Gly Glu Arg Gly
65 70 75 80

Phe Pro Gly Leu Leu Gly Pro Tyr Gly Pro Lys Gly Asp Lys Gly Pro
85 90 95

Met Gly Val Pro Gly Phe Leu Gly Ile Asn Gly Ile Pro Gly His Pro
100 105 110

Gly Gln Pro Gly Pro Arg Gly Pro Pro Gly Leu Asp Gly Cys Asn Gly
115 120 125

Thr Gln Gly Ala Val Gly Phe Pro Gly Pro Asp Gly Tyr Pro Gly Leu

```
    130                 135                 140

Leu Gly Pro Pro Gly Leu Pro Gly Gln Lys Gly Ser Lys Gly Asp Pro
145                 150                 155                 160

Val Leu Ala Pro Gly Ser Phe Lys Gly Met Lys Gly Asp Pro Gly Leu
                165                 170                 175

Pro Gly Leu Asp Gly Ile Thr Gly Pro Gln Gly Ala Pro Gly Phe Pro
            180                 185                 190

Gly Ala Val Gly Pro Ala Gly Pro Pro Gly Leu Gln Gly Pro Pro Gly
        195                 200                 205

Pro Pro Gly Pro Leu Gly Pro Asp Gly Asn Met Gly Leu Gly Phe Gln
    210                 215                 220

Gly Glu Lys Gly Val Lys Gly Asp Val Gly Leu Pro Gly Pro Ala Gly
225                 230                 235                 240

Pro Pro Pro Ser Thr Gly Glu Leu Glu Phe Met Gly Phe Pro Lys Gly
                245                 250                 255

Lys Lys Gly Ser Lys Gly Glu Pro Gly Pro Lys Gly Phe Pro Gly Ile
            260                 265                 270

Ser Gly Pro Pro Gly Phe Pro Gly Leu Gly Thr Thr Gly Glu Lys Gly
        275                 280                 285

Glu Lys Gly Glu Lys Gly Ile Pro Gly Leu Pro Gly Pro Arg Gly Pro
    290                 295                 300

Met Gly Ser Glu Gly Val Gln Gly Pro Pro Gly Gln Gln Gly Lys Lys
305                 310                 315                 320

Gly Thr Leu Gly Phe Pro Gly Leu Asn Gly Phe Gln Gly Ile Glu Gly
                325                 330                 335

Gln Lys Gly Asp Ile Gly Leu Pro Gly Pro Asp Val Phe Ile Asp Ile
            340                 345                 350

Asp Gly Ala Val Ile Ser Gly Asn Pro Gly Asp Pro Gly Val Pro Gly
        355                 360                 365

Leu Pro Gly Leu Lys Gly Asp Glu Gly Ile Gln Gly Leu Arg Gly Pro
    370                 375                 380

Ser Gly Val Pro Gly Leu Pro Ala Leu Ser Gly Val Pro Gly Ala Leu
385                 390                 395                 400

Gly Pro Gln Gly Phe Pro Gly Leu Lys Gly Asp Gln Gly Asn Pro Gly
```

405 410 415

Arg Thr Thr Ile Gly Ala Ala Gly Leu Pro Gly Arg Asp Gly Leu Pro
420 425 430

Gly Pro Pro Gly Pro Pro Gly Pro Pro Ser Pro Glu Phe Glu Thr Glu
435 440 445

Thr Leu His Asn Lys Glu Ser Gly Phe Pro Gly Leu Arg Gly Glu Gln
450 455 460

Gly Pro Lys Gly Asn Leu Gly Leu Lys Gly Ile Lys Gly Asp Ser Gly
465 470 475 480

Phe Cys Ala Cys Asp Gly Gly Val Pro Asn Thr Gly Pro Pro Gly Glu
485 490 495

Pro Gly Pro Pro Gly Pro Trp Gly Leu Ile Gly Leu Pro Gly Leu Lys
500 505 510

Gly Ala Arg Gly Asp Arg Gly Ser Gly Gly Ala Gln Gly Pro Ala Gly
515 520 525

Ala Pro Gly Leu Val Gly Pro Leu Gly Pro Ser Gly Pro Lys Gly Lys
530 535 540

Lys Gly Glu Pro Ile Leu Ser Thr Ile Gln Gly Met Pro Gly Asp Arg
545 550 555 560

Gly Asp Ser Gly Ser Gln Gly Phe Arg Gly Val Ile Gly Glu Pro Gly
565 570 575

Lys Asp Gly Val Pro Gly Leu Pro Gly Leu Pro Gly Leu Pro Gly Asp
580 585 590

Gly Gly Gln Gly Phe Pro Gly Glu Lys Gly Leu Pro Gly Leu Pro Gly
595 600 605

Glu Lys Gly His Pro Gly Pro Pro Gly Leu Pro Gly Asn Gly Leu Pro
610 615 620

Gly Leu Pro Gly Pro Arg Gly Leu Pro Gly Asp Lys Gly Lys Asp Gly
625 630 635 640

Leu Pro Gly Gln Gln Gly Leu Pro Gly Ser Lys Gly Ile Thr Leu Pro
645 650 655

Cys Ile Ile Pro Gly Ser Tyr Gly Pro Ser Gly Phe Pro Gly Thr Pro
660 665 670

Gly Phe Pro Gly Pro Lys Gly Ser Arg Gly Leu Pro Gly Thr Pro Gly

675 680 685

Gln Pro Gly Ser Ser Gly Ser Lys Gly Glu Pro Gly Ser Pro Gly Leu
690 695 700

Val His Leu Pro Glu Leu Pro Gly Phe Pro Gly Pro Arg Gly Glu Lys
705 710 715 720

Gly Leu Pro Gly Phe Pro Gly Leu Pro Gly Lys Asp Gly Leu Pro Gly
725 730 735

Met Ile Gly Ser Pro Gly Leu Pro Gly Ser Lys Gly Ala Thr Gly Asp
740 745 750

Ile Phe Gly Ala Glu Asn Gly Ala Pro Gly Glu Gln Gly Leu Gln Gly
755 760 765

Leu Thr Gly His Lys Gly Phe Leu Gly Asp Ser Gly Leu Pro Gly Leu
770 775 780

Lys Gly Val His Gly Lys Pro Gly Leu Leu Gly Pro Lys Gly Glu Arg
785 790 795 800

Gly Ser Pro Gly Thr Pro Gly Gln Val Gly Gln Pro Gly Thr Pro Gly
805 810 815

Ser Ser Gly Pro Tyr Gly Ile Lys Gly Lys Ser Gly Leu Pro Gly Ala
820 825 830

Pro Gly Phe Pro Gly Ile Ser Gly His Pro Gly Lys Lys Gly Thr Arg
835 840 845

Gly Lys Lys Gly Pro Pro Gly Ser Ile Val Lys Lys Gly Leu Pro Gly
850 855 860

Leu Lys Gly Leu Pro Gly Asn Pro Gly Leu Val Gly Leu Lys Gly Ser
865 870 875 880

Pro Gly Ser Pro Gly Val Ala Gly Leu Pro Ala Leu Ser Gly Pro Lys
885 890 895

Gly Glu Lys Gly Ser Val Gly Phe Val Gly Phe Pro Gly Ile Pro Gly
900 905 910

Leu Pro Gly Ile Pro Gly Thr Arg Gly Leu Lys Gly Ile Pro Gly Ser
915 920 925

Thr Gly Lys Met Gly Pro Ser Gly Arg Ala Gly Thr Pro Gly Glu Lys
930 935 940

Gly Asp Arg Gly Asn Pro Gly Pro Val Gly Ile Pro Ser Pro Arg Arg

945 950 955 960

Pro Met Ser Asn Leu Trp Leu Lys Gly Asp Lys Gly Ser Gln Gly Ser
965 970 975

Ala Gly Ser Asn Gly Phe Pro Gly Pro Arg Gly Asp Lys Gly Glu Ala
980 985 990

Gly Arg Pro Gly Pro Pro Gly Leu Pro Gly Ala Pro Gly Leu Pro Gly
995 1000 1005

Ile Ile Lys Gly Val Ser Gly Lys Pro Gly Pro Pro Gly Phe Met
1010 1015 1020

Gly Ile Arg Gly Leu Pro Gly Leu Lys Gly Ser Ser Gly Ile Thr
1025 1030 1035

Gly Phe Pro Gly Met Pro Gly Glu Ser Gly Ser Gln Gly Ile Arg
1040 1045 1050

Gly Ser Pro Gly Leu Pro Gly Ala Ser Gly Leu Pro Gly Leu Lys
1055 1060 1065

Gly Asp Asn Gly Gln Thr Val Glu Ile Ser Gly Ser Pro Gly Pro
1070 1075 1080

Lys Gly Gln Pro Gly Glu Ser Gly Phe Lys Gly Thr Lys Gly Arg
1085 1090 1095

Asp Gly Leu Ile Gly Asn Ile Gly Phe Pro Gly Asn Lys Gly Glu
1100 1105 1110

Asp Gly Lys Val Gly Val Ser Gly Asp Val Gly Leu Pro Gly Ala
1115 1120 1125

Pro Gly Phe Pro Gly Val Ala Gly Met Arg Gly Glu Pro Gly Leu
1130 1135 1140

Pro Gly Ser Ser Gly His Gln Gly Ala Ile Gly Pro Leu Gly Ser
1145 1150 1155

Pro Gly Leu Ile Gly Pro Lys Gly Phe Pro Gly Phe Pro Gly Leu
1160 1165 1170

His Gly Leu Asn Gly Leu Pro Gly Thr Lys Gly Thr His Gly Thr
1175 1180 1185

Pro Gly Pro Ser Ile Thr Gly Val Pro Gly Pro Ala Gly Leu Pro
1190 1195 1200

Gly Pro Lys Gly Glu Lys Gly Tyr Pro Gly Ile Gly Ile Gly Ala

1205 1210 1215

Pro Gly Lys Pro Gly Leu Arg Gly Gln Lys Gly Asp Arg Gly Phe
1220 1225 1230

Pro Gly Leu Gln Gly Pro Ala Gly Leu Pro Gly Ala Pro Gly Ile
1235 1240 1245

Ser Leu Pro Ser Leu Ile Ala Gly Gln Pro Gly Asp Pro Gly Arg
1250 1255 1260

Pro Gly Leu Asp Gly Glu Arg Gly Arg Pro Gly Pro Ala Gly Pro
1265 1270 1275

Pro Gly Pro Pro Gly Pro Ser Ser Asn Gln Gly Asp Thr Gly Asp
1280 1285 1290

Pro Gly Phe Pro Gly Ile Pro Gly Pro Lys Gly Pro Lys Gly Asp
1295 1300 1305

Gln Gly Ile Pro Gly Phe Ser Gly Leu Pro Gly Glu Leu Gly Leu
1310 1315 1320

Lys Gly Met Arg Gly Glu Pro Gly Phe Met Gly Thr Pro Gly Lys
1325 1330 1335

Val Gly Pro Pro Gly Asp Pro Gly Phe Pro Gly Met Lys Gly Lys
1340 1345 1350

Ala Gly Pro Arg Gly Ser Ser Gly Leu Gln Gly Asp Pro Gly Gln
1355 1360 1365

Thr Pro Thr Ala Glu Ala Val Gln Val Pro Pro Gly Pro Leu Gly
1370 1375 1380

Leu Pro Gly Ile Asp Gly Ile Pro Gly Leu Thr Gly Asp Pro Gly
1385 1390 1395

Ala Gln Gly Pro Val Gly Leu Gln Gly Ser Lys Gly Leu Pro Gly
1400 1405 1410

Ile Pro Gly Lys Asp Gly Pro Ser Gly Leu Pro Gly Pro Pro Gly
1415 1420 1425

Ala Leu Gly Asp Pro Gly Leu Pro Gly Leu Gln Gly Pro Pro Gly
1430 1435 1440

Phe Glu Gly Ala Pro Gly Gln Gln Gly Pro Phe Gly Met Pro Gly
1445 1450 1455

Met Pro Gly Gln Ser Met Arg Val Gly Tyr Thr Leu Val Lys His

1460 1465 1470

Ser Gln Ser Glu Gln Val Pro Pro Cys Pro Ile Gly Met Ser Gln
1475 1480 1485

Leu Trp Val Gly Tyr Ser Leu Leu Phe Val Glu Gly Gln Glu Lys
1490 1495 1500

Ala His Asn Gln Asp Leu Gly Phe Ala Gly Ser Cys Leu Pro Arg
1505 1510 1515

Phe Ser Thr Met Pro Phe Ile Tyr Cys Asn Ile Asn Glu Val Cys
1520 1525 1530

His Tyr Ala Arg Arg Asn Asp Lys Ser Tyr Trp Leu Ser Thr Thr
1535 1540 1545

Ala Pro Ile Pro Met Met Pro Val Ser Gln Thr Gln Ile Pro Gln
1550 1555 1560

Tyr Ile Ser Arg Cys Ser Val Cys Glu Ala Pro Ser Gln Ala Ile
1565 1570 1575

Ala Val His Ser Gln Asp Ile Thr Ile Pro Gln Cys Pro Leu Gly
1580 1585 1590

Trp Arg Ser Leu Trp Ile Gly Tyr Ser Phe Leu Met His Thr Ala
1595 1600 1605

Ala Gly Ala Glu Gly Gly Gly Gln Ser Leu Val Ser Pro Gly Ser
1610 1615 1620

Cys Leu Glu Asp Phe Arg Ala Thr Pro Phe Ile Glu Cys Ser Gly
1625 1630 1635

Ala Arg Gly Thr Cys His Tyr Phe Ala Asn Lys Tyr Ser Phe Trp
1640 1645 1650

Leu Thr Thr Val Glu Glu Arg Gln Gln Phe Gly Glu Leu Pro Val
1655 1660 1665

Ser Glu Thr Leu Lys Ala Gly Gln Leu His Thr Arg Val Ser Arg
1670 1675 1680

Cys Gln Val Cys Met Lys Ser Leu
1685 1690

<210> 72
<211> 1838
<212> PRT
<213> Homo sapiens

<400> 72

```
Met Asp Val His Thr Arg Trp Lys Ala Arg Ser Ala Leu Arg Pro Gly
1               5                  10                  15

Ala Pro Leu Leu Pro Pro Leu Leu Leu Leu Leu Leu Trp Ala Pro Pro
            20                  25                  30

Pro Ser Arg Ala Ala Gln Pro Ala Asp Leu Leu Lys Val Leu Asp Phe
        35                  40                  45

His Asn Leu Pro Asp Gly Ile Thr Lys Thr Thr Gly Phe Cys Ala Thr
    50                  55                  60

Arg Arg Ser Ser Lys Gly Pro Asp Val Ala Tyr Arg Val Thr Lys Asp
65                  70                  75                  80

Ala Gln Leu Ser Ala Pro Thr Lys Gln Leu Tyr Pro Ala Ser Ala Phe
                85                  90                  95

Pro Glu Asp Phe Ser Ile Leu Thr Thr Val Lys Ala Lys Lys Gly Ser
            100                 105                 110

Gln Ala Phe Leu Val Ser Ile Tyr Asn Glu Gln Gly Ile Gln Gln Ile
        115                 120                 125

Gly Leu Glu Leu Gly Arg Ser Pro Val Phe Leu Tyr Glu Asp His Thr
    130                 135                 140

Gly Lys Pro Gly Pro Glu Asp Tyr Pro Leu Phe Arg Gly Ile Asn Leu
145                 150                 155                 160

Ser Asp Gly Lys Trp His Arg Ile Ala Leu Ser Val His Lys Lys Asn
                165                 170                 175

Val Thr Leu Ile Leu Asp Cys Lys Lys Lys Thr Thr Lys Phe Leu Asp
            180                 185                 190

Arg Ser Asp His Pro Met Ile Asp Ile Asn Gly Ile Ile Val Phe Gly
        195                 200                 205

Thr Arg Ile Leu Asp Glu Glu Val Phe Glu Gly Asp Ile Gln Gln Leu
    210                 215                 220

Leu Phe Val Ser Asp His Arg Ala Ala Tyr Asp Tyr Cys Glu His Tyr
225                 230                 235                 240

Ser Pro Asp Cys Asp Thr Ala Val Pro Asp Thr Pro Gln Ser Gln Asp
                245                 250                 255

Pro Asn Pro Asp Glu Tyr Tyr Thr Glu Gly Asp Gly Glu Gly Glu Thr
            260                 265                 270
```

```
Tyr Tyr Tyr Glu Tyr Pro Tyr Tyr Glu Asp Pro Glu Asp Leu Gly Lys
        275                 280                 285

Glu Pro Thr Pro Ser Lys Lys Pro Val Glu Ala Ala Lys Glu Thr Thr
    290                 295                 300

Glu Val Pro Glu Glu Leu Thr Pro Thr Pro Thr Glu Ala Ala Pro Met
305                 310                 315                 320

Pro Glu Thr Ser Glu Gly Ala Gly Lys Glu Glu Asp Val Gly Ile Gly
                325                 330                 335

Asp Tyr Asp Tyr Val Pro Ser Glu Asp Tyr Tyr Thr Pro Ser Pro Tyr
            340                 345                 350

Asp Asp Leu Thr Tyr Gly Glu Gly Glu Glu Asn Pro Asp Gln Pro Thr
        355                 360                 365

Asp Pro Gly Ala Gly Ala Glu Ile Pro Thr Ser Thr Ala Asp Thr Ser
    370                 375                 380

Asn Ser Ser Asn Pro Ala Pro Pro Pro Gly Glu Gly Ala Asp Asp Leu
385                 390                 395                 400

Glu Gly Glu Phe Thr Glu Glu Thr Ile Arg Asn Leu Asp Glu Asn Tyr
                405                 410                 415

Tyr Asp Pro Tyr Tyr Asp Pro Thr Ser Ser Pro Ser Glu Ile Gly Pro
            420                 425                 430

Gly Met Pro Ala Asn Gln Asp Thr Ile Tyr Glu Gly Ile Gly Gly Pro
        435                 440                 445

Arg Gly Glu Lys Gly Gln Lys Gly Glu Pro Ala Ile Ile Glu Pro Gly
    450                 455                 460

Met Leu Ile Glu Gly Pro Pro Gly Pro Glu Gly Pro Ala Gly Leu Pro
465                 470                 475                 480

Gly Pro Pro Gly Thr Met Gly Pro Thr Gly Gln Val Gly Asp Pro Gly
                485                 490                 495

Glu Arg Gly Pro Pro Gly Arg Pro Gly Leu Pro Gly Ala Asp Gly Leu
            500                 505                 510

Pro Gly Pro Pro Gly Thr Met Leu Met Leu Pro Phe Arg Phe Gly Gly
        515                 520                 525

Gly Gly Asp Ala Gly Ser Lys Gly Pro Met Val Ser Ala Gln Glu Ser
    530                 535                 540
```

```
Gln Ala Gln Ala Ile Leu Gln Gln Ala Arg Leu Ala Leu Arg Gly Pro
545                 550                 555                 560

Ala Gly Pro Met Gly Leu Thr Gly Arg Pro Gly Pro Val Gly Pro Pro
                565                 570                 575

Gly Ser Gly Gly Leu Lys Gly Glu Pro Gly Asp Val Gly Pro Gln Gly
            580                 585                 590

Pro Arg Gly Val Gln Gly Pro Pro Gly Pro Ala Gly Lys Pro Gly Arg
        595                 600                 605

Arg Gly Arg Ala Gly Ser Asp Gly Ala Arg Gly Met Pro Gly Gln Thr
    610                 615                 620

Gly Pro Lys Gly Asp Arg Gly Phe Asp Gly Leu Ala Gly Leu Pro Gly
625                 630                 635                 640

Glu Lys Gly His Arg Gly Asp Pro Gly Pro Ser Gly Pro Pro Gly Pro
                645                 650                 655

Pro Gly Asp Asp Gly Glu Arg Gly Asp Asp Gly Glu Val Gly Pro Arg
            660                 665                 670

Gly Leu Pro Gly Glu Pro Gly Pro Arg Gly Leu Leu Gly Pro Lys Gly
        675                 680                 685

Pro Pro Gly Pro Pro Gly Pro Pro Gly Val Thr Gly Met Asp Gly Gln
    690                 695                 700

Pro Gly Pro Lys Gly Asn Val Gly Pro Gln Gly Glu Pro Gly Pro Pro
705                 710                 715                 720

Gly Gln Gln Gly Asn Pro Gly Ala Gln Gly Leu Pro Gly Pro Gln Gly
                725                 730                 735

Ala Ile Gly Pro Pro Gly Glu Lys Gly Pro Leu Gly Lys Pro Gly Leu
            740                 745                 750

Pro Gly Met Pro Gly Ala Asp Gly Pro Pro Gly His Pro Gly Lys Glu
        755                 760                 765

Gly Pro Pro Gly Glu Lys Gly Gly Gln Gly Pro Pro Gly Pro Gln Gly
    770                 775                 780

Pro Ile Gly Tyr Pro Gly Pro Arg Gly Val Lys Gly Ala Asp Gly Ile
785                 790                 795                 800

Arg Gly Leu Lys Gly Thr Lys Gly Glu Lys Gly Glu Asp Gly Phe Pro
                805                 810                 815
```

```
Gly Phe Lys Gly Asp Met Gly Ile Lys Gly Asp Arg Gly Glu Ile Gly
            820                 825                 830

Pro Pro Gly Pro Arg Gly Glu Asp Gly Pro Glu Gly Pro Lys Gly Arg
        835                 840                 845

Gly Gly Pro Asn Gly Asp Pro Gly Pro Leu Gly Pro Pro Gly Glu Lys
    850                 855                 860

Gly Lys Leu Gly Val Pro Gly Leu Pro Gly Tyr Pro Gly Arg Gln Gly
865                 870                 875                 880

Pro Lys Gly Ser Ile Gly Phe Pro Gly Phe Pro Gly Ala Asn Gly Glu
                885                 890                 895

Lys Gly Gly Arg Gly Thr Pro Gly Lys Pro Gly Pro Arg Gly Gln Arg
            900                 905                 910

Gly Pro Thr Gly Pro Arg Gly Glu Arg Gly Pro Arg Gly Ile Thr Gly
        915                 920                 925

Lys Pro Gly Pro Lys Gly Asn Ser Gly Gly Asp Gly Pro Ala Gly Pro
    930                 935                 940

Pro Gly Glu Arg Gly Pro Asn Gly Pro Gln Gly Pro Thr Gly Phe Pro
945                 950                 955                 960

Gly Pro Lys Gly Pro Pro Gly Pro Pro Gly Lys Asp Gly Leu Pro Gly
                965                 970                 975

His Pro Gly Gln Arg Gly Glu Thr Gly Phe Gln Gly Lys Thr Gly Pro
            980                 985                 990

Pro Gly Pro Pro Gly Val Val Gly  Pro Gln Gly Pro Thr  Gly Glu Thr
        995                 1000                1005

Gly Pro  Met Gly Glu Arg Gly  His Pro Gly Pro Pro  Gly Pro Pro
    1010                1015                1020

Gly Glu  Gln Gly Leu Pro Gly  Leu Ala Gly Lys Glu  Gly Thr Lys
    1025                1030                1035

Gly Asp  Pro Gly Pro Ala Gly  Leu Pro Gly Lys Asp  Gly Pro Pro
    1040                1045                1050

Gly Leu  Arg Gly Phe Pro Gly  Asp Arg Gly Leu Pro  Gly Pro Val
    1055                1060                1065

Gly Ala  Leu Gly Leu Lys Gly  Asn Glu Gly Pro Pro  Gly Pro Pro
    1070                1075                1080
```

```
Gly Pro  Ala Gly Ser Pro Gly  Glu Arg Gly Pro Ala  Gly Ala Ala
    1085                 1090                 1095

Gly Pro  Ile Gly Ile Pro Gly  Arg Pro Gly Pro Gln  Gly Pro Pro
    1100                 1105                 1110

Gly Pro  Ala Gly Glu Lys Gly  Ala Pro Gly Glu Lys  Gly Pro Gln
    1115                 1120                 1125

Gly Pro  Ala Gly Arg Asp Gly  Leu Gln Gly Pro Val  Gly Leu Pro
    1130                 1135                 1140

Gly Pro  Ala Gly Pro Val Gly  Pro Pro Gly Glu Asp  Gly Asp Lys
    1145                 1150                 1155

Gly Glu  Ile Gly Glu Pro Gly  Gln Lys Gly Ser Lys  Gly Asp Lys
    1160                 1165                 1170

Gly Glu  Gln Gly Pro Pro Gly  Pro Thr Gly Pro Gln  Gly Pro Ile
    1175                 1180                 1185

Gly Gln  Pro Gly Pro Ser Gly  Ala Asp Gly Glu Pro  Gly Pro Arg
    1190                 1195                 1200

Gly Gln  Gln Gly Leu Phe Gly  Gln Lys Gly Asp Glu  Gly Pro Arg
    1205                 1210                 1215

Gly Phe  Pro Gly Pro Pro Gly  Pro Val Gly Leu Gln  Gly Leu Pro
    1220                 1225                 1230

Gly Pro  Pro Gly Glu Lys Gly  Glu Thr Gly Asp Val  Gly Gln Met
    1235                 1240                 1245

Gly Pro  Pro Gly Pro Pro Gly  Pro Arg Gly Pro Ser  Gly Ala Pro
    1250                 1255                 1260

Gly Ala  Asp Gly Pro Gln Gly  Pro Pro Gly Gly Ile  Gly Asn Pro
    1265                 1270                 1275

Gly Ala  Val Gly Glu Lys Gly  Glu Pro Gly Glu Ala  Gly Glu Pro
    1280                 1285                 1290

Gly Leu  Pro Gly Glu Gly Gly  Pro Pro Gly Pro Lys  Gly Glu Arg
    1295                 1300                 1305

Gly Glu  Lys Gly Glu Ser Gly  Pro Ser Gly Ala Ala  Gly Pro Pro
    1310                 1315                 1320

Gly Pro  Lys Gly Pro Pro Gly  Asp Asp Gly Pro Lys  Gly Ser Pro
    1325                 1330                 1335
```

```
Gly Pro  Val Gly Phe Pro Gly  Asp Pro Gly Pro Pro  Gly Glu Pro
    1340                1345                1350

Gly Pro  Ala Gly Gln Asp Gly  Pro Pro Gly Asp Lys  Gly Asp Asp
    1355                1360                1365

Gly Glu  Pro Gly Gln Thr Gly  Ser Pro Gly Pro Thr  Gly Glu Pro
    1370                1375                1380

Gly Pro  Ser Gly Pro Pro Gly  Lys Arg Gly Pro Pro  Gly Pro Ala
    1385                1390                1395

Gly Pro  Glu Gly Arg Gln Gly  Glu Lys Gly Ala Lys  Gly Glu Ala
    1400                1405                1410

Gly Leu  Glu Gly Pro Pro Gly  Lys Thr Gly Pro Ile  Gly Pro Gln
    1415                1420                1425

Gly Ala  Pro Gly Lys Pro Gly  Pro Asp Gly Leu Arg  Gly Ile Pro
    1430                1435                1440

Gly Pro  Val Gly Glu Gln Gly  Leu Pro Gly Ser Pro  Gly Pro Asp
    1445                1450                1455

Gly Pro  Pro Gly Pro Met Gly  Pro Pro Gly Leu Pro  Gly Leu Lys
    1460                1465                1470

Gly Asp  Ser Gly Pro Lys Gly  Glu Lys Gly His Pro  Gly Leu Ile
    1475                1480                1485

Gly Leu  Ile Gly Pro Pro Gly  Glu Gln Gly Glu Lys  Gly Asp Arg
    1490                1495                1500

Gly Leu  Pro Gly Pro Gln Gly  Ser Ser Gly Pro Lys  Gly Glu Gln
    1505                1510                1515

Gly Ile  Thr Gly Pro Ser Gly  Pro Ile Gly Pro Pro  Gly Pro Pro
    1520                1525                1530

Gly Leu  Pro Gly Pro Pro Gly  Pro Lys Gly Ala Lys  Gly Ser Ser
    1535                1540                1545

Gly Pro  Thr Gly Pro Lys Gly  Glu Ala Gly His Pro  Gly Pro Pro
    1550                1555                1560

Gly Pro  Pro Gly Pro Pro Gly  Glu Val Ile Gln Pro  Leu Pro Ile
    1565                1570                1575

Gln Ala  Ser Arg Thr Arg Arg  Asn Ile Asp Ala Ser  Gln Leu Leu
    1580                1585                1590
```

```
Asp Asp  Gly Asn Gly Glu Asn  Tyr Val Asp Tyr Ala  Asp Gly Met
    1595                1600                1605

Glu Glu  Ile Phe Gly Ser Leu  Asn Ser Leu Lys Leu  Glu Ile Glu
    1610                1615                1620

Gln Met  Lys Arg Pro Leu Gly  Thr Gln Gln Asn Pro  Ala Arg Thr
    1625                1630                1635

Cys Lys  Asp Leu Gln Leu Cys  His Pro Asp Phe Pro  Asp Gly Glu
    1640                1645                1650

Tyr Trp  Val Asp Pro Asn Gln  Gly Cys Ser Arg Asp  Ser Phe Lys
    1655                1660                1665

Val Tyr  Cys Asn Phe Thr Ala  Gly Gly Ser Thr Cys  Val Phe Pro
    1670                1675                1680

Asp Lys  Lys Ser Glu Gly Ala  Arg Ile Thr Ser Trp  Pro Lys Glu
    1685                1690                1695

Asn Pro  Gly Ser Trp Phe Ser  Glu Phe Lys Arg Gly  Lys Leu Leu
    1700                1705                1710

Ser Tyr  Val Asp Ala Glu Gly  Asn Pro Val Gly Val  Val Gln Met
    1715                1720                1725

Thr Phe  Leu Arg Leu Leu Ser  Ala Ser Ala His Gln  Asn Val Thr
    1730                1735                1740

Tyr His  Cys Tyr Gln Ser Val  Ala Trp Gln Asp Ala  Ala Thr Gly
    1745                1750                1755

Ser Tyr  Asp Lys Ala Leu Arg  Phe Leu Gly Ser Asn  Asp Glu Glu
    1760                1765                1770

Met Ser  Tyr Asp Asn Asn Pro  Tyr Ile Arg Ala Leu  Val Asp Gly
    1775                1780                1785

Cys Ala  Thr Lys Lys Gly Tyr  Gln Lys Thr Val Leu  Glu Ile Asp
    1790                1795                1800

Thr Pro  Lys Val Glu Gln Val  Pro Ile Val Asp Ile  Met Phe Asn
    1805                1810                1815

Asp Phe  Gly Glu Ala Ser Gln  Lys Phe Gly Phe Glu  Val Gly Pro
    1820                1825                1830

Ala Cys  Phe Met Gly
    1835
```

<210> 73
<211> 1499
<212> PRT
<213> Homo sapiens

<400> 73

```
Met Met Ala Asn Trp Ala Glu Ala Arg Pro Leu Leu Ile Leu Ile Val
1               5                  10                  15

Leu Leu Gly Gln Phe Val Ser Ile Lys Ala Gln Glu Glu Asp Glu Asp
            20                  25                  30

Glu Gly Tyr Gly Glu Glu Ile Ala Cys Thr Gln Asn Gly Gln Met Tyr
        35                  40                  45

Leu Asn Arg Asp Ile Trp Lys Pro Ala Pro Cys Gln Ile Cys Val Cys
    50                  55                  60

Asp Asn Gly Ala Ile Leu Cys Asp Lys Ile Glu Cys Gln Asp Val Leu
65                  70                  75                  80

Asp Cys Ala Asp Pro Val Thr Pro Pro Gly Glu Cys Cys Pro Val Cys
                85                  90                  95

Ser Gln Thr Pro Gly Gly Gly Asn Thr Asn Phe Gly Arg Gly Arg Lys
            100                 105                 110

Gly Gln Lys Gly Glu Pro Gly Leu Val Pro Val Val Thr Gly Ile Arg
        115                 120                 125

Gly Arg Pro Gly Pro Ala Gly Pro Pro Gly Ser Gln Gly Pro Arg Gly
    130                 135                 140

Glu Arg Gly Pro Lys Gly Arg Pro Gly Pro Arg Gly Pro Gln Gly Ile
145                 150                 155                 160

Asp Gly Glu Pro Gly Val Pro Gly Gln Pro Gly Ala Pro Gly Pro Pro
                165                 170                 175

Gly His Pro Ser His Pro Gly Pro Asp Gly Leu Ser Arg Pro Phe Ser
            180                 185                 190

Ala Gln Met Ala Gly Leu Asp Glu Lys Ser Gly Leu Gly Ser Gln Val
        195                 200                 205

Gly Leu Met Pro Gly Ser Val Gly Pro Val Gly Pro Arg Gly Pro Gln
    210                 215                 220

Gly Leu Gln Gly Gln Gln Gly Gly Ala Gly Pro Thr Gly Pro Pro Gly
225                 230                 235                 240
```

```
Glu Pro Gly Asp Pro Gly Pro Met Gly Pro Ile Gly Ser Arg Gly Pro
                245                 250                 255

Glu Gly Pro Pro Gly Lys Pro Gly Glu Asp Gly Glu Pro Gly Arg Asn
            260                 265                 270

Gly Asn Pro Gly Glu Val Gly Phe Ala Gly Ser Pro Gly Ala Arg Gly
        275                 280                 285

Phe Pro Gly Ala Pro Gly Leu Pro Gly Leu Lys Gly His Arg Gly His
    290                 295                 300

Lys Gly Leu Glu Gly Pro Lys Gly Glu Val Gly Ala Pro Gly Ser Lys
305                 310                 315                 320

Gly Glu Ala Gly Pro Thr Gly Pro Met Gly Ala Met Gly Pro Leu Gly
                325                 330                 335

Pro Arg Gly Met Pro Gly Glu Arg Gly Arg Leu Gly Pro Gln Gly Ala
            340                 345                 350

Pro Gly Gln Arg Gly Ala His Gly Met Pro Gly Lys Pro Gly Pro Met
        355                 360                 365

Gly Pro Leu Gly Ile Pro Gly Ser Ser Gly Phe Pro Gly Asn Pro Gly
    370                 375                 380

Met Lys Gly Glu Ala Gly Pro Thr Gly Ala Arg Gly Pro Glu Gly Pro
385                 390                 395                 400

Gln Gly Gln Arg Gly Glu Thr Gly Pro Pro Gly Pro Val Gly Ser Pro
                405                 410                 415

Gly Leu Pro Gly Ala Ile Gly Thr Asp Gly Thr Pro Gly Ala Lys Gly
            420                 425                 430

Pro Thr Gly Ser Pro Gly Thr Ser Gly Pro Pro Gly Ser Ala Gly Pro
        435                 440                 445

Pro Gly Ser Pro Gly Pro Gln Gly Ser Thr Gly Pro Gln Gly Ile Arg
    450                 455                 460

Gly Gln Pro Gly Asp Pro Gly Val Pro Gly Phe Lys Gly Glu Ala Gly
465                 470                 475                 480

Pro Lys Gly Glu Pro Gly Pro His Gly Ile Gln Gly Pro Ile Gly Pro
                485                 490                 495

Pro Gly Glu Glu Gly Lys Arg Gly Pro Arg Gly Asp Pro Gly Thr Val
            500                 505                 510
```

```
Gly Pro Pro Gly Pro Val Gly Glu Arg Gly Ala Pro Gly Asn Arg Gly
        515                 520                 525

Phe Pro Gly Ser Asp Gly Leu Pro Gly Pro Lys Gly Ala Gln Gly Glu
    530                 535                 540

Arg Gly Pro Val Gly Ser Ser Gly Pro Lys Gly Ser Gln Gly Asp Pro
545                 550                 555                 560

Gly Arg Pro Gly Glu Pro Gly Leu Pro Gly Ala Arg Gly Leu Thr Gly
                565                 570                 575

Asn Pro Gly Val Gln Gly Pro Glu Gly Lys Leu Gly Pro Leu Gly Ala
            580                 585                 590

Pro Gly Glu Asp Gly Arg Pro Gly Pro Pro Gly Ser Ile Gly Ile Arg
        595                 600                 605

Gly Gln Pro Gly Ser Met Gly Leu Pro Gly Pro Lys Gly Ser Ser Gly
    610                 615                 620

Asp Pro Gly Lys Pro Gly Glu Ala Gly Asn Ala Gly Val Pro Gly Gln
625                 630                 635                 640

Arg Gly Ala Pro Gly Lys Asp Gly Glu Val Gly Pro Ser Gly Pro Val
                645                 650                 655

Gly Pro Pro Gly Leu Ala Gly Glu Arg Gly Glu Gln Gly Pro Pro Gly
            660                 665                 670

Pro Thr Gly Phe Gln Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Glu
        675                 680                 685

Gly Gly Lys Pro Gly Asp Gln Gly Val Pro Gly Asp Pro Gly Ala Val
    690                 695                 700

Gly Pro Leu Gly Pro Arg Gly Glu Arg Gly Asn Pro Gly Glu Arg Gly
705                 710                 715                 720

Glu Pro Gly Ile Thr Gly Leu Pro Gly Glu Lys Gly Met Ala Gly Gly
                725                 730                 735

His Gly Pro Asp Gly Pro Lys Gly Ser Pro Gly Pro Ser Gly Thr Pro
            740                 745                 750

Gly Asp Thr Gly Pro Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly
        755                 760                 765

Ile Ala Gly Thr Pro Gly Pro Lys Gly Asp Arg Gly Gly Ile Gly Glu
    770                 775                 780
```

```
Lys Gly Ala Glu Gly Thr Ala Gly Asn Asp Gly Ala Arg Gly Leu Pro
785                 790                 795                 800

Gly Pro Leu Gly Pro Pro Gly Pro Ala Gly Pro Thr Gly Glu Lys Gly
                805                 810                 815

Glu Pro Gly Pro Arg Gly Leu Val Gly Pro Pro Gly Ser Arg Gly Asn
            820                 825                 830

Pro Gly Ser Arg Gly Glu Asn Gly Pro Thr Gly Ala Val Gly Phe Ala
        835                 840                 845

Gly Pro Gln Gly Pro Asp Gly Gln Pro Gly Val Lys Gly Glu Pro Gly
    850                 855                 860

Glu Pro Gly Gln Lys Gly Asp Ala Gly Ser Pro Gly Pro Gln Gly Leu
865                 870                 875                 880

Ala Gly Ser Pro Gly Pro His Gly Pro Asn Gly Val Pro Gly Leu Lys
                885                 890                 895

Gly Gly Arg Gly Thr Gln Gly Pro Pro Gly Ala Thr Gly Phe Pro Gly
            900                 905                 910

Ser Ala Gly Arg Val Gly Pro Pro Gly Pro Ala Gly Ala Pro Gly Pro
        915                 920                 925

Ala Gly Pro Leu Gly Glu Pro Gly Lys Glu Gly Pro Pro Gly Leu Arg
    930                 935                 940

Gly Asp Pro Gly Ser His Gly Arg Val Gly Asp Arg Gly Pro Ala Gly
945                 950                 955                 960

Pro Pro Gly Gly Pro Gly Asp Lys Gly Asp Pro Gly Glu Asp Gly Gln
                965                 970                 975

Pro Gly Pro Asp Gly Pro Pro Gly Pro Ala Gly Thr Thr Gly Gln Arg
            980                 985                 990

Gly Ile Val Gly Met Pro Gly Gln  Arg Gly Glu Arg Gly  Met Pro Gly
        995                 1000                1005

Leu Pro  Gly Pro Ala Gly Thr  Pro Gly Lys Val Gly  Pro Thr Gly
    1010                1015                1020

Ala Thr  Gly Asp Lys Gly Pro  Pro Gly Pro Val Gly  Pro Pro Gly
    1025                1030                1035

Ser Asn  Gly Pro Val Gly Glu  Pro Gly Pro Glu Gly  Pro Ala Gly
    1040                1045                1050
```

```
Asn Asp  Gly Thr Pro Gly Arg  Asp Gly Ala Val Gly  Glu Arg Gly
    1055                 1060                 1065

Asp Arg  Gly Asp Pro Gly Pro  Ala Gly Leu Pro Gly  Ser Gln Gly
    1070                 1075                 1080

Ala Pro  Gly Thr Pro Gly Pro  Val Gly Ala Pro Gly  Asp Ala Gly
    1085                 1090                 1095

Gln Arg  Gly Asp Pro Gly Ser  Arg Gly Pro Ile Gly  Pro Pro Gly
    1100                 1105                 1110

Arg Ala  Gly Lys Arg Gly Leu  Pro Gly Pro Gln Gly  Pro Arg Gly
    1115                 1120                 1125

Asp Lys  Gly Asp His Gly Asp  Arg Gly Asp Arg Gly  Gln Lys Gly
    1130                 1135                 1140

His Arg  Gly Phe Thr Gly Leu  Gln Gly Leu Pro Gly  Pro Pro Gly
    1145                 1150                 1155

Pro Asn  Gly Glu Gln Gly Ser  Ala Gly Ile Pro Gly  Pro Phe Gly
    1160                 1165                 1170

Pro Arg  Gly Pro Pro Gly Pro  Val Gly Pro Ser Gly  Lys Glu Gly
    1175                 1180                 1185

Asn Pro  Gly Pro Leu Gly Pro  Ile Gly Pro Pro Gly  Val Arg Gly
    1190                 1195                 1200

Ser Val  Gly Glu Ala Gly Pro  Glu Gly Pro Pro Gly  Glu Pro Gly
    1205                 1210                 1215

Pro Pro  Gly Pro Pro Gly Pro  Pro Gly His Leu Thr  Ala Ala Leu
    1220                 1225                 1230

Gly Asp  Ile Met Gly His Tyr  Asp Glu Ser Met Pro  Asp Pro Leu
    1235                 1240                 1245

Pro Glu  Phe Thr Glu Asp Gln  Ala Ala Pro Asp Asp  Lys Asn Lys
    1250                 1255                 1260

Thr Asp  Pro Gly Val His Ala  Thr Leu Lys Ser Leu  Ser Ser Gln
    1265                 1270                 1275

Ile Glu  Thr Met Arg Ser Pro  Asp Gly Ser Lys Lys  His Pro Ala
    1280                 1285                 1290

Arg Thr  Cys Asp Asp Leu Lys  Leu Cys His Ser Ala  Lys Gln Ser
    1295                 1300                 1305
```

```
Gly Glu  Tyr Trp Ile Asp Pro  Asn Gln Gly Ser Val  Glu Asp Ala
    1310                 1315                 1320

Ile Lys  Val Tyr Cys Asn Met  Glu Thr Gly Glu Thr  Cys Ile Ser
    1325                 1330                 1335

Ala Asn  Pro Ser Ser Val Pro  Arg Lys Thr Trp Trp  Ala Ser Lys
    1340                 1345                 1350

Ser Pro  Asp Asn Lys Pro Val  Trp Tyr Gly Leu Asp  Met Asn Arg
    1355                 1360                 1365

Gly Ser  Gln Phe Ala Tyr Gly  Asp His Gln Ser Pro  Asn Thr Ala
    1370                 1375                 1380

Ile Thr  Gln Met Thr Phe Leu  Arg Leu Leu Ser Lys  Glu Ala Ser
    1385                 1390                 1395

Gln Asn  Ile Thr Tyr Ile Cys  Lys Asn Ser Val Gly  Tyr Met Asp
    1400                 1405                 1410

Asp Gln  Ala Lys Asn Leu Lys  Lys Ala Val Val Leu  Lys Gly Ala
    1415                 1420                 1425

Asn Asp  Leu Asp Ile Lys Ala  Glu Gly Asn Ile Arg  Phe Arg Tyr
    1430                 1435                 1440

Ile Val  Leu Gln Asp Thr Cys  Ser Lys Arg Asn Gly  Asn Val Gly
    1445                 1450                 1455

Lys Thr  Val Phe Glu Tyr Arg  Thr Gln Asn Val Ala  Arg Leu Pro
    1460                 1465                 1470

Ile Ile  Asp Leu Ala Pro Val  Asp Val Gly Gly Thr  Asp Gln Glu
    1475                 1480                 1485

Phe Gly  Val Glu Ile Gly Pro  Val Cys Phe Val
    1490                 1495


<210>  74
<211>  1745
<212>  PRT
<213>  Homo sapiens

<400>  74

Met Gly Asn Arg Arg Asp Leu Gly Gln Pro Arg Ala Gly Leu Cys Leu
1               5                  10                  15

Leu Leu Ala Ala Leu Gln Leu Leu Pro Gly Thr Gln Ala Asp Pro Val
            20                  25                  30
```

```
Asp Val Leu Lys Ala Leu Gly Val Gln Gly Gly Gln Ala Gly Val Pro
        35                  40                  45

Glu Gly Pro Gly Phe Cys Pro Gln Arg Thr Pro Glu Gly Asp Arg Ala
    50                  55                  60

Phe Arg Ile Gly Gln Ala Ser Thr Leu Gly Ile Pro Thr Trp Glu Leu
65                  70                  75                  80

Phe Pro Glu Gly His Phe Pro Glu Asn Phe Ser Leu Leu Ile Thr Leu
                85                  90                  95

Arg Gly Gln Pro Ala Asn Gln Ser Val Leu Leu Ser Ile Tyr Asp Glu
            100                 105                 110

Arg Gly Ala Arg Gln Leu Gly Leu Ala Leu Gly Pro Ala Leu Gly Leu
        115                 120                 125

Leu Gly Asp Pro Phe Arg Pro Leu Pro Gln Gln Val Asn Leu Thr Asp
    130                 135                 140

Gly Arg Trp His Arg Val Ala Val Ser Ile Asp Gly Glu Met Val Thr
145                 150                 155                 160

Leu Val Ala Asp Cys Glu Ala Gln Pro Pro Val Leu Gly His Gly Pro
                165                 170                 175

Arg Phe Ile Ser Ile Ala Gly Leu Thr Val Leu Gly Thr Gln Asp Leu
            180                 185                 190

Gly Glu Lys Thr Phe Glu Gly Asp Ile Gln Glu Leu Leu Ile Ser Pro
        195                 200                 205

Asp Pro Gln Ala Ala Phe Gln Ala Cys Glu Arg Tyr Leu Pro Asp Cys
    210                 215                 220

Asp Asn Leu Ala Pro Ala Ala Thr Val Ala Pro Gln Gly Glu Pro Glu
225                 230                 235                 240

Thr Pro Arg Pro Arg Arg Lys Gly Lys Gly Lys Gly Arg Lys Lys Gly
                245                 250                 255

Arg Gly Arg Lys Gly Lys Gly Arg Lys Lys Asn Lys Glu Ile Trp Thr
            260                 265                 270

Ser Ser Pro Pro Pro Asp Ser Ala Glu Asn Gln Thr Ser Thr Asp Ile
        275                 280                 285

Pro Lys Thr Glu Thr Pro Ala Pro Asn Leu Pro Pro Thr Pro Thr Pro
    290                 295                 300
```

```
Leu Val Val Thr Ser Thr Val Thr Thr Gly Leu Asn Ala Thr Ile Leu
305                 310                 315                 320

Glu Arg Ser Leu Asp Pro Asp Ser Gly Thr Glu Leu Gly Thr Leu Glu
                325                 330                 335

Thr Lys Ala Ala Arg Glu Asp Glu Glu Gly Asp Asp Ser Thr Met Gly
            340                 345                 350

Pro Asp Phe Arg Ala Ala Glu Tyr Pro Ser Arg Thr Gln Phe Gln Ile
        355                 360                 365

Phe Pro Gly Ala Gly Glu Lys Gly Ala Lys Gly Glu Pro Ala Val Ile
    370                 375                 380

Glu Lys Gly Gln Gln Phe Glu Gly Pro Pro Gly Ala Pro Gly Pro Gln
385                 390                 395                 400

Gly Val Val Gly Pro Ser Gly Pro Pro Gly Pro Pro Gly Phe Pro Gly
                405                 410                 415

Asp Pro Gly Pro Pro Gly Pro Ala Gly Leu Pro Gly Ile Pro Gly Ile
            420                 425                 430

Asp Gly Ile Arg Gly Pro Pro Gly Thr Val Ile Met Met Pro Phe Gln
        435                 440                 445

Phe Ala Gly Gly Ser Phe Lys Gly Pro Pro Val Ser Phe Gln Gln Ala
    450                 455                 460

Gln Ala Gln Ala Val Leu Gln Gln Thr Gln Leu Ser Met Lys Gly Pro
465                 470                 475                 480

Pro Gly Pro Val Gly Leu Thr Gly Arg Pro Gly Pro Val Gly Leu Pro
                485                 490                 495

Gly His Pro Gly Leu Lys Gly Glu Glu Gly Ala Glu Gly Pro Gln Gly
            500                 505                 510

Pro Arg Gly Leu Gln Gly Pro His Gly Pro Pro Gly Arg Val Gly Lys
        515                 520                 525

Met Gly Arg Pro Gly Ala Asp Gly Ala Arg Gly Leu Pro Gly Asp Thr
    530                 535                 540

Gly Pro Lys Gly Asp Arg Gly Phe Asp Gly Leu Pro Gly Leu Pro Gly
545                 550                 555                 560

Glu Lys Gly Gln Arg Gly Asp Phe Gly His Val Gly Gln Pro Gly Pro
                565                 570                 575
```

```
Pro Gly Glu Asp Gly Glu Arg Gly Ala Glu Gly Pro Pro Gly Pro Thr
            580                 585                 590

Gly Gln Ala Gly Glu Pro Gly Pro Arg Gly Leu Leu Gly Pro Arg Gly
        595                 600                 605

Ser Pro Gly Pro Thr Gly Arg Pro Gly Val Thr Gly Ile Asp Gly Ala
    610                 615                 620

Pro Gly Ala Lys Gly Asn Val Gly Pro Pro Gly Glu Pro Gly Pro Pro
625                 630                 635                 640

Gly Gln Gln Gly Asn His Gly Ser Gln Gly Leu Pro Gly Pro Gln Gly
                645                 650                 655

Leu Ile Gly Thr Pro Gly Glu Lys Gly Pro Pro Gly Asn Pro Gly Ile
            660                 665                 670

Pro Gly Leu Pro Gly Ser Asp Gly Pro Leu Gly His Pro Gly His Glu
        675                 680                 685

Gly Pro Thr Gly Glu Lys Gly Ala Gln Gly Pro Pro Gly Ser Ala Gly
    690                 695                 700

Pro Pro Gly Tyr Pro Gly Pro Arg Gly Val Lys Gly Thr Ser Gly Asn
705                 710                 715                 720

Arg Gly Leu Gln Gly Glu Lys Gly Glu Lys Gly Glu Asp Gly Phe Pro
                725                 730                 735

Gly Phe Lys Gly Asp Val Gly Leu Lys Gly Asp Gln Gly Lys Pro Gly
            740                 745                 750

Ala Pro Gly Pro Arg Gly Glu Asp Gly Pro Glu Gly Pro Lys Gly Gln
        755                 760                 765

Ala Gly Gln Ala Gly Glu Glu Gly Pro Pro Gly Ser Ala Gly Glu Lys
    770                 775                 780

Gly Lys Leu Gly Val Pro Gly Leu Pro Gly Tyr Pro Gly Arg Pro Gly
785                 790                 795                 800

Pro Lys Gly Ser Ile Gly Phe Pro Gly Pro Leu Gly Pro Ile Gly Glu
                805                 810                 815

Lys Gly Lys Ser Gly Lys Thr Gly Gln Pro Gly Leu Glu Gly Glu Arg
            820                 825                 830

Gly Pro Pro Gly Ser Arg Gly Glu Arg Gly Gln Pro Gly Ala Thr Gly
        835                 840                 845
```

```
Gln Pro Gly Pro Lys Gly Asp Val Gly Gln Asp Gly Ala Pro Gly Ile
    850                 855                 860

Pro Gly Glu Lys Gly Leu Pro Gly Leu Gln Gly Pro Pro Gly Phe Pro
865                 870                 875                 880

Gly Pro Lys Gly Pro Pro Gly His Gln Gly Lys Asp Gly Arg Pro Gly
                885                 890                 895

His Pro Gly Gln Arg Gly Glu Leu Gly Phe Gln Gly Gln Thr Gly Pro
            900                 905                 910

Pro Gly Pro Ala Gly Val Leu Gly Pro Gln Gly Lys Thr Gly Glu Val
        915                 920                 925

Gly Pro Leu Gly Glu Arg Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly
    930                 935                 940

Glu Gln Gly Leu Pro Gly Leu Glu Gly Arg Glu Gly Ala Lys Gly Glu
945                 950                 955                 960

Leu Gly Pro Pro Gly Pro Leu Gly Lys Glu Gly Pro Ala Gly Leu Arg
                965                 970                 975

Gly Phe Pro Gly Pro Lys Gly Gly Pro Gly Asp Pro Gly Pro Thr Gly
            980                 985                 990

Leu Lys Gly Asp Lys Gly Pro Pro  Gly Pro Val Gly Ala  Asn Gly Ser
        995                 1000                1005

Pro Gly  Glu Arg Gly Pro Leu  Gly Pro Ala Gly Gly  Ile Gly Leu
    1010                1015                1020

Pro Gly  Gln Ser Gly Ser Glu  Gly Pro Val Gly Pro  Ala Gly Lys
    1025                1030                1035

Lys Gly  Ser Arg Gly Glu Arg  Gly Pro Pro Gly Pro  Thr Gly Lys
    1040                1045                1050

Asp Gly  Ile Pro Gly Pro Leu  Gly Pro Leu Gly Pro  Pro Gly Ala
    1055                1060                1065

Ala Gly  Pro Ser Gly Glu Glu  Gly Asp Lys Gly Asp  Val Gly Ala
    1070                1075                1080

Pro Gly  His Lys Gly Ser Lys  Gly Asp Lys Gly Asp  Ala Gly Pro
    1085                1090                1095

Pro Gly  Gln Pro Gly Ile Arg  Gly Pro Ala Gly His  Pro Gly Pro
    1100                1105                1110
```

```
Pro Gly  Ala Asp Gly Ala Gln  Gly Arg Arg Gly Pro  Pro Gly Leu
    1115                1120                1125

Phe Gly  Gln Lys Gly Asp Asp  Gly Val Arg Gly Phe  Val Gly Val
    1130                1135                1140

Ile Gly  Pro Pro Gly Leu Gln  Gly Leu Pro Gly Pro  Pro Gly Glu
    1145                1150                1155

Lys Gly  Glu Val Gly Asp Val  Gly Ser Met Gly Pro  His Gly Ala
    1160                1165                1170

Pro Gly  Pro Arg Gly Pro Gln  Gly Pro Thr Gly Ser  Glu Gly Thr
    1175                1180                1185

Pro Gly  Leu Pro Gly Gly Val  Gly Gln Pro Gly Ala  Val Gly Glu
    1190                1195                1200

Lys Gly  Glu Arg Gly Asp Ala  Gly Asp Pro Gly Pro  Pro Gly Ala
    1205                1210                1215

Pro Gly  Ile Pro Gly Pro Lys  Gly Asp Ile Gly Glu  Lys Gly Asp
    1220                1225                1230

Ser Gly  Pro Ser Gly Ala Ala  Gly Pro Pro Gly Lys  Lys Gly Pro
    1235                1240                1245

Pro Gly  Glu Asp Gly Ala Lys  Gly Ser Val Gly Pro  Thr Gly Leu
    1250                1255                1260

Pro Gly  Asp Leu Gly Pro Pro  Gly Asp Pro Gly Val  Ser Gly Ile
    1265                1270                1275

Asp Gly  Ser Pro Gly Glu Lys  Gly Asp Pro Gly Asp  Val Gly Gly
    1280                1285                1290

Pro Gly  Pro Pro Gly Ala Ser  Gly Glu Pro Gly Ala  Pro Gly Pro
    1295                1300                1305

Pro Gly  Lys Arg Gly Pro Ser  Gly His Met Gly Arg  Glu Gly Arg
    1310                1315                1320

Glu Gly  Glu Lys Gly Ala Lys  Gly Glu Pro Gly Pro  Asp Gly Pro
    1325                1330                1335

Pro Gly  Arg Thr Gly Pro Met  Gly Ala Arg Gly Pro  Pro Gly Arg
    1340                1345                1350

Val Gly  Pro Glu Gly Leu Arg  Gly Ile Pro Gly Pro  Val Gly Glu
    1355                1360                1365
```

```
Pro Gly  Leu Leu Gly Ala Pro  Gly Gln Met Gly Pro  Pro Gly Pro
    1370                1375                1380

Leu Gly  Pro Ser Gly Leu Pro  Gly Leu Lys Gly Asp  Thr Gly Pro
    1385                1390                1395

Lys Gly  Glu Lys Gly His Ile  Gly Leu Ile Gly Leu  Ile Gly Pro
    1400                1405                1410

Pro Gly  Glu Ala Gly Glu Lys  Gly Asp Gln Gly Leu  Pro Gly Val
    1415                1420                1425

Gln Gly  Pro Pro Gly Pro Lys  Gly Asp Pro Gly Pro  Pro Gly Pro
    1430                1435                1440

Ile Gly  Ser Leu Gly His Pro  Gly Pro Pro Gly Val  Ala Gly Pro
    1445                1450                1455

Leu Gly  Gln Lys Gly Ser Lys  Gly Ser Pro Gly Ser  Met Gly Pro
    1460                1465                1470

Arg Gly  Asp Thr Gly Pro Ala  Gly Pro Pro Gly Pro  Pro Gly Ala
    1475                1480                1485

Pro Ala  Glu Leu His Gly Leu  Arg Arg Arg Arg Arg  Phe Val Pro
    1490                1495                1500

Val Pro  Leu Pro Val Val Glu  Gly Gly Leu Glu Glu  Val Leu Ala
    1505                1510                1515

Ser Leu  Thr Ser Leu Ser Leu  Glu Leu Glu Gln Leu  Arg Arg Pro
    1520                1525                1530

Pro Gly  Thr Ala Glu Arg Pro  Gly Leu Val Cys His  Glu Leu His
    1535                1540                1545

Arg Asn  His Pro His Leu Pro  Asp Gly Glu Tyr Trp  Ile Asp Pro
    1550                1555                1560

Asn Gln  Gly Cys Ala Arg Asp  Ser Phe Arg Val Phe  Cys Asn Phe
    1565                1570                1575

Thr Ala  Gly Gly Glu Thr Cys  Leu Tyr Pro Asp Lys  Lys Phe Glu
    1580                1585                1590

Ile Val  Lys Leu Ala Ser Trp  Ser Lys Glu Lys Pro  Gly Gly Trp
    1595                1600                1605

Tyr Ser  Thr Phe Arg Arg Gly  Lys Lys Phe Ser Tyr  Val Asp Ala
    1610                1615                1620
```

```
Asp Gly  Ser Pro Val Asn Val  Val Gln Leu Asn Phe  Leu Lys Leu
    1625                1630                1635


Leu Ser  Ala Thr Ala Arg Gln  Asn Phe Thr Tyr Ser  Cys Gln Asn
    1640                1645                1650


Ala Ala  Ala Trp Leu Asp Glu  Ala Thr Gly Asp Tyr  Ser His Ser
    1655                1660                1665


Ala Arg  Phe Leu Gly Thr Asn  Gly Glu Glu Leu Ser  Phe Asn Gln
    1670                1675                1680


Thr Thr  Ala Ala Thr Val Ser  Val Pro Gln Asp Gly  Cys Arg Leu
    1685                1690                1695


Arg Lys  Gly Gln Thr Lys Thr  Leu Phe Glu Phe Ser  Ser Ser Arg
    1700                1705                1710


Ala Gly  Phe Leu Pro Leu Trp  Asp Val Ala Ala Thr  Asp Phe Gly
    1715                1720                1725


Gln Thr  Asn Gln Lys Phe Gly  Phe Glu Leu Gly Pro  Val Cys Phe
    1730                1735                1740


Ser Ser
    1745


<210>  75
<211>  1028
<212>  PRT
<213>  Homo sapiens

<400>  75

Met Arg Ala Ala Arg Ala Leu Leu Pro Leu Leu Leu Gln Ala Cys Trp
1               5                  10                  15


Thr Ala Ala Gln Asp Glu Pro Glu Thr Pro Arg Ala Val Ala Phe Gln
            20                  25                  30


Asp Cys Pro Val Asp Leu Phe Phe Val Leu Asp Thr Ser Glu Ser Val
        35                  40                  45


Ala Leu Arg Leu Lys Pro Tyr Gly Ala Leu Val Asp Lys Val Lys Ser
    50                  55                  60


Phe Thr Lys Arg Phe Ile Asp Asn Leu Arg Asp Arg Tyr Tyr Arg Cys
65                  70                  75                  80


Asp Arg Asn Leu Val Trp Asn Ala Gly Ala Leu His Tyr Ser Asp Glu
                85                  90                  95


Val Glu Ile Ile Gln Gly Leu Thr Arg Met Pro Gly Gly Arg Asp Ala
```

```
            100                 105                 110

Leu Lys Ser Ser Val Asp Ala Val Lys Tyr Phe Gly Lys Gly Thr Tyr
        115                 120                 125

Thr Asp Cys Ala Ile Lys Lys Gly Leu Glu Gln Leu Leu Val Gly Gly
    130                 135                 140

Ser His Leu Lys Glu Asn Lys Tyr Leu Ile Val Val Thr Asp Gly His
145                 150                 155                 160

Pro Leu Glu Gly Tyr Lys Glu Pro Cys Gly Gly Leu Glu Asp Ala Val
                165                 170                 175

Asn Glu Ala Lys His Leu Gly Val Lys Val Phe Ser Val Ala Ile Thr
            180                 185                 190

Pro Asp His Leu Glu Pro Arg Leu Ser Ile Ile Ala Thr Asp His Thr
        195                 200                 205

Tyr Arg Arg Asn Phe Thr Ala Ala Asp Trp Gly Gln Ser Arg Asp Ala
    210                 215                 220

Glu Glu Ala Ile Ser Gln Thr Ile Asp Thr Ile Val Asp Met Ile Lys
225                 230                 235                 240

Asn Asn Val Glu Gln Val Cys Cys Ser Phe Glu Cys Gln Pro Ala Arg
                245                 250                 255

Gly Pro Pro Gly Leu Arg Gly Asp Pro Gly Phe Glu Gly Glu Arg Gly
            260                 265                 270

Lys Pro Gly Leu Pro Gly Glu Lys Gly Glu Ala Gly Asp Pro Gly Arg
        275                 280                 285

Pro Gly Asp Leu Gly Pro Val Gly Tyr Gln Gly Met Lys Gly Glu Lys
    290                 295                 300

Gly Ser Arg Gly Glu Lys Gly Ser Arg Gly Pro Lys Gly Tyr Lys Gly
305                 310                 315                 320

Glu Lys Gly Lys Arg Gly Ile Asp Gly Val Asp Gly Val Lys Gly Glu
                325                 330                 335

Met Gly Tyr Pro Gly Leu Pro Gly Cys Lys Gly Ser Pro Gly Phe Asp
            340                 345                 350

Gly Ile Gln Gly Pro Pro Gly Pro Lys Gly Asp Pro Gly Ala Phe Gly
        355                 360                 365

Leu Lys Gly Glu Lys Gly Glu Pro Gly Ala Asp Gly Glu Ala Gly Arg
```

```
    370                 375                 380

Pro Gly Ser Ser Gly Pro Ser Gly Asp Glu Gly Gln Pro Gly Glu Pro
385                 390                 395                 400

Gly Pro Pro Gly Glu Lys Gly Glu Ala Gly Asp Glu Gly Asn Pro Gly
                405                 410                 415

Pro Asp Gly Ala Pro Gly Glu Arg Gly Gly Pro Gly Glu Arg Gly Pro
            420                 425                 430

Arg Gly Thr Pro Gly Thr Arg Gly Pro Arg Gly Asp Pro Gly Glu Ala
        435                 440                 445

Gly Pro Gln Gly Asp Gln Gly Arg Glu Gly Pro Val Gly Val Pro Gly
    450                 455                 460

Asp Pro Gly Glu Ala Gly Pro Ile Gly Pro Lys Gly Tyr Arg Gly Asp
465                 470                 475                 480

Glu Gly Pro Pro Gly Ser Glu Gly Ala Arg Gly Ala Pro Gly Pro Ala
                485                 490                 495

Gly Pro Pro Gly Asp Pro Gly Leu Met Gly Glu Arg Gly Glu Asp Gly
            500                 505                 510

Pro Ala Gly Asn Gly Thr Glu Gly Phe Pro Gly Phe Pro Gly Tyr Pro
        515                 520                 525

Gly Asn Arg Gly Ala Pro Gly Ile Asn Gly Thr Lys Gly Tyr Pro Gly
    530                 535                 540

Leu Lys Gly Asp Glu Gly Glu Ala Gly Asp Pro Gly Asp Asp Asn Asn
545                 550                 555                 560

Asp Ile Ala Pro Arg Gly Val Lys Gly Ala Lys Gly Tyr Arg Gly Pro
                565                 570                 575

Glu Gly Pro Gln Gly Pro Pro Gly His Gln Gly Pro Pro Gly Pro Asp
            580                 585                 590

Glu Cys Glu Ile Leu Asp Ile Ile Met Lys Met Cys Ser Cys Cys Glu
        595                 600                 605

Cys Lys Cys Gly Pro Ile Asp Leu Leu Phe Val Leu Asp Ser Ser Glu
    610                 615                 620

Ser Ile Gly Leu Gln Asn Phe Glu Ile Ala Lys Asp Phe Val Val Lys
625                 630                 635                 640

Val Ile Asp Arg Leu Ser Arg Asp Glu Leu Val Lys Phe Glu Pro Gly
```

645 650 655

Gln Ser Tyr Ala Gly Val Val Gln Tyr Ser His Ser Gln Met Gln Glu
660 665 670

His Val Ser Leu Arg Ser Pro Ser Ile Arg Asn Val Gln Glu Leu Lys
675 680 685

Glu Ala Ile Lys Ser Leu Gln Trp Met Ala Gly Gly Thr Phe Thr Gly
690 695 700

Glu Ala Leu Gln Tyr Thr Arg Asp Gln Leu Leu Pro Pro Ser Pro Asn
705 710 715 720

Asn Arg Ile Ala Leu Val Ile Thr Asp Gly Arg Ser Asp Thr Gln Arg
725 730 735

Asp Thr Thr Pro Leu Asn Val Leu Cys Ser Pro Gly Ile Gln Val Val
740 745 750

Ser Val Gly Ile Lys Asp Val Phe Asp Phe Ile Pro Gly Ser Asp Gln
755 760 765

Leu Asn Val Ile Ser Cys Gln Gly Leu Ala Pro Ser Gln Gly Arg Pro
770 775 780

Gly Leu Ser Leu Val Lys Glu Asn Tyr Ala Glu Leu Leu Glu Asp Ala
785 790 795 800

Phe Leu Lys Asn Val Thr Ala Gln Ile Cys Ile Asp Lys Lys Cys Pro
805 810 815

Asp Tyr Thr Cys Pro Ile Thr Phe Ser Ser Pro Ala Asp Ile Thr Ile
820 825 830

Leu Leu Asp Gly Ser Ala Ser Val Gly Ser His Asn Phe Asp Thr Thr
835 840 845

Lys Arg Phe Ala Lys Arg Leu Ala Glu Arg Phe Leu Thr Ala Gly Arg
850 855 860

Thr Asp Pro Ala His Asp Val Arg Val Ala Val Val Gln Tyr Ser Gly
865 870 875 880

Thr Gly Gln Gln Arg Pro Glu Arg Ala Ser Leu Gln Phe Leu Gln Asn
885 890 895

Tyr Thr Ala Leu Ala Ser Ala Val Asp Ala Met Asp Phe Ile Asn Asp
900 905 910

Ala Thr Asp Val Asn Asp Ala Leu Gly Tyr Val Thr Arg Phe Tyr Arg

915 920 925

Glu Ala Ser Ser Gly Ala Ala Lys Lys Arg Leu Leu Leu Phe Ser Asp
930 935 940

Gly Asn Ser Gln Gly Ala Thr Pro Ala Ala Ile Glu Lys Ala Val Gln
945 950 955 960

Glu Ala Gln Arg Ala Gly Ile Glu Ile Phe Val Val Val Val Gly Arg
965 970 975

Gln Val Asn Glu Pro His Ile Arg Val Leu Val Thr Gly Lys Thr Ala
980 985 990

Glu Tyr Asp Val Ala Tyr Gly Glu Ser His Leu Phe Arg Val Pro Ser
995 1000 1005

Tyr Gln Ala Leu Leu Arg Gly Val Phe His Gln Thr Val Ser Arg
1010 1015 1020

Lys Val Ala Leu Gly
1025

<210> 76
<211> 1019
<212> PRT
<213> Homo sapiens

<400> 76

Met Leu Gln Gly Thr Cys Ser Val Leu Leu Leu Trp Gly Ile Leu Gly
1 5 10 15

Ala Ile Gln Ala Gln Gln Gln Glu Val Ile Ser Pro Asp Thr Thr Glu
20 25 30

Arg Asn Asn Asn Cys Pro Glu Lys Thr Asp Cys Pro Ile His Val Tyr
35 40 45

Phe Val Leu Asp Thr Ser Glu Ser Val Thr Met Gln Ser Pro Thr Asp
50 55 60

Ile Leu Leu Phe His Met Lys Gln Phe Val Pro Gln Phe Ile Ser Gln
65 70 75 80

Leu Gln Asn Glu Phe Tyr Leu Asp Gln Val Ala Leu Ser Trp Arg Tyr
85 90 95

Gly Gly Leu His Phe Ser Asp Gln Val Glu Val Phe Ser Pro Pro Gly
100 105 110

Ser Asp Arg Ala Ser Phe Ile Lys Asn Leu Gln Gly Ile Ser Ser Phe
115 120 125

```
Arg Arg Gly Thr Phe Thr Asp Cys Ala Leu Ala Asn Met Thr Glu Gln
    130                 135                 140

Ile Arg Gln Asp Arg Ser Lys Gly Thr Val His Phe Ala Val Val Ile
145                 150                 155                 160

Thr Asp Gly His Val Thr Gly Ser Pro Cys Gly Gly Ile Lys Leu Gln
                165                 170                 175

Ala Glu Arg Ala Arg Glu Glu Gly Ile Arg Leu Phe Ala Val Ala Pro
            180                 185                 190

Asn Gln Asn Leu Lys Glu Gln Gly Leu Arg Asp Ile Ala Ser Thr Pro
        195                 200                 205

His Glu Leu Tyr Arg Asn Asp Tyr Ala Thr Met Leu Pro Asp Ser Thr
    210                 215                 220

Glu Ile Asp Gln Asp Thr Ile Asn Arg Ile Ile Lys Val Met Lys His
225                 230                 235                 240

Glu Ala Tyr Gly Glu Cys Tyr Lys Val Ser Cys Leu Glu Ile Pro Gly
                245                 250                 255

Pro Ser Gly Pro Lys Gly Tyr Arg Gly Gln Lys Gly Ala Lys Gly Asn
            260                 265                 270

Met Gly Glu Pro Gly Glu Pro Gly Gln Lys Gly Arg Gln Gly Asp Pro
        275                 280                 285

Gly Ile Glu Gly Pro Ile Gly Phe Pro Gly Pro Lys Gly Val Pro Gly
    290                 295                 300

Phe Lys Gly Glu Lys Gly Glu Phe Gly Ala Asp Gly Arg Lys Gly Ala
305                 310                 315                 320

Pro Gly Leu Ala Gly Lys Asn Gly Thr Asp Gly Gln Lys Gly Lys Leu
                325                 330                 335

Gly Arg Ile Gly Pro Pro Gly Cys Lys Gly Asp Pro Gly Asn Arg Gly
            340                 345                 350

Pro Asp Gly Tyr Pro Gly Glu Ala Gly Ser Pro Gly Glu Arg Gly Asp
        355                 360                 365

Gln Gly Gly Lys Gly Asp Pro Gly Arg Pro Gly Arg Arg Gly Pro Pro
    370                 375                 380

Gly Glu Ile Gly Ala Lys Gly Ser Lys Gly Tyr Gln Gly Asn Ser Gly
385                 390                 395                 400
```

```
Ala Pro Gly Ser Pro Gly Val Lys Gly Ala Lys Gly Gly Pro Gly Pro
                405                 410                 415

Arg Gly Pro Lys Gly Glu Pro Gly Arg Arg Gly Asp Pro Gly Thr Lys
            420                 425                 430

Gly Ser Pro Gly Ser Asp Gly Pro Lys Gly Glu Lys Gly Asp Pro Gly
        435                 440                 445

Pro Glu Gly Pro Arg Gly Leu Ala Gly Glu Val Gly Asn Lys Gly Ala
    450                 455                 460

Lys Gly Asp Arg Gly Leu Pro Gly Pro Arg Gly Pro Gln Gly Ala Leu
465                 470                 475                 480

Gly Glu Pro Gly Lys Gln Gly Ser Arg Gly Asp Pro Gly Asp Ala Gly
                485                 490                 495

Pro Arg Gly Asp Ser Gly Gln Pro Gly Pro Lys Gly Asp Pro Gly Arg
            500                 505                 510

Pro Gly Phe Ser Tyr Pro Gly Pro Arg Gly Ala Pro Gly Glu Lys Gly
        515                 520                 525

Glu Pro Gly Pro Arg Gly Pro Glu Gly Gly Arg Gly Asp Phe Gly Leu
    530                 535                 540

Lys Gly Glu Pro Gly Arg Lys Gly Glu Lys Gly Glu Pro Ala Asp Pro
545                 550                 555                 560

Gly Pro Pro Gly Glu Pro Gly Pro Arg Gly Pro Arg Gly Val Pro Gly
                565                 570                 575

Pro Glu Gly Glu Pro Gly Pro Pro Gly Asp Pro Gly Leu Thr Glu Cys
            580                 585                 590

Asp Val Met Thr Tyr Val Arg Glu Thr Cys Gly Cys Cys Asp Cys Glu
        595                 600                 605

Lys Arg Cys Gly Ala Leu Asp Val Val Phe Val Ile Asp Ser Ser Glu
    610                 615                 620

Ser Ile Gly Tyr Thr Asn Phe Thr Leu Glu Lys Asn Phe Val Ile Asn
625                 630                 635                 640

Val Val Asn Arg Leu Gly Ala Ile Ala Lys Asp Pro Lys Ser Glu Thr
                645                 650                 655

Gly Thr Arg Val Gly Val Val Gln Tyr Ser His Glu Gly Thr Phe Glu
            660                 665                 670
```

```
Ala Ile Gln Leu Asp Asp Glu Arg Ile Asp Ser Leu Ser Ser Phe Lys
        675                 680                 685

Glu Ala Val Lys Asn Leu Glu Trp Ile Ala Gly Gly Thr Trp Thr Pro
    690                 695                 700

Ser Ala Leu Lys Phe Ala Tyr Asp Arg Leu Ile Lys Glu Ser Arg Arg
705                 710                 715                 720

Gln Lys Thr Arg Val Phe Ala Val Val Ile Thr Asp Gly Arg His Asp
                725                 730                 735

Pro Arg Asp Asp Asp Leu Asn Leu Arg Ala Leu Cys Asp Arg Asp Val
            740                 745                 750

Thr Val Thr Ala Ile Gly Ile Gly Asp Met Phe His Glu Lys His Glu
        755                 760                 765

Ser Glu Asn Leu Tyr Ser Ile Ala Cys Asp Lys Pro Gln Gln Val Arg
    770                 775                 780

Asn Met Thr Leu Phe Ser Asp Leu Val Ala Glu Lys Phe Ile Asp Asp
785                 790                 795                 800

Met Glu Asp Val Leu Cys Pro Asp Pro Gln Ile Val Cys Pro Asp Leu
                805                 810                 815

Pro Cys Gln Thr Glu Leu Ser Val Ala Gln Cys Thr Gln Arg Pro Val
            820                 825                 830

Asp Ile Val Phe Leu Leu Asp Gly Ser Glu Arg Leu Gly Glu Gln Asn
        835                 840                 845

Phe His Lys Ala Arg Arg Phe Val Glu Gln Val Ala Arg Arg Leu Thr
    850                 855                 860

Leu Ala Arg Arg Asp Asp Asp Pro Leu Asn Ala Arg Val Ala Leu Leu
865                 870                 875                 880

Gln Phe Gly Gly Pro Gly Glu Gln Gln Val Ala Phe Pro Leu Ser His
                885                 890                 895

Asn Leu Thr Ala Ile His Glu Ala Leu Glu Thr Thr Gln Tyr Leu Asn
            900                 905                 910

Ser Phe Ser His Val Gly Ala Gly Val Val His Ala Ile Asn Ala Ile
        915                 920                 925

Val Arg Ser Pro Arg Gly Gly Ala Arg Arg His Ala Glu Leu Ser Phe
    930                 935                 940
```

```
Val Phe Leu Thr Asp Gly Val Thr Gly Asn Asp Ser Leu His Glu Ser
945                 950                 955                 960


Ala His Ser Met Arg Lys Gln Asn Val Val Pro Thr Val Leu Ala Leu
                965                 970                 975


Gly Ser Asp Val Asp Met Asp Val Leu Thr Thr Leu Ser Leu Gly Asp
            980                 985                 990


Arg Ala Ala Val Phe His Glu Lys  Asp Tyr Asp Ser Leu  Ala Gln Pro
        995                 1000                1005


Gly Phe  Phe Asp Arg Phe Ile  Arg Trp Ile Cys
    1010                1015


<210>  77
<211>  3177
<212>  PRT
<213>  Homo sapiens

<400>  77

Met Arg Lys His Arg His Leu Pro Leu Val Ala Val Phe Cys Leu Phe
1               5                   10                  15


Leu Ser Gly Phe Pro Thr Thr His Ala Gln Gln Gln Gln Ala Asp Val
            20                  25                  30


Lys Asn Gly Ala Ala Ala Asp Ile Ile Phe Leu Val Asp Ser Ser Trp
        35                  40                  45


Thr Ile Gly Glu Glu His Phe Gln Leu Val Arg Glu Phe Leu Tyr Asp
    50                  55                  60


Val Val Lys Ser Leu Ala Val Gly Glu Asn Asp Phe His Phe Ala Leu
65                  70                  75                  80


Val Gln Phe Asn Gly Asn Pro His Thr Glu Phe Leu Leu Asn Thr Tyr
                85                  90                  95


Arg Thr Lys Gln Glu Val Leu Ser His Ile Ser Asn Met Ser Tyr Ile
            100                 105                 110


Gly Gly Thr Asn Gln Thr Gly Lys Gly Leu Glu Tyr Ile Met Gln Ser
        115                 120                 125


His Leu Thr Lys Ala Ala Gly Ser Arg Ala Gly Asp Gly Val Pro Gln
    130                 135                 140


Val Ile Val Val Leu Thr Asp Gly His Ser Lys Asp Gly Leu Ala Leu
145                 150                 155                 160
```

```
Pro Ser Ala Glu Leu Lys Ser Ala Asp Val Asn Val Phe Ala Ile Gly
                165                 170                 175

Val Glu Asp Ala Asp Glu Gly Ala Leu Lys Glu Ile Ala Ser Glu Pro
            180                 185                 190

Leu Asn Met His Met Phe Asn Leu Glu Asn Phe Thr Ser Leu His Asp
        195                 200                 205

Ile Val Gly Asn Leu Val Ser Cys Val His Ser Ser Val Ser Pro Glu
    210                 215                 220

Arg Ala Gly Asp Thr Glu Thr Leu Lys Asp Ile Thr Ala Gln Asp Ser
225                 230                 235                 240

Ala Asp Ile Ile Phe Leu Ile Asp Gly Ser Asn Asn Thr Gly Ser Val
                245                 250                 255

Asn Phe Ala Val Ile Leu Asp Phe Leu Val Asn Leu Leu Glu Lys Leu
            260                 265                 270

Pro Ile Gly Thr Gln Gln Ile Arg Val Gly Val Val Gln Phe Ser Asp
        275                 280                 285

Glu Pro Arg Thr Met Phe Ser Leu Asp Thr Tyr Ser Thr Lys Ala Gln
    290                 295                 300

Val Leu Gly Ala Val Lys Ala Leu Gly Phe Ala Gly Gly Glu Leu Ala
305                 310                 315                 320

Asn Ile Gly Leu Ala Leu Asp Phe Val Val Glu Asn His Phe Thr Arg
                325                 330                 335

Ala Gly Gly Ser Arg Val Glu Glu Gly Val Pro Gln Val Leu Val Leu
            340                 345                 350

Ile Ser Ala Gly Pro Ser Ser Asp Glu Ile Arg Tyr Gly Val Val Ala
        355                 360                 365

Leu Lys Gln Ala Ser Val Phe Ser Phe Gly Leu Gly Ala Gln Ala Ala
    370                 375                 380

Ser Arg Ala Glu Leu Gln His Ile Ala Thr Asp Asp Asn Leu Val Phe
385                 390                 395                 400

Thr Val Pro Glu Phe Arg Ser Phe Gly Asp Leu Gln Glu Lys Leu Leu
                405                 410                 415

Pro Tyr Ile Val Gly Val Ala Gln Arg His Ile Val Leu Lys Pro Pro
            420                 425                 430
```

```
Thr Ile Val Thr Gln Val Ile Glu Val Asn Lys Arg Asp Ile Val Phe
        435                 440                 445

Leu Val Asp Gly Ser Ser Ala Leu Gly Leu Ala Asn Phe Asn Ala Ile
    450                 455                 460

Arg Asp Phe Ile Ala Lys Val Ile Gln Arg Leu Glu Ile Gly Gln Asp
465                 470                 475                 480

Leu Ile Gln Val Ala Val Ala Gln Tyr Ala Asp Thr Val Arg Pro Glu
                485                 490                 495

Phe Tyr Phe Asn Thr His Pro Thr Lys Arg Glu Val Ile Thr Ala Val
            500                 505                 510

Arg Lys Met Lys Pro Leu Asp Gly Ser Ala Leu Tyr Thr Gly Ser Ala
        515                 520                 525

Leu Asp Phe Val Arg Asn Asn Leu Phe Thr Ser Ser Ala Gly Tyr Arg
    530                 535                 540

Ala Ala Glu Gly Ile Pro Lys Leu Leu Val Leu Ile Thr Gly Gly Lys
545                 550                 555                 560

Ser Leu Asp Glu Ile Ser Gln Pro Ala Gln Glu Leu Lys Arg Ser Ser
                565                 570                 575

Ile Met Ala Phe Ala Ile Gly Asn Lys Gly Ala Asp Gln Ala Glu Leu
            580                 585                 590

Glu Glu Ile Ala Phe Asp Ser Ser Leu Val Phe Ile Pro Ala Glu Phe
        595                 600                 605

Arg Ala Ala Pro Leu Gln Gly Met Leu Pro Gly Leu Leu Ala Pro Leu
    610                 615                 620

Arg Thr Leu Ser Gly Thr Pro Glu Val His Ser Asn Lys Arg Asp Ile
625                 630                 635                 640

Ile Phe Leu Leu Asp Gly Ser Ala Asn Val Gly Lys Thr Asn Phe Pro
                645                 650                 655

Tyr Val Arg Asp Phe Val Met Asn Leu Val Asn Ser Leu Asp Ile Gly
            660                 665                 670

Asn Asp Asn Ile Arg Val Gly Leu Val Gln Phe Ser Asp Thr Pro Val
        675                 680                 685

Thr Glu Phe Ser Leu Asn Thr Tyr Gln Thr Lys Ser Asp Ile Leu Gly
    690                 695                 700
```

```
His Leu Arg Gln Leu Gln Leu Gln Gly Gly Ser Gly Leu Asn Thr Gly
705                 710                 715                 720

Ser Ala Leu Ser Tyr Val Tyr Ala Asn His Phe Thr Glu Ala Gly Gly
                725                 730                 735

Ser Arg Ile Arg Glu His Val Pro Gln Leu Leu Leu Leu Leu Thr Ala
            740                 745                 750

Gly Gln Ser Glu Asp Ser Tyr Leu Gln Ala Ala Asn Ala Leu Thr Arg
        755                 760                 765

Ala Gly Ile Leu Thr Phe Cys Val Gly Ala Ser Gln Ala Asn Lys Ala
    770                 775                 780

Glu Leu Glu Gln Ile Ala Phe Asn Pro Ser Leu Val Tyr Leu Met Asp
785                 790                 795                 800

Asp Phe Ser Ser Leu Pro Ala Leu Pro Gln Gln Leu Ile Gln Pro Leu
                805                 810                 815

Thr Thr Tyr Val Ser Gly Gly Val Glu Glu Val Pro Leu Ala Gln Pro
            820                 825                 830

Glu Ser Lys Arg Asp Ile Leu Phe Leu Phe Asp Gly Ser Ala Asn Leu
        835                 840                 845

Val Gly Gln Phe Pro Val Val Arg Asp Phe Leu Tyr Lys Ile Ile Asp
    850                 855                 860

Glu Leu Asn Val Lys Pro Glu Gly Thr Arg Ile Ala Val Ala Gln Tyr
865                 870                 875                 880

Ser Asp Asp Val Lys Val Glu Ser Arg Phe Asp Glu His Gln Ser Lys
                885                 890                 895

Pro Glu Ile Leu Asn Leu Val Lys Arg Met Lys Ile Lys Thr Gly Lys
            900                 905                 910

Ala Leu Asn Leu Gly Tyr Ala Leu Asp Tyr Ala Gln Arg Tyr Ile Phe
        915                 920                 925

Val Lys Ser Ala Gly Ser Arg Ile Glu Asp Gly Val Leu Gln Phe Leu
    930                 935                 940

Val Leu Leu Val Ala Gly Arg Ser Ser Asp Arg Val Asp Gly Pro Ala
945                 950                 955                 960

Ser Asn Leu Lys Gln Ser Gly Val Val Pro Phe Ile Phe Gln Ala Lys
                965                 970                 975
```

```
Asn Ala Asp Pro Ala Glu Leu Glu Gln Ile Val Leu Ser Pro Ala Phe
            980                 985                 990

Ile Leu Ala Ala Glu Ser Leu Pro  Lys Ile Gly Asp Leu  His Pro Gln
        995                 1000                1005

Ile Val  Asn Leu Leu Lys Ser  Val His Asn Gly Ala  Pro Ala Pro
    1010                1015                1020

Val Ser  Gly Glu Lys Asp Val  Val Phe Leu Leu Asp  Gly Ser Glu
    1025                1030                1035

Gly Val  Arg Ser Gly Phe Pro  Leu Leu Lys Glu Phe  Val Gln Arg
    1040                1045                1050

Val Val  Glu Ser Leu Asp Val  Gly Gln Asp Arg Val  Arg Val Ala
    1055                1060                1065

Val Val  Gln Tyr Ser Asp Arg  Thr Arg Pro Glu Phe  Tyr Leu Asn
    1070                1075                1080

Ser Tyr  Met Asn Lys Gln Asp  Val Val Asn Ala Val  Arg Gln Leu
    1085                1090                1095

Thr Leu  Leu Gly Gly Pro Thr  Pro Asn Thr Gly Ala  Ala Leu Glu
    1100                1105                1110

Phe Val  Leu Arg Asn Ile Leu  Val Ser Ser Ala Gly  Ser Arg Ile
    1115                1120                1125

Thr Glu  Gly Val Pro Gln Leu  Leu Ile Val Leu Thr  Ala Asp Arg
    1130                1135                1140

Ser Gly  Asp Asp Val Arg Asn  Pro Ser Val Val Val  Lys Arg Gly
    1145                1150                1155

Gly Ala  Val Pro Ile Gly Ile  Gly Ile Gly Asn Ala  Asp Ile Thr
    1160                1165                1170

Glu Met  Gln Thr Ile Ser Phe  Ile Pro Asp Phe Ala  Val Ala Ile
    1175                1180                1185

Pro Thr  Phe Arg Gln Leu Gly  Thr Val Gln Gln Val  Ile Ser Glu
    1190                1195                1200

Arg Val  Thr Gln Leu Thr Arg  Glu Glu Leu Ser Arg  Leu Gln Pro
    1205                1210                1215

Val Leu  Gln Pro Leu Pro Ser  Pro Gly Val Gly Gly  Lys Arg Asp
    1220                1225                1230
```

```
Val Val  Phe Leu Ile Asp Gly  Ser Gln Ser Ala Gly  Pro Glu Phe
    1235                 1240                 1245

Gln Tyr  Val Arg Thr Leu Ile  Glu Arg Leu Val Asp  Tyr Leu Asp
    1250                 1255                 1260

Val Gly  Phe Asp Thr Thr Arg  Val Ala Val Ile Gln  Phe Ser Asp
    1265                 1270                 1275

Asp Pro  Lys Val Glu Phe Leu  Leu Asn Ala His Ser  Ser Lys Asp
    1280                 1285                 1290

Glu Val  Gln Asn Ala Val Gln  Arg Leu Arg Pro Lys  Gly Gly Arg
    1295                 1300                 1305

Gln Ile  Asn Val Gly Asn Ala  Leu Glu Tyr Val Ser  Arg Asn Ile
    1310                 1315                 1320

Phe Lys  Arg Pro Leu Gly Ser  Arg Ile Glu Glu Gly  Val Pro Gln
    1325                 1330                 1335

Phe Leu  Val Leu Ile Ser Ser  Gly Lys Ser Asp Asp  Glu Val Asp
    1340                 1345                 1350

Asp Pro  Ala Val Glu Leu Lys  Gln Phe Gly Val Ala  Pro Phe Thr
    1355                 1360                 1365

Ile Ala  Arg Asn Ala Asp Gln  Glu Glu Leu Val Lys  Ile Ser Leu
    1370                 1375                 1380

Ser Pro  Glu Tyr Val Phe Ser  Val Ser Thr Phe Arg  Glu Leu Pro
    1385                 1390                 1395

Ser Leu  Glu Gln Lys Leu Leu  Thr Pro Ile Thr Thr  Leu Thr Ser
    1400                 1405                 1410

Glu Gln  Ile Gln Lys Leu Leu  Ala Ser Thr Arg Tyr  Pro Pro Pro
    1415                 1420                 1425

Ala Val  Glu Ser Asp Ala Ala  Asp Ile Val Phe Leu  Ile Asp Ser
    1430                 1435                 1440

Ser Glu  Gly Val Arg Pro Asp  Gly Phe Ala His Ile  Arg Asp Phe
    1445                 1450                 1455

Val Ser  Arg Ile Val Arg Arg  Leu Asn Ile Gly Pro  Ser Lys Val
    1460                 1465                 1470

Arg Val  Gly Val Val Gln Phe  Ser Asn Asp Val Phe  Pro Glu Phe
    1475                 1480                 1485
```

```
Tyr Leu  Lys Thr Tyr Arg Ser  Gln Ala Pro Val Leu  Asp Ala Ile
    1490                 1495                 1500

Arg Arg  Leu Arg Leu Arg Gly  Gly Ser Pro Leu Asn  Thr Gly Lys
    1505                 1510                 1515

Ala Leu  Glu Phe Val Ala Arg  Asn Leu Phe Val Lys  Ser Ala Gly
    1520                 1525                 1530

Ser Arg  Ile Glu Asp Gly Val  Pro Gln His Leu Val  Leu Val Leu
    1535                 1540                 1545

Gly Gly  Lys Ser Gln Asp Asp  Val Ser Arg Phe Ala  Gln Val Ile
    1550                 1555                 1560

Arg Ser  Ser Gly Ile Val Ser  Leu Gly Val Gly Asp  Arg Asn Ile
    1565                 1570                 1575

Asp Arg  Thr Glu Leu Gln Thr  Ile Thr Asn Asp Pro  Arg Leu Val
    1580                 1585                 1590

Phe Thr  Val Arg Glu Phe Arg  Glu Leu Pro Asn Ile  Glu Glu Arg
    1595                 1600                 1605

Ile Met  Asn Ser Phe Gly Pro  Ser Ala Ala Thr Pro  Ala Pro Pro
    1610                 1615                 1620

Gly Val  Asp Thr Pro Pro Pro  Ser Arg Pro Glu Lys  Lys Lys Ala
    1625                 1630                 1635

Asp Ile  Val Phe Leu Leu Asp  Gly Ser Ile Asn Phe  Arg Arg Asp
    1640                 1645                 1650

Ser Phe  Gln Glu Val Leu Arg  Phe Val Ser Glu Ile  Val Asp Thr
    1655                 1660                 1665

Val Tyr  Glu Asp Gly Asp Ser  Ile Gln Val Gly Leu  Val Gln Tyr
    1670                 1675                 1680

Asn Ser  Asp Pro Thr Asp Glu  Phe Phe Leu Lys Asp  Phe Ser Thr
    1685                 1690                 1695

Lys Arg  Gln Ile Ile Asp Ala  Ile Asn Lys Val Val  Tyr Lys Gly
    1700                 1705                 1710

Gly Arg  His Ala Asn Thr Lys  Val Gly Leu Glu His  Leu Arg Val
    1715                 1720                 1725

Asn His  Phe Val Pro Glu Ala  Gly Ser Arg Leu Asp  Gln Arg Val
    1730                 1735                 1740
```

```
Pro Gln  Ile Ala Phe Val Ile  Thr Gly Gly Lys Ser  Val Glu Asp
    1745                1750                1755

Ala Gln  Asp Val Ser Leu Ala  Leu Thr Gln Arg Gly  Val Lys Val
    1760                1765                1770

Phe Ala  Val Gly Val Arg Asn  Ile Asp Ser Glu Glu  Val Gly Lys
    1775                1780                1785

Ile Ala  Ser Asn Ser Ala Thr  Ala Phe Arg Val Gly  Asn Val Gln
    1790                1795                1800

Glu Leu  Ser Glu Leu Ser Glu  Gln Val Leu Glu Thr  Leu His Asp
    1805                1810                1815

Ala Met  His Glu Thr Leu Cys  Pro Gly Val Thr Asp  Ala Ala Lys
    1820                1825                1830

Ala Cys  Asn Leu Asp Val Ile  Leu Gly Phe Asp Gly  Ser Arg Asp
    1835                1840                1845

Gln Asn  Val Phe Val Ala Gln  Lys Gly Phe Glu Ser  Lys Val Asp
    1850                1855                1860

Ala Ile  Leu Asn Arg Ile Ser  Gln Met His Arg Val  Ser Cys Ser
    1865                1870                1875

Gly Gly  Arg Ser Pro Thr Val  Arg Val Ser Val Val  Ala Asn Thr
    1880                1885                1890

Pro Ser  Gly Pro Val Glu Ala  Phe Asp Phe Asp Glu  Tyr Gln Pro
    1895                1900                1905

Glu Met  Leu Glu Lys Phe Arg  Asn Met Arg Ser Gln  His Pro Tyr
    1910                1915                1920

Val Leu  Thr Glu Asp Thr Leu  Lys Val Tyr Leu Asn  Lys Phe Arg
    1925                1930                1935

Gln Ser  Ser Pro Asp Ser Val  Lys Val Val Ile His  Phe Thr Asp
    1940                1945                1950

Gly Ala  Asp Gly Asp Leu Ala  Asp Leu His Arg Ala  Ser Glu Asn
    1955                1960                1965

Leu Arg  Gln Glu Gly Val Arg  Ala Leu Ile Leu Val  Gly Leu Glu
    1970                1975                1980

Arg Val  Val Asn Leu Glu Arg  Leu Met His Leu Glu  Phe Gly Arg
    1985                1990                1995
```

```
Gly Phe  Met Tyr Asp Arg Pro  Leu Arg Leu Asn Leu  Leu Asp Leu
    2000                 2005                 2010

Asp Tyr  Glu Leu Ala Glu Gln  Leu Asp Asn Ile Ala  Glu Lys Ala
    2015                 2020                 2025

Cys Cys  Gly Val Pro Cys Lys  Cys Ser Gly Gln Arg  Gly Asp Arg
    2030                 2035                 2040

Gly Pro  Ile Gly Ser Ile Gly  Pro Lys Gly Ile Pro  Gly Glu Asp
    2045                 2050                 2055

Gly Tyr  Arg Gly Tyr Pro Gly  Asp Glu Gly Gly Pro  Gly Glu Arg
    2060                 2065                 2070

Gly Pro  Pro Gly Val Asn Gly  Thr Gln Gly Phe Gln  Gly Cys Pro
    2075                 2080                 2085

Gly Gln  Arg Gly Val Lys Gly  Ser Arg Gly Phe Pro  Gly Glu Lys
    2090                 2095                 2100

Gly Glu  Val Gly Glu Ile Gly  Leu Asp Gly Leu Asp  Gly Glu Asp
    2105                 2110                 2115

Gly Asp  Lys Gly Leu Pro Gly  Ser Ser Gly Glu Lys  Gly Asn Pro
    2120                 2125                 2130

Gly Arg  Arg Gly Asp Lys Gly  Pro Arg Gly Glu Lys  Gly Glu Arg
    2135                 2140                 2145

Gly Asp  Val Gly Ile Arg Gly  Asp Pro Gly Asn Pro  Gly Gln Asp
    2150                 2155                 2160

Ser Gln  Glu Arg Gly Pro Lys  Gly Glu Thr Gly Asp  Leu Gly Pro
    2165                 2170                 2175

Met Gly  Val Pro Gly Arg Asp  Gly Val Pro Gly Gly  Pro Gly Glu
    2180                 2185                 2190

Thr Gly  Lys Asn Gly Gly Phe  Gly Arg Arg Gly Pro  Pro Gly Ala
    2195                 2200                 2205

Lys Gly  Asn Lys Gly Gly Pro  Gly Gln Pro Gly Phe  Glu Gly Glu
    2210                 2215                 2220

Gln Gly  Thr Arg Gly Ala Gln  Gly Pro Ala Gly Pro  Ala Gly Pro
    2225                 2230                 2235

Pro Gly  Leu Ile Gly Glu Gln  Gly Ile Ser Gly Pro  Arg Gly Ser
    2240                 2245                 2250
```

```
Gly Gly  Ala Ala Gly Ala Pro  Gly Glu Arg Gly Arg  Thr Gly Pro
    2255                 2260                 2265

Leu Gly  Arg Lys Gly Glu Pro  Gly Glu Pro Gly Pro  Lys Gly Gly
    2270                 2275                 2280

Ile Gly  Asn Arg Gly Pro Arg  Gly Glu Thr Gly Asp  Asp Gly Arg
    2285                 2290                 2295

Asp Gly  Val Gly Ser Glu Gly  Arg Arg Gly Lys Lys  Gly Glu Arg
    2300                 2305                 2310

Gly Phe  Pro Gly Tyr Pro Gly  Pro Lys Gly Asn Pro  Gly Glu Pro
    2315                 2320                 2325

Gly Leu  Asn Gly Thr Thr Gly  Pro Lys Gly Ile Arg  Gly Arg Arg
    2330                 2335                 2340

Gly Asn  Ser Gly Pro Pro Gly  Ile Val Gly Gln Lys  Gly Asp Pro
    2345                 2350                 2355

Gly Tyr  Pro Gly Pro Ala Gly  Pro Lys Gly Asn Arg  Gly Asp Ser
    2360                 2365                 2370

Ile Asp  Gln Cys Ala Leu Ile  Gln Ser Ile Lys Asp  Lys Cys Pro
    2375                 2380                 2385

Cys Cys  Tyr Gly Pro Leu Glu  Cys Pro Val Phe Pro  Thr Glu Leu
    2390                 2395                 2400

Ala Phe  Ala Leu Asp Thr Ser  Glu Gly Val Asn Gln  Asp Thr Phe
    2405                 2410                 2415

Gly Arg  Met Arg Asp Val Val  Leu Ser Ile Val Asn  Asp Leu Thr
    2420                 2425                 2430

Ile Ala  Glu Ser Asn Cys Pro  Arg Gly Ala Arg Val  Ala Val Val
    2435                 2440                 2445

Thr Tyr  Asn Asn Glu Val Thr  Thr Glu Ile Arg Phe  Ala Asp Ser
    2450                 2455                 2460

Lys Arg  Lys Ser Val Leu Leu  Asp Lys Ile Lys Asn  Leu Gln Val
    2465                 2470                 2475

Ala Leu  Thr Ser Lys Gln Gln  Ser Leu Glu Thr Ala  Met Ser Phe
    2480                 2485                 2490

Val Ala  Arg Asn Thr Phe Lys  Arg Val Arg Asn Gly  Phe Leu Met
    2495                 2500                 2505
```

```
Arg Lys  Val Ala Val Phe Phe  Ser Asn Thr Pro Thr  Arg Ala Ser
    2510                 2515                 2520

Pro Gln  Leu Arg Glu Ala Val  Leu Lys Leu Ser Asp  Ala Gly Ile
    2525                 2530                 2535

Thr Pro  Leu Phe Leu Thr Arg  Gln Glu Asp Arg Gln  Leu Ile Asn
    2540                 2545                 2550

Ala Leu  Gln Ile Asn Asn Thr  Ala Val Gly His Ala  Leu Val Leu
    2555                 2560                 2565

Pro Ala  Gly Arg Asp Leu Thr  Asp Phe Leu Glu Asn  Val Leu Thr
    2570                 2575                 2580

Cys His  Val Cys Leu Asp Ile  Cys Asn Ile Asp Pro  Ser Cys Gly
    2585                 2590                 2595

Phe Gly  Ser Trp Arg Pro Ser  Phe Arg Asp Arg Arg  Ala Ala Gly
    2600                 2605                 2610

Ser Asp  Val Asp Ile Asp Met  Ala Phe Ile Leu Asp  Ser Ala Glu
    2615                 2620                 2625

Thr Thr  Thr Leu Phe Gln Phe  Asn Glu Met Lys Lys  Tyr Ile Ala
    2630                 2635                 2640

Tyr Leu  Val Arg Gln Leu Asp  Met Ser Pro Asp Pro  Lys Ala Ser
    2645                 2650                 2655

Gln His  Phe Ala Arg Val Ala  Val Val Gln His Ala  Pro Ser Glu
    2660                 2665                 2670

Ser Val  Asp Asn Ala Ser Met  Pro Pro Val Lys Val  Glu Phe Ser
    2675                 2680                 2685

Leu Thr  Asp Tyr Gly Ser Lys  Glu Lys Leu Val Asp  Phe Leu Ser
    2690                 2695                 2700

Arg Gly  Met Thr Gln Leu Gln  Gly Thr Arg Ala Leu  Gly Ser Ala
    2705                 2710                 2715

Ile Glu  Tyr Thr Ile Glu Asn  Val Phe Glu Ser Ala  Pro Asn Pro
    2720                 2725                 2730

Arg Asp  Leu Lys Ile Val Val  Leu Met Leu Thr Gly  Glu Val Pro
    2735                 2740                 2745

Glu Gln  Gln Leu Glu Glu Ala  Gln Arg Val Ile Leu  Gln Ala Lys
    2750                 2755                 2760
```

```
Cys Lys  Gly Tyr Phe Phe Val  Val Leu Gly Ile Gly  Arg Lys Val
    2765                 2770                 2775

Asn Ile  Lys Glu Val Tyr Thr  Phe Ala Ser Glu Pro  Asn Asp Val
    2780                 2785                 2790

Phe Phe  Lys Leu Val Asp Lys  Ser Thr Glu Leu Asn  Glu Glu Pro
    2795                 2800                 2805

Leu Met  Arg Phe Gly Arg Leu  Leu Pro Ser Phe Val  Ser Ser Glu
    2810                 2815                 2820

Asn Ala  Phe Tyr Leu Ser Pro  Asp Ile Arg Lys Gln  Cys Asp Trp
    2825                 2830                 2835

Phe Gln  Gly Asp Gln Pro Thr  Lys Asn Leu Val Lys  Phe Gly His
    2840                 2845                 2850

Lys Gln  Val Asn Val Pro Asn  Asn Val Thr Ser Ser  Pro Thr Ser
    2855                 2860                 2865

Asn Pro  Val Thr Thr Thr Lys  Pro Val Thr Thr Thr  Lys Pro Val
    2870                 2875                 2880

Thr Thr  Thr Thr Lys Pro Val  Thr Thr Thr Thr Lys  Pro Val Thr
    2885                 2890                 2895

Ile Ile  Asn Gln Pro Ser Val  Lys Pro Ala Ala Ala  Lys Pro Ala
    2900                 2905                 2910

Pro Ala  Lys Pro Val Ala Ala  Lys Pro Val Ala Thr  Lys Met Ala
    2915                 2920                 2925

Thr Val  Arg Pro Pro Val Ala  Val Lys Pro Ala Thr  Ala Ala Lys
    2930                 2935                 2940

Pro Val  Ala Ala Lys Pro Ala  Ala Val Arg Pro Pro  Ala Ala Ala
    2945                 2950                 2955

Ala Ala  Lys Pro Val Ala Thr  Lys Pro Glu Val Pro  Arg Pro Gln
    2960                 2965                 2970

Ala Ala  Lys Pro Ala Ala Thr  Lys Pro Ala Thr Thr  Lys Pro Met
    2975                 2980                 2985

Val Lys  Met Ser Arg Glu Val  Gln Val Phe Glu Ile  Thr Glu Asn
    2990                 2995                 3000

Ser Ala  Lys Leu His Trp Glu  Arg Ala Glu Pro Pro  Gly Pro Tyr
    3005                 3010                 3015
```

```
Phe Tyr  Asp Leu Thr Val Thr  Ser Ala His Asp Gln  Ser Leu Val
    3020                 3025                 3030


Leu Lys  Gln Asn Leu Thr Val  Thr Asp Arg Val Ile  Gly Gly Leu
    3035                 3040                 3045


Leu Ala  Gly Gln Thr Tyr His  Val Ala Val Val Cys  Tyr Leu Arg
    3050                 3055                 3060


Ser Gln  Val Arg Ala Thr Tyr  His Gly Ser Phe Ser  Thr Lys Lys
    3065                 3070                 3075


Ser Gln  Pro Pro Pro Pro Gln  Pro Ala Arg Ser Ala  Ser Ser Ser
    3080                 3085                 3090


Thr Ile  Asn Leu Met Val Ser  Thr Glu Pro Leu Ala  Leu Thr Glu
    3095                 3100                 3105


Thr Asp  Ile Cys Lys Leu Pro  Lys Asp Glu Gly Thr  Cys Arg Asp
    3110                 3115                 3120


Phe Ile  Leu Lys Trp Tyr Tyr  Asp Pro Asn Thr Lys  Ser Cys Ala
    3125                 3130                 3135


Arg Phe  Trp Tyr Gly Gly Cys  Gly Gly Asn Glu Asn  Lys Phe Gly
    3140                 3145                 3150


Ser Gln  Lys Glu Cys Glu Lys  Val Cys Ala Pro Val  Leu Ala Lys
    3155                 3160                 3165


Pro Gly  Val Ile Ser Val Met  Gly Thr
    3170                 3175


<210>  78
<211>  2944
<212>  PRT
<213>  Homo sapiens

<400>  78

Met Thr Leu Arg Leu Leu Val Ala Ala Leu Cys Ala Gly Ile Leu Ala
1               5                  10                  15


Glu Ala Pro Arg Val Arg Ala Gln His Arg Glu Arg Val Thr Cys Thr
            20                  25                  30


Arg Leu Tyr Ala Ala Asp Ile Val Phe Leu Leu Asp Gly Ser Ser Ser
        35                  40                  45


Ile Gly Arg Ser Asn Phe Arg Glu Val Arg Ser Phe Leu Glu Gly Leu
    50                  55                  60
```

```
Val Leu Pro Phe Ser Gly Ala Ala Ser Ala Gln Gly Val Arg Phe Ala
65                  70                  75                  80

Thr Val Gln Tyr Ser Asp Asp Pro Arg Thr Glu Phe Gly Leu Asp Ala
                85                  90                  95

Leu Gly Ser Gly Gly Asp Val Ile Arg Ala Ile Arg Glu Leu Ser Tyr
            100                 105                 110

Lys Gly Gly Asn Thr Arg Thr Gly Ala Ala Ile Leu His Val Ala Asp
        115                 120                 125

His Val Phe Leu Pro Gln Leu Ala Arg Pro Gly Val Pro Lys Val Cys
    130                 135                 140

Ile Leu Ile Thr Asp Gly Lys Ser Gln Asp Leu Val Asp Thr Ala Ala
145                 150                 155                 160

Gln Arg Leu Lys Gly Gln Gly Val Lys Leu Phe Ala Val Gly Ile Lys
                165                 170                 175

Asn Ala Asp Pro Glu Glu Leu Lys Arg Val Ala Ser Gln Pro Thr Ser
            180                 185                 190

Asp Phe Phe Phe Phe Val Asn Asp Phe Ser Ile Leu Arg Thr Leu Leu
        195                 200                 205

Pro Leu Val Ser Arg Arg Val Cys Thr Thr Ala Gly Gly Val Pro Val
    210                 215                 220

Thr Arg Pro Pro Asp Asp Ser Thr Ser Ala Pro Arg Asp Leu Val Leu
225                 230                 235                 240

Ser Glu Pro Ser Ser Gln Ser Leu Arg Val Gln Trp Thr Ala Ala Ser
                245                 250                 255

Gly Pro Val Thr Gly Tyr Lys Val Gln Tyr Thr Pro Leu Thr Gly Leu
            260                 265                 270

Gly Gln Pro Leu Pro Ser Glu Arg Gln Glu Val Asn Val Pro Ala Gly
        275                 280                 285

Glu Thr Ser Val Arg Leu Arg Gly Leu Arg Pro Leu Thr Glu Tyr Gln
    290                 295                 300

Val Thr Val Ile Ala Leu Tyr Ala Asn Ser Ile Gly Glu Ala Val Ser
305                 310                 315                 320

Gly Thr Ala Arg Thr Thr Ala Leu Glu Gly Pro Glu Leu Thr Ile Gln
                325                 330                 335
```

```
Asn Thr Thr Ala His Ser Leu Leu Val Ala Trp Arg Ser Val Pro Gly
            340                 345                 350

Ala Thr Gly Tyr Arg Val Thr Trp Arg Val Leu Ser Gly Gly Pro Thr
        355                 360                 365

Gln Gln Gln Glu Leu Gly Pro Gly Gln Gly Ser Val Leu Leu Arg Asp
    370                 375                 380

Leu Glu Pro Gly Thr Asp Tyr Glu Val Thr Val Ser Thr Leu Phe Gly
385                 390                 395                 400

Arg Ser Val Gly Pro Ala Thr Ser Leu Met Ala Arg Thr Asp Ala Ser
                405                 410                 415

Val Glu Gln Thr Leu Arg Pro Val Ile Leu Gly Pro Thr Ser Ile Leu
            420                 425                 430

Leu Ser Trp Asn Leu Val Pro Glu Ala Arg Gly Tyr Arg Leu Glu Trp
        435                 440                 445

Arg Arg Glu Thr Gly Leu Glu Pro Pro Gln Lys Val Val Leu Pro Ser
    450                 455                 460

Asp Val Thr Arg Tyr Gln Leu Asp Gly Leu Gln Pro Gly Thr Glu Tyr
465                 470                 475                 480

Arg Leu Thr Leu Tyr Thr Leu Leu Glu Gly His Glu Val Ala Thr Pro
                485                 490                 495

Ala Thr Val Val Pro Thr Gly Pro Glu Leu Pro Val Ser Pro Val Thr
            500                 505                 510

Asp Leu Gln Ala Thr Glu Leu Pro Gly Gln Arg Val Arg Val Ser Trp
        515                 520                 525

Ser Pro Val Pro Gly Ala Thr Gln Tyr Arg Ile Ile Val Arg Ser Thr
    530                 535                 540

Gln Gly Val Glu Arg Thr Leu Val Leu Pro Gly Ser Gln Thr Ala Phe
545                 550                 555                 560

Asp Leu Asp Asp Val Gln Ala Gly Leu Ser Tyr Thr Val Arg Val Ser
                565                 570                 575

Ala Arg Val Gly Pro Arg Glu Gly Ser Ala Ser Val Leu Thr Val Arg
            580                 585                 590

Arg Glu Pro Glu Thr Pro Leu Ala Val Pro Gly Leu Arg Val Val Val
        595                 600                 605
```

```
Ser Asp Ala Thr Arg Val Arg Val Ala Trp Gly Pro Val Pro Gly Ala
    610                 615                 620

Ser Gly Phe Arg Ile Ser Trp Ser Thr Gly Ser Gly Pro Glu Ser Ser
625                 630                 635                 640

Gln Thr Leu Pro Pro Asp Ser Thr Ala Thr Asp Ile Thr Gly Leu Gln
                645                 650                 655

Pro Gly Thr Thr Tyr Gln Val Ala Val Ser Val Leu Arg Gly Arg Glu
            660                 665                 670

Glu Gly Pro Ala Ala Val Ile Val Ala Arg Thr Asp Pro Leu Gly Pro
        675                 680                 685

Val Arg Thr Val His Val Thr Gln Ala Ser Ser Ser Ser Val Thr Ile
    690                 695                 700

Thr Trp Thr Arg Val Pro Gly Ala Thr Gly Tyr Arg Val Ser Trp His
705                 710                 715                 720

Ser Ala His Gly Pro Glu Lys Ser Gln Leu Val Ser Gly Glu Ala Thr
                725                 730                 735

Val Ala Glu Leu Asp Gly Leu Glu Pro Asp Thr Glu Tyr Thr Val His
            740                 745                 750

Val Arg Ala His Val Ala Gly Val Asp Gly Pro Pro Ala Ser Val Val
        755                 760                 765

Val Arg Thr Ala Pro Glu Pro Val Gly Arg Val Ser Arg Leu Gln Ile
    770                 775                 780

Leu Asn Ala Ser Ser Asp Val Leu Arg Ile Thr Trp Val Gly Val Thr
785                 790                 795                 800

Gly Ala Thr Ala Tyr Arg Leu Ala Trp Gly Arg Ser Glu Gly Gly Pro
                805                 810                 815

Met Arg His Gln Ile Leu Pro Gly Asn Thr Asp Ser Ala Glu Ile Arg
            820                 825                 830

Gly Leu Glu Gly Gly Val Ser Tyr Ser Val Arg Val Thr Ala Leu Val
        835                 840                 845

Gly Asp Arg Glu Gly Thr Pro Val Ser Ile Val Val Thr Thr Pro Pro
    850                 855                 860

Glu Ala Pro Pro Ala Leu Gly Thr Leu His Val Val Gln Arg Gly Glu
865                 870                 875                 880
```

```
His Ser Leu Arg Leu Arg Trp Glu Pro Val Pro Arg Ala Gln Gly Phe
                885                 890                 895

Leu Leu His Trp Gln Pro Glu Gly Gly Gln Glu Gln Ser Arg Val Leu
            900                 905                 910

Gly Pro Glu Leu Ser Ser Tyr His Leu Asp Gly Leu Glu Pro Ala Thr
        915                 920                 925

Gln Tyr Arg Val Arg Leu Ser Val Leu Gly Pro Ala Gly Glu Gly Pro
    930                 935                 940

Ser Ala Glu Val Thr Ala Arg Thr Glu Ser Pro Arg Val Pro Ser Ile
945                 950                 955                 960

Glu Leu Arg Val Val Asp Thr Ser Ile Asp Ser Val Thr Leu Ala Trp
                965                 970                 975

Thr Pro Val Ser Arg Ala Ser Ser Tyr Ile Leu Ser Trp Arg Pro Leu
            980                 985                 990

Arg Gly Pro Gly Gln Glu Val Pro  Gly Ser Pro Gln Thr  Leu Pro Gly
        995                 1000                1005

Ile Ser  Ser Ser Gln Arg Val  Thr Gly Leu Glu Pro  Gly Val Ser
    1010                1015                1020

Tyr Ile  Phe Ser Leu Thr Pro  Val Leu Asp Gly Val  Arg Gly Pro
    1025                1030                1035

Glu Ala  Ser Val Thr Gln Thr  Pro Val Cys Pro Arg  Gly Leu Ala
    1040                1045                1050

Asp Val  Val Phe Leu Pro His  Ala Thr Gln Asp Asn  Ala His Arg
    1055                1060                1065

Ala Glu  Ala Thr Arg Arg Val  Leu Glu Arg Leu Val  Leu Ala Leu
    1070                1075                1080

Gly Pro  Leu Gly Pro Gln Ala  Val Gln Val Gly Leu  Leu Ser Tyr
    1085                1090                1095

Ser His  Arg Pro Ser Pro Leu  Phe Pro Leu Asn Gly  Ser His Asp
    1100                1105                1110

Leu Gly  Ile Ile Leu Gln Arg  Ile Arg Asp Met Pro  Tyr Met Asp
    1115                1120                1125

Pro Ser  Gly Asn Asn Leu Gly  Thr Ala Val Val Thr  Ala His Arg
    1130                1135                1140
```

```
Tyr Met  Leu Ala Pro Asp Ala  Pro Gly Arg Arg Gln  His Val Pro
    1145                1150                1155

Gly Val  Met Val Leu Leu Val  Asp Glu Pro Leu Arg  Gly Asp Ile
    1160                1165                1170

Phe Ser  Pro Ile Arg Glu Ala  Gln Ala Ser Gly Leu  Asn Val Val
    1175                1180                1185

Met Leu  Gly Met Ala Gly Ala  Asp Pro Glu Gln Leu  Arg Arg Leu
    1190                1195                1200

Ala Pro  Gly Met Asp Ser Val  Gln Thr Phe Phe Ala  Val Asp Asp
    1205                1210                1215

Gly Pro  Ser Leu Asp Gln Ala  Val Ser Gly Leu Ala  Thr Ala Leu
    1220                1225                1230

Cys Gln  Ala Ser Phe Thr Thr  Gln Pro Arg Pro Glu  Pro Cys Pro
    1235                1240                1245

Val Tyr  Cys Pro Lys Gly Gln  Lys Gly Glu Pro Gly  Glu Met Gly
    1250                1255                1260

Leu Arg  Gly Gln Val Gly Pro  Pro Gly Asp Pro Gly  Leu Pro Gly
    1265                1270                1275

Arg Thr  Gly Ala Pro Gly Pro  Gln Gly Pro Pro Gly  Ser Ala Thr
    1280                1285                1290

Ala Lys  Gly Glu Arg Gly Phe  Pro Gly Ala Asp Gly  Arg Pro Gly
    1295                1300                1305

Ser Pro  Gly Arg Ala Gly Asn  Pro Gly Thr Pro Gly  Ala Pro Gly
    1310                1315                1320

Leu Lys  Gly Ser Pro Gly Leu  Pro Gly Pro Arg Gly  Asp Pro Gly
    1325                1330                1335

Glu Arg  Gly Pro Arg Gly Pro  Lys Gly Glu Pro Gly  Ala Pro Gly
    1340                1345                1350

Gln Val  Ile Gly Gly Glu Gly  Pro Gly Leu Pro Gly  Arg Lys Gly
    1355                1360                1365

Asp Pro  Gly Pro Ser Gly Pro  Pro Gly Pro Arg Gly  Pro Leu Gly
    1370                1375                1380

Asp Pro  Gly Pro Arg Gly Pro  Pro Gly Leu Pro Gly  Thr Ala Met
    1385                1390                1395
```

```
Lys Gly  Asp Lys Gly Asp Arg  Gly Glu Arg Gly Pro  Pro Gly Pro
    1400                 1405                 1410

Gly Glu  Gly Gly Ile Ala Pro  Gly Glu Pro Gly Leu  Pro Gly Leu
    1415                 1420                 1425

Pro Gly  Ser Pro Gly Pro Gln  Gly Pro Val Gly Pro  Pro Gly Lys
    1430                 1435                 1440

Lys Gly  Glu Lys Gly Asp Ser  Glu Asp Gly Ala Pro  Gly Leu Pro
    1445                 1450                 1455

Gly Gln  Pro Gly Ser Pro Gly  Glu Gln Gly Pro Arg  Gly Pro Pro
    1460                 1465                 1470

Gly Ala  Ile Gly Pro Lys Gly  Asp Arg Gly Phe Pro  Gly Pro Leu
    1475                 1480                 1485

Gly Glu  Ala Gly Glu Lys Gly  Glu Arg Gly Pro Pro  Gly Pro Ala
    1490                 1495                 1500

Gly Ser  Arg Gly Leu Pro Gly  Val Ala Gly Arg Pro  Gly Ala Lys
    1505                 1510                 1515

Gly Pro  Glu Gly Pro Pro Gly  Pro Thr Gly Arg Gln  Gly Glu Lys
    1520                 1525                 1530

Gly Glu  Pro Gly Arg Pro Gly  Asp Pro Ala Val Val  Gly Pro Ala
    1535                 1540                 1545

Val Ala  Gly Pro Lys Gly Glu  Lys Gly Asp Val Gly  Pro Ala Gly
    1550                 1555                 1560

Pro Arg  Gly Ala Thr Gly Val  Gln Gly Glu Arg Gly  Pro Pro Gly
    1565                 1570                 1575

Leu Val  Leu Pro Gly Asp Pro  Gly Pro Lys Gly Asp  Pro Gly Asp
    1580                 1585                 1590

Arg Gly  Pro Ile Gly Leu Thr  Gly Arg Ala Gly Pro  Pro Gly Asp
    1595                 1600                 1605

Ser Gly  Pro Pro Gly Glu Lys  Gly Asp Pro Gly Arg  Pro Gly Pro
    1610                 1615                 1620

Pro Gly  Pro Val Gly Pro Arg  Gly Arg Asp Gly Glu  Val Gly Glu
    1625                 1630                 1635

Lys Gly  Asp Glu Gly Pro Pro  Gly Asp Pro Gly Leu  Pro Gly Lys
    1640                 1645                 1650
```

```
Ala Gly  Glu Arg Gly Leu Arg  Gly Ala Pro Gly Val  Arg Gly Pro
    1655                1660                1665

Val Gly  Glu Lys Gly Asp Gln  Gly Asp Pro Gly Glu  Asp Gly Arg
    1670                1675                1680

Asn Gly  Ser Pro Gly Ser Ser  Gly Pro Lys Gly Asp  Arg Gly Glu
    1685                1690                1695

Pro Gly  Pro Pro Gly Pro Pro  Gly Arg Leu Val Asp  Thr Gly Pro
    1700                1705                1710

Gly Ala  Arg Glu Lys Gly Glu  Pro Gly Asp Arg Gly  Gln Glu Gly
    1715                1720                1725

Pro Arg  Gly Pro Lys Gly Asp  Pro Gly Leu Pro Gly  Ala Pro Gly
    1730                1735                1740

Glu Arg  Gly Ile Glu Gly Phe  Arg Gly Pro Pro Gly  Pro Gln Gly
    1745                1750                1755

Asp Pro  Gly Val Arg Gly Pro  Ala Gly Glu Lys Gly  Asp Arg Gly
    1760                1765                1770

Pro Pro  Gly Leu Asp Gly Arg  Ser Gly Leu Asp Gly  Lys Pro Gly
    1775                1780                1785

Ala Ala  Gly Pro Ser Gly Pro  Asn Gly Ala Ala Gly  Lys Ala Gly
    1790                1795                1800

Asp Pro  Gly Arg Asp Gly Leu  Pro Gly Leu Arg Gly  Glu Gln Gly
    1805                1810                1815

Leu Pro  Gly Pro Ser Gly Pro  Pro Gly Leu Pro Gly  Lys Pro Gly
    1820                1825                1830

Glu Asp  Gly Lys Pro Gly Leu  Asn Gly Lys Asn Gly  Glu Pro Gly
    1835                1840                1845

Asp Pro  Gly Glu Asp Gly Arg  Lys Gly Glu Lys Gly  Asp Ser Gly
    1850                1855                1860

Ala Ser  Gly Arg Glu Gly Arg  Asp Gly Pro Lys Gly  Glu Arg Gly
    1865                1870                1875

Ala Pro  Gly Ile Leu Gly Pro  Gln Gly Pro Pro Gly  Leu Pro Gly
    1880                1885                1890

Pro Val  Gly Pro Pro Gly Gln  Gly Phe Pro Gly Val  Pro Gly Gly
    1895                1900                1905
```

```
Thr Gly  Pro Lys Gly Asp Arg  Gly Glu Thr Gly Ser  Lys Gly Glu
    1910                 1915                 1920

Gln Gly  Leu Pro Gly Glu Arg  Gly Leu Arg Gly Glu  Pro Gly Ser
    1925                 1930                 1935

Val Pro  Asn Val Asp Arg Leu  Leu Glu Thr Ala Gly  Ile Lys Ala
    1940                 1945                 1950

Ser Ala  Leu Arg Glu Ile Val  Glu Thr Trp Asp Glu  Ser Ser Gly
    1955                 1960                 1965

Ser Phe  Leu Pro Val Pro Glu  Arg Arg Arg Gly Pro  Lys Gly Asp
    1970                 1975                 1980

Ser Gly  Glu Gln Gly Pro Pro  Gly Lys Glu Gly Pro  Ile Gly Phe
    1985                 1990                 1995

Pro Gly  Glu Arg Gly Leu Lys  Gly Asp Arg Gly Asp  Pro Gly Pro
    2000                 2005                 2010

Gln Gly  Pro Pro Gly Leu Ala  Leu Gly Glu Arg Gly  Pro Pro Gly
    2015                 2020                 2025

Pro Ser  Gly Leu Ala Gly Glu  Pro Gly Lys Pro Gly  Ile Pro Gly
    2030                 2035                 2040

Leu Pro  Gly Arg Ala Gly Gly  Val Gly Glu Ala Gly  Arg Pro Gly
    2045                 2050                 2055

Glu Arg  Gly Glu Arg Gly Glu  Lys Gly Glu Arg Gly  Glu Gln Gly
    2060                 2065                 2070

Arg Asp  Gly Pro Pro Gly Leu  Pro Gly Thr Pro Gly  Pro Pro Gly
    2075                 2080                 2085

Pro Pro  Gly Pro Lys Val Ser  Val Asp Glu Pro Gly  Pro Gly Leu
    2090                 2095                 2100

Ser Gly  Glu Gln Gly Pro Pro  Gly Leu Lys Gly Ala  Lys Gly Glu
    2105                 2110                 2115

Pro Gly  Ser Asn Gly Asp Gln  Gly Pro Lys Gly Asp  Arg Gly Val
    2120                 2125                 2130

Pro Gly  Ile Lys Gly Asp Arg  Gly Glu Pro Gly Pro  Arg Gly Gln
    2135                 2140                 2145

Asp Gly  Asn Pro Gly Leu Pro  Gly Glu Arg Gly Met  Ala Gly Pro
    2150                 2155                 2160
```

```
Glu Gly  Lys Pro Gly Leu Gln  Gly Pro Arg Gly Pro  Pro Gly Pro
    2165                 2170                 2175

Val Gly  Gly His Gly Asp Pro  Gly Pro Pro Gly Ala  Pro Gly Leu
    2180                 2185                 2190

Ala Gly  Pro Ala Gly Pro Gln  Gly Pro Ser Gly Leu  Lys Gly Glu
    2195                 2200                 2205

Pro Gly  Glu Thr Gly Pro Pro  Gly Arg Gly Leu Thr  Gly Pro Thr
    2210                 2215                 2220

Gly Ala  Val Gly Leu Pro Gly  Pro Pro Gly Pro Ser  Gly Leu Val
    2225                 2230                 2235

Gly Pro  Gln Gly Ser Pro Gly  Leu Pro Gly Gln Val  Gly Glu Thr
    2240                 2245                 2250

Gly Lys  Pro Gly Ala Pro Gly  Arg Asp Gly Ala Ser  Gly Lys Asp
    2255                 2260                 2265

Gly Asp  Arg Gly Ser Pro Gly  Val Pro Gly Ser Pro  Gly Leu Pro
    2270                 2275                 2280

Gly Pro  Val Gly Pro Lys Gly  Glu Pro Gly Pro Thr  Gly Ala Pro
    2285                 2290                 2295

Gly Gln  Ala Val Val Gly Leu  Pro Gly Ala Lys Gly  Glu Lys Gly
    2300                 2305                 2310

Ala Pro  Gly Gly Leu Ala Gly  Asp Leu Val Gly Glu  Pro Gly Ala
    2315                 2320                 2325

Lys Gly  Asp Arg Gly Leu Pro  Gly Pro Arg Gly Glu  Lys Gly Glu
    2330                 2335                 2340

Ala Gly  Arg Ala Gly Glu Pro  Gly Asp Pro Gly Glu  Asp Gly Gln
    2345                 2350                 2355

Lys Gly  Ala Pro Gly Pro Lys  Gly Phe Lys Gly Asp  Pro Gly Val
    2360                 2365                 2370

Gly Val  Pro Gly Ser Pro Gly  Pro Pro Gly Pro Pro  Gly Val Lys
    2375                 2380                 2385

Gly Asp  Leu Gly Leu Pro Gly  Leu Pro Gly Ala Pro  Gly Val Val
    2390                 2395                 2400

Gly Phe  Pro Gly Gln Thr Gly  Pro Arg Gly Glu Met  Gly Gln Pro
    2405                 2410                 2415
```

```
Gly Pro  Ser Gly Glu Arg Gly  Leu Ala Gly Pro Pro  Gly Arg Glu
    2420                 2425                 2430

Gly Ile  Pro Gly Pro Leu Gly  Pro Pro Gly Pro Pro  Gly Ser Val
    2435                 2440                 2445

Gly Pro  Pro Gly Ala Ser Gly  Leu Lys Gly Asp Lys  Gly Asp Pro
    2450                 2455                 2460

Gly Val  Gly Leu Pro Gly Pro  Arg Gly Glu Arg Gly  Glu Pro Gly
    2465                 2470                 2475

Ile Arg  Gly Glu Asp Gly Arg  Pro Gly Gln Glu Gly  Pro Arg Gly
    2480                 2485                 2490

Leu Thr  Gly Pro Pro Gly Ser  Arg Gly Glu Arg Gly  Glu Lys Gly
    2495                 2500                 2505

Asp Val  Gly Ser Ala Gly Leu  Lys Gly Asp Lys Gly  Asp Ser Ala
    2510                 2515                 2520

Val Ile  Leu Gly Pro Pro Gly  Pro Arg Gly Ala Lys  Gly Asp Met
    2525                 2530                 2535

Gly Glu  Arg Gly Pro Arg Gly  Leu Asp Gly Asp Lys  Gly Pro Arg
    2540                 2545                 2550

Gly Asp  Asn Gly Asp Pro Gly  Asp Lys Gly Ser Lys  Gly Glu Pro
    2555                 2560                 2565

Gly Asp  Lys Gly Ser Ala Gly  Leu Pro Gly Leu Arg  Gly Leu Leu
    2570                 2575                 2580

Gly Pro  Gln Gly Gln Pro Gly  Ala Ala Gly Ile Pro  Gly Asp Pro
    2585                 2590                 2595

Gly Ser  Pro Gly Lys Asp Gly  Val Pro Gly Ile Arg  Gly Glu Lys
    2600                 2605                 2610

Gly Asp  Val Gly Phe Met Gly  Pro Arg Gly Leu Lys  Gly Glu Arg
    2615                 2620                 2625

Gly Val  Lys Gly Ala Cys Gly  Leu Asp Gly Glu Lys  Gly Asp Lys
    2630                 2635                 2640

Gly Glu  Ala Gly Pro Pro Gly  Arg Pro Gly Leu Ala  Gly His Lys
    2645                 2650                 2655

Gly Glu  Met Gly Glu Pro Gly  Val Pro Gly Gln Ser  Gly Ala Pro
    2660                 2665                 2670
```

```
Gly Lys  Glu Gly Leu Ile Gly  Pro Lys Gly Asp Arg  Gly Phe Asp
    2675                2680                2685

Gly Gln  Pro Gly Pro Lys Gly  Asp Gln Gly Glu Lys  Gly Glu Arg
    2690                2695                2700

Gly Thr  Pro Gly Ile Gly Gly  Phe Pro Gly Pro Ser  Gly Asn Asp
    2705                2710                2715

Gly Ser  Ala Gly Pro Pro Gly  Pro Pro Gly Ser Val  Gly Pro Arg
    2720                2725                2730

Gly Pro  Glu Gly Leu Gln Gly  Gln Lys Gly Glu Arg  Gly Pro Pro
    2735                2740                2745

Gly Glu  Arg Val Val Gly Ala  Pro Gly Val Pro Gly  Ala Pro Gly
    2750                2755                2760

Glu Arg  Gly Glu Gln Gly Arg  Pro Gly Pro Ala Gly  Pro Arg Gly
    2765                2770                2775

Glu Lys  Gly Glu Ala Ala Leu  Thr Glu Asp Asp Ile  Arg Gly Phe
    2780                2785                2790

Val Arg  Gln Glu Met Ser Gln  His Cys Ala Cys Gln  Gly Gln Phe
    2795                2800                2805

Ile Ala  Ser Gly Ser Arg Pro  Leu Pro Ser Tyr Ala  Ala Asp Thr
    2810                2815                2820

Ala Gly  Ser Gln Leu His Ala  Val Pro Val Leu Arg  Val Ser His
    2825                2830                2835

Ala Glu  Glu Glu Glu Arg Val  Pro Pro Glu Asp Asp  Glu Tyr Ser
    2840                2845                2850

Glu Tyr  Ser Glu Tyr Ser Val  Glu Glu Tyr Gln Asp  Pro Glu Ala
    2855                2860                2865

Pro Trp  Asp Ser Asp Asp Pro  Cys Ser Leu Pro Leu  Asp Glu Gly
    2870                2875                2880

Ser Cys  Thr Ala Tyr Thr Leu  Arg Trp Tyr His Arg  Ala Val Thr
    2885                2890                2895

Gly Ser  Thr Glu Ala Cys His  Pro Phe Val Tyr Gly  Gly Cys Gly
    2900                2905                2910

Gly Asn  Ala Asn Arg Phe Gly  Thr Arg Glu Ala Cys  Glu Arg Arg
    2915                2920                2925
```

Cys Pro Pro Arg Val Val Gln Ser Gln Gly Thr Gly Thr Ala Gln
2930 2935 2940

Asp

<210> 79
<211> 724
<212> PRT
<213> Homo sapiens

<400> 79

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1 5 10 15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
20 25 30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
35 40 45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
50 55 60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65 70 75 80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
85 90 95

Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
100 105 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Gly Ala Val
115 120 125

Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val
130 135 140

Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe
145 150 155 160

Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys
165 170 175

Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val
180 185 190

Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile
195 200 205

Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu Pro Tyr Thr Thr Gly

```
    210                 215                 220

Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly
225                 230                 235                 240

Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala
                245                 250                 255

Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly
            260                 265                 270

Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala
        275                 280                 285

Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala
    290                 295                 300

Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala
305                 310                 315                 320

Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val
                325                 330                 335

Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro
            340                 345                 350

Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val
        355                 360                 365

Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly
    370                 375                 380

Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly
385                 390                 395                 400

Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly Gly Ile Pro Gly
                405                 410                 415

Val Ala Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly Gly Val
            420                 425                 430

Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala Ala Ala Ala Ala Lys
        435                 440                 445

Ala Ala Lys Tyr Gly Val Gly Thr Pro Ala Ala Ala Ala Ala Lys Ala
    450                 455                 460

Ala Ala Lys Ala Ala Gln Phe Gly Leu Val Pro Gly Val Gly Val Ala
465                 470                 475                 480

Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly
```

485 490 495

Leu Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly
500 505 510

Val Gly Val Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Ala Ala Ala
515 520 525

Lys Ser Ala Ala Lys Val Ala Ala Lys Ala Gln Leu Arg Ala Ala Ala
530 535 540

Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly Val Pro
545 550 555 560

Gly Leu Gly Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly Ala Gly
565 570 575

Val Pro Gly Phe Gly Ala Val Pro Gly Ala Leu Ala Ala Ala Lys Ala
580 585 590

Ala Lys Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu Gly Ala
595 600 605

Leu Gly Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly Pro Ala
610 615 620

Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly
625 630 635 640

Leu Val Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly Leu Gly
645 650 655

Val Pro Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala Ala Ala
660 665 670

Lys Ala Ala Lys Tyr Gly Ala Ala Gly Leu Gly Gly Val Leu Gly Gly
675 680 685

Ala Gly Gln Phe Pro Leu Gly Gly Val Ala Ala Arg Pro Gly Phe Gly
690 695 700

Leu Ser Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly
705 710 715 720

Arg Lys Arg Lys

<210> 80
<211> 677
<212> PRT
<213> Homo sapiens

<400> 80

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1 5 10 15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
20 25 30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Ala Leu Gly Pro
35 40 45

Gly Gly Lys Pro Leu Lys Pro Val Pro Gly Gly Leu Ala Gly Ala Gly
50 55 60

Leu Gly Ala Gly Leu Gly Ala Phe Pro Ala Val Thr Phe Pro Gly Ala
65 70 75 80

Leu Val Pro Gly Gly Val Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala
85 90 95

Lys Ala Gly Ala Gly Leu Gly Gly Val Pro Gly Val Gly Gly Leu Gly
100 105 110

Val Ser Ala Gly Ala Val Val Pro Gln Pro Gly Ala Gly Val Lys Pro
115 120 125

Gly Lys Val Pro Gly Val Gly Leu Pro Gly Val Tyr Pro Gly Gly Val
130 135 140

Leu Pro Gly Ala Arg Phe Pro Gly Val Gly Val Leu Pro Gly Val Pro
145 150 155 160

Thr Gly Ala Gly Val Lys Pro Lys Ala Pro Gly Val Gly Gly Ala Phe
165 170 175

Ala Gly Ile Pro Gly Val Gly Pro Phe Gly Gly Pro Gln Pro Gly Val
180 185 190

Pro Leu Gly Tyr Pro Ile Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly
195 200 205

Leu Pro Tyr Thr Thr Gly Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly
210 215 220

Val Ala Gly Ala Ala Gly Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val
225 230 235 240

Gly Pro Gln Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe
245 250 255

Gly Ala Gly Ala Ala Gly Val Leu Pro Gly Val Gly Gly Ala Gly Val
260 265 270

```
Pro Gly Val Pro Gly Ala Ile Pro Gly Ile Gly Gly Ile Ala Gly Val
        275                 280                 285

Gly Thr Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala
    290                 295                 300

Lys Tyr Gly Ala Ala Ala Gly Leu Val Pro Gly Gly Pro Gly Phe Gly
305                 310                 315                 320

Pro Gly Val Val Gly Val Pro Gly Ala Gly Val Pro Gly Val Gly Val
                325                 330                 335

Pro Gly Ala Gly Ile Pro Val Val Pro Gly Ala Gly Ile Pro Gly Ala
            340                 345                 350

Ala Val Pro Gly Val Val Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala
        355                 360                 365

Lys Ala Ala Lys Tyr Gly Ala Arg Pro Gly Val Gly Val Gly Gly Ile
    370                 375                 380

Pro Thr Tyr Gly Val Gly Ala Gly Gly Phe Pro Gly Phe Gly Val Gly
385                 390                 395                 400

Val Gly Gly Ile Pro Gly Val Ala Gly Val Pro Gly Val Gly Gly Val
                405                 410                 415

Pro Gly Val Gly Gly Val Pro Gly Val Gly Ile Ser Pro Glu Ala Gln
            420                 425                 430

Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Leu Val Pro Gly Val
        435                 440                 445

Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro
    450                 455                 460

Gly Val Gly Leu Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val
465                 470                 475                 480

Ala Pro Gly Val Gly Val Ala Pro Gly Ile Gly Pro Gly Gly Val Ala
                485                 490                 495

Ala Ala Ala Lys Ser Ala Ala Lys Val Ala Ala Lys Ala Gln Leu Arg
            500                 505                 510

Ala Ala Ala Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly Val Gly Val
        515                 520                 525

Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly Leu Gly Val
    530                 535                 540
```

```
Gly Ala Gly Val Pro Gly Phe Gly Ala Val Pro Gly Ala Leu Ala Ala
545                 550                 555                 560

Ala Lys Ala Ala Lys Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly
                565                 570                 575

Leu Gly Ala Leu Gly Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala
            580                 585                 590

Gly Pro Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala
        595                 600                 605

Gln Phe Gly Leu Val Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly
    610                 615                 620

Gly Leu Gly Val Pro Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala
625                 630                 635                 640

Ala Ala Ala Lys Ala Ala Lys Tyr Gly Val Ala Ala Arg Pro Gly Phe
                645                 650                 655

Gly Leu Ser Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys
            660                 665                 670

Gly Arg Lys Arg Lys
        675


<210>  81
<211>  692
<212>  PRT
<213>  Homo sapiens

<400>  81

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
        35                  40                  45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
    50                  55                  60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65                  70                  75                  80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
                85                  90                  95
```

```
Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
            100                 105                 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Ala Pro Ser
        115                 120                 125

Val Pro Gly Ala Val Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly
    130                 135                 140

Lys Val Pro Gly Val Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu
145                 150                 155                 160

Pro Gly Ala Arg Phe Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr
                165                 170                 175

Gly Ala Gly Val Lys Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala
            180                 185                 190

Gly Ile Pro Gly Val Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro
        195                 200                 205

Leu Gly Tyr Pro Ile Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu
    210                 215                 220

Pro Tyr Thr Thr Gly Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val
225                 230                 235                 240

Ala Gly Ala Ala Gly Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly
                245                 250                 255

Pro Gln Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly
            260                 265                 270

Ala Gly Ala Ala Gly Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro
        275                 280                 285

Gly Val Pro Gly Ala Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly
    290                 295                 300

Thr Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys
305                 310                 315                 320

Tyr Gly Ala Ala Ala Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro
                325                 330                 335

Gly Val Val Gly Val Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro
            340                 345                 350

Gly Ala Gly Ile Pro Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala
        355                 360                 365
```

```
Val Pro Gly Val Val Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys
    370                 375                 380

Ala Ala Lys Tyr Gly Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro
385                 390                 395                 400

Thr Tyr Gly Val Gly Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val
                405                 410                 415

Gly Gly Ile Pro Gly Val Ala Gly Val Pro Gly Val Gly Gly Val Pro
            420                 425                 430

Gly Val Gly Gly Val Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala
        435                 440                 445

Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Leu Val Pro Gly Val Gly
    450                 455                 460

Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly
465                 470                 475                 480

Val Gly Leu Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala
                485                 490                 495

Pro Gly Val Gly Val Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Ala
            500                 505                 510

Ala Ala Lys Ser Ala Ala Lys Val Ala Ala Lys Ala Gln Leu Arg Ala
        515                 520                 525

Ala Ala Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly
    530                 535                 540

Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly
545                 550                 555                 560

Ala Gly Val Pro Gly Phe Gly Ala Val Pro Gly Ala Leu Ala Ala Ala
                565                 570                 575

Lys Ala Ala Lys Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu
            580                 585                 590

Gly Ala Leu Gly Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly
        595                 600                 605

Pro Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln
    610                 615                 620

Phe Gly Leu Val Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly
625                 630                 635                 640
```

```
Leu Gly Val Pro Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala
                645                 650                 655

Ala Ala Lys Ala Ala Lys Tyr Gly Val Ala Ala Arg Pro Gly Phe Gly
            660                 665                 670

Leu Ser Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly
        675                 680                 685

Arg Lys Arg Lys
    690
```

<210> 82
<211> 711
<212> PRT
<213> Homo sapiens

<400> 82

```
Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
        35                  40                  45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
    50                  55                  60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65                  70                  75                  80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
                85                  90                  95

Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
            100                 105                 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Ala Pro Ser
        115                 120                 125

Val Pro Gly Ala Val Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly
    130                 135                 140

Lys Val Pro Gly Val Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu
145                 150                 155                 160

Pro Gly Ala Arg Phe Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr
                165                 170                 175
```

```
Gly Ala Gly Val Lys Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala
            180                 185                 190

Gly Ile Pro Gly Val Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro
        195                 200                 205

Leu Gly Tyr Pro Ile Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu
    210                 215                 220

Pro Tyr Thr Thr Gly Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val
225                 230                 235                 240

Ala Gly Ala Ala Gly Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly
                245                 250                 255

Pro Gln Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly
            260                 265                 270

Ala Gly Ala Ala Gly Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro
        275                 280                 285

Gly Val Pro Gly Ala Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly
    290                 295                 300

Thr Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys
305                 310                 315                 320

Tyr Gly Ala Ala Ala Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro
                325                 330                 335

Gly Val Val Gly Val Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro
            340                 345                 350

Gly Ala Gly Ile Pro Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala
        355                 360                 365

Val Pro Gly Val Val Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys
    370                 375                 380

Ala Ala Lys Tyr Gly Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro
385                 390                 395                 400

Thr Tyr Gly Val Gly Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val
                405                 410                 415

Gly Gly Ile Pro Gly Val Ala Gly Val Pro Gly Val Gly Gly Val Pro
            420                 425                 430

Gly Val Gly Gly Val Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala
        435                 440                 445
```

```
Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Val Gly Thr Pro Ala Ala
    450                 455                 460

Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly Leu Val Pro
465                 470                 475                 480

Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val
                485                 490                 495

Ala Pro Gly Val Gly Leu Ala Pro Gly Val Gly Val Ala Pro Gly Val
            500                 505                 510

Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Ile Gly Pro Gly Gly
        515                 520                 525

Val Ala Ala Ala Ala Lys Ser Ala Ala Lys Val Ala Ala Lys Ala Gln
    530                 535                 540

Leu Arg Ala Ala Ala Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly Val
545                 550                 555                 560

Gly Val Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly Leu
                565                 570                 575

Gly Val Gly Ala Gly Val Pro Gly Phe Gly Ala Val Pro Gly Ala Leu
            580                 585                 590

Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Val Pro Gly Val Leu
        595                 600                 605

Gly Gly Leu Gly Ala Leu Gly Gly Val Gly Ile Pro Gly Gly Val Val
    610                 615                 620

Gly Ala Gly Pro Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys
625                 630                 635                 640

Ala Ala Gln Phe Gly Leu Val Gly Ala Ala Gly Leu Gly Gly Leu Gly
                645                 650                 655

Val Gly Gly Leu Gly Val Pro Gly Val Gly Gly Leu Gly Gly Ile Pro
            660                 665                 670

Pro Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Val Ala Ala Arg Pro
        675                 680                 685

Gly Phe Gly Leu Ser Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys
    690                 695                 700

Ala Cys Gly Arg Lys Arg Lys
705                 710
```

<210> 83
<211> 705
<212> PRT
<213> Homo sapiens

<400> 83

```
Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
        35                  40                  45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
    50                  55                  60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65                  70                  75                  80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
                85                  90                  95

Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
            100                 105                 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Gly Ala Val
        115                 120                 125

Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val
    130                 135                 140

Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe
145                 150                 155                 160

Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys
                165                 170                 175

Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val
            180                 185                 190

Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile
        195                 200                 205

Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu Pro Tyr Thr Thr Gly
    210                 215                 220

Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly
225                 230                 235                 240

Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala
```

245 250 255

Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly
260 265 270

Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala
275 280 285

Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala
290 295 300

Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala
305 310 315 320

Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val
325 330 335

Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro
340 345 350

Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val
355 360 365

Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly
370 375 380

Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly
385 390 395 400

Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly Gly Ile Pro Gly
405 410 415

Val Ala Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly Gly Val
420 425 430

Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala Ala Ala Ala Ala Lys
435 440 445

Ala Ala Lys Tyr Gly Leu Val Pro Gly Val Gly Val Ala Pro Gly Val
450 455 460

Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Leu Ala Pro
465 470 475 480

Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val
485 490 495

Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Ala Ala Ala Lys Ser Ala
500 505 510

Ala Lys Val Ala Ala Lys Ala Gln Leu Arg Ala Ala Ala Gly Leu Gly

515 520 525

Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly Val Pro Gly Leu Gly
530 535 540

Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly
545 550 555 560

Phe Gly Ala Val Pro Gly Ala Leu Ala Ala Ala Lys Ala Ala Lys Tyr
565 570 575

Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu Gly Ala Leu Gly Gly
580 585 590

Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly Pro Ala Ala Ala Ala
595 600 605

Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly Leu Val Gly
610 615 620

Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly Leu Gly Val Pro Gly
625 630 635 640

Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala Ala Ala Lys Ala Ala
645 650 655

Lys Tyr Gly Ala Ala Gly Leu Gly Gly Val Leu Gly Gly Ala Gly Gln
660 665 670

Phe Pro Leu Gly Gly Val Ala Ala Arg Pro Gly Phe Gly Leu Ser Pro
675 680 685

Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly Arg Lys Arg
690 695 700

Lys
705

<210> 84
<211> 706
<212> PRT
<213> Homo sapiens

<400> 84

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1 5 10 15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
20 25 30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
35 40 45

```
Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
    50                  55                  60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65                  70                  75                  80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
                85                  90                  95

Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
            100                 105                 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Gly Ala Val
        115                 120                 125

Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val
    130                 135                 140

Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe
145                 150                 155                 160

Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys
                165                 170                 175

Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val
            180                 185                 190

Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile
        195                 200                 205

Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu Pro Tyr Thr Thr Gly
    210                 215                 220

Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly
225                 230                 235                 240

Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala
                245                 250                 255

Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly
            260                 265                 270

Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala
        275                 280                 285

Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala
    290                 295                 300

Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala
305                 310                 315                 320
```

```
Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val
                325                 330                 335

Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro
            340                 345                 350

Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val
        355                 360                 365

Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly
    370                 375                 380

Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly
385                 390                 395                 400

Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly Gly Ile Pro Gly
                405                 410                 415

Val Ala Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly Gly Val
            420                 425                 430

Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala Ala Ala Ala Ala Lys
        435                 440                 445

Ala Ala Lys Tyr Gly Val Gly Thr Pro Ala Ala Ala Ala Ala Lys Ala
    450                 455                 460

Ala Ala Lys Ala Ala Gln Phe Gly Leu Val Pro Gly Val Gly Val Ala
465                 470                 475                 480

Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly
                485                 490                 495

Leu Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly
            500                 505                 510

Val Gly Val Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Ala Ala Ala
        515                 520                 525

Lys Ser Ala Ala Lys Val Ala Ala Lys Ala Gln Leu Arg Ala Ala Ala
    530                 535                 540

Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly Val Pro
545                 550                 555                 560

Gly Leu Gly Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly Ala Gly
                565                 570                 575

Val Pro Gly Phe Gly Ala Val Pro Gly Ala Leu Ala Ala Ala Lys Ala
            580                 585                 590
```

```
Ala Lys Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu Gly Ala
        595                 600                 605

Leu Gly Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly Pro Ala
    610                 615                 620

Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly
625                 630                 635                 640

Leu Val Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly Leu Gly
                645                 650                 655

Val Pro Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala Ala Ala
            660                 665                 670

Lys Ala Ala Lys Tyr Gly Val Ala Ala Arg Pro Gly Phe Gly Leu Ser
        675                 680                 685

Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly Arg Lys
    690                 695                 700

Arg Lys
705
```

<210> 85
<211> 643
<212> PRT
<213> Homo sapiens

<400> 85

```
Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
        35                  40                  45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
    50                  55                  60

Pro Gly Leu Gly Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val
65                  70                  75                  80

Pro Gly Gly Val Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala
                85                  90                  95

Gly Ala Gly Leu Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser
            100                 105                 110
```

```
Ala Gly Ala Val Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys
        115                 120                 125

Val Pro Gly Val Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro
    130                 135                 140

Gly Ala Arg Phe Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly
145                 150                 155                 160

Ala Gly Val Lys Pro Lys Ala Pro Gly Val Gly Pro Phe Gly Gly Pro
                165                 170                 175

Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile Lys Ala Pro Lys Leu Pro
            180                 185                 190

Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly Lys Ala Gly Tyr
        195                 200                 205

Pro Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala Ala Ala Ala Ala
    210                 215                 220

Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly Val Leu Pro Gly
225                 230                 235                 240

Val Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala Ile Pro Gly Ile
                245                 250                 255

Gly Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala Ala Ala Ala Ala
            260                 265                 270

Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala Gly Leu Val Pro
        275                 280                 285

Gly Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val Pro Gly Ala Gly
    290                 295                 300

Val Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro Val Val Pro Gly
305                 310                 315                 320

Ala Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val Ser Pro Glu Ala
                325                 330                 335

Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Arg Pro Gly
            340                 345                 350

Val Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly Ala Gly Gly Phe
        355                 360                 365

Pro Gly Phe Gly Val Gly Val Gly Ala Glu Ala Gln Ala Ala Ala Ala
    370                 375                 380
```

```
Ala Lys Ala Ala Lys Tyr Gly Leu Val Pro Gly Val Gly Val Ala Pro
385                 390                 395                 400

Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Leu
                405                 410                 415

Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val
            420                 425                 430

Gly Val Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Ala Ala Ala Lys
        435                 440                 445

Ser Ala Ala Lys Val Ala Ala Lys Ala Gln Leu Arg Ala Ala Ala Gly
    450                 455                 460

Leu Gly Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly Val Pro Gly
465                 470                 475                 480

Leu Gly Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val
                485                 490                 495

Pro Gly Phe Gly Ala Val Pro Gly Ala Leu Ala Ala Ala Lys Ala Ala
            500                 505                 510

Lys Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu Gly Ala Leu
        515                 520                 525

Gly Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly Pro Ala Ala
    530                 535                 540

Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly Leu
545                 550                 555                 560

Val Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly Leu Gly Val
                565                 570                 575

Pro Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala Ala Ala Lys
            580                 585                 590

Ala Ala Lys Tyr Gly Ala Ala Gly Leu Gly Gly Val Leu Gly Gly Ala
        595                 600                 605

Gly Gln Phe Pro Leu Gly Gly Val Ala Ala Arg Pro Gly Phe Gly Leu
    610                 615                 620

Ser Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly Arg
625                 630                 635                 640

Lys Arg Lys
```

<210> 86
<211> 700
<212> PRT
<213> Homo sapiens

<400> 86

```
Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Ala Leu Gly Pro
        35                  40                  45

Gly Gly Lys Pro Leu Lys Pro Val Pro Gly Gly Leu Ala Gly Ala Gly
    50                  55                  60

Leu Gly Ala Gly Leu Gly Ala Phe Pro Ala Val Thr Phe Pro Gly Ala
65                  70                  75                  80

Leu Val Pro Gly Gly Val Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala
                85                  90                  95

Lys Ala Gly Ala Gly Leu Gly Gly Val Pro Gly Val Gly Gly Leu Gly
            100                 105                 110

Val Ser Ala Ala Pro Ser Val Pro Gly Ala Val Val Pro Gln Pro Gly
        115                 120                 125

Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val Gly Leu Pro Gly Val
    130                 135                 140

Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe Pro Gly Val Gly Val
145                 150                 155                 160

Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys Pro Lys Ala Pro Gly
                165                 170                 175

Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val Gly Pro Phe Gly Gly
            180                 185                 190

Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile Lys Ala Pro Lys Leu
        195                 200                 205

Pro Gly Gly Tyr Gly Leu Pro Tyr Thr Thr Gly Lys Leu Pro Tyr Gly
    210                 215                 220

Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly Lys Ala Gly Tyr Pro
225                 230                 235                 240
```

```
Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala Ala Ala Ala Lys
                245                 250                 255

Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly Val Leu Pro Gly Val
            260                 265                 270

Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala Ile Pro Gly Ile Gly
        275                 280                 285

Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala Ala Ala Ala Ala Ala
    290                 295                 300

Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala Gly Leu Val Pro Gly
305                 310                 315                 320

Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val Pro Gly Ala Gly Val
                325                 330                 335

Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro Val Val Pro Gly Ala
            340                 345                 350

Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val Ser Pro Glu Ala Ala
        355                 360                 365

Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Arg Pro Gly Val
    370                 375                 380

Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly Ala Gly Gly Phe Pro
385                 390                 395                 400

Gly Phe Gly Val Gly Val Gly Gly Ile Pro Gly Val Ala Gly Val Pro
                405                 410                 415

Gly Val Gly Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly Ile
            420                 425                 430

Ser Pro Glu Ala Gln Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly
        435                 440                 445

Leu Val Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly
    450                 455                 460

Val Gly Val Ala Pro Gly Val Gly Leu Ala Pro Gly Val Gly Val Ala
465                 470                 475                 480

Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Ile Gly
                485                 490                 495

Pro Gly Gly Val Ala Ala Ala Ala Lys Ser Ala Ala Lys Val Ala Ala
            500                 505                 510
```

```
Lys Ala Gln Leu Arg Ala Ala Ala Gly Leu Gly Ala Gly Ile Pro Gly
        515                 520                 525

Leu Gly Val Gly Val Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val
    530                 535                 540

Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly Phe Gly Ala Val Pro
545                 550                 555                 560

Gly Ala Leu Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Val Pro
                565                 570                 575

Gly Val Leu Gly Gly Leu Gly Ala Leu Gly Gly Val Gly Ile Pro Gly
            580                 585                 590

Gly Val Val Gly Ala Gly Pro Ala Ala Ala Ala Ala Ala Ala Lys Ala
        595                 600                 605

Ala Ala Lys Ala Ala Gln Phe Gly Leu Val Gly Ala Ala Gly Leu Gly
    610                 615                 620

Gly Leu Gly Val Gly Gly Leu Gly Val Pro Gly Val Gly Gly Leu Gly
625                 630                 635                 640

Gly Ile Pro Pro Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala
                645                 650                 655

Gly Leu Gly Gly Val Leu Gly Gly Ala Gly Gln Phe Pro Leu Gly Gly
            660                 665                 670

Val Ala Ala Arg Pro Gly Phe Gly Leu Ser Pro Ile Phe Pro Gly Gly
        675                 680                 685

Ala Cys Leu Gly Lys Ala Cys Gly Arg Lys Arg Lys
    690                 695                 700


<210>  87
<211>  730
<212>  PRT
<213>  Homo sapiens

<400>  87

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
        35                  40                  45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
```

```
    50                  55                  60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65                  70                  75                  80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
                85                  90                  95

Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
            100                 105                 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Gly Ala Val
        115                 120                 125

Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val
    130                 135                 140

Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe
145                 150                 155                 160

Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys
                165                 170                 175

Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val
            180                 185                 190

Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile
        195                 200                 205

Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu Pro Tyr Thr Thr Gly
    210                 215                 220

Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly
225                 230                 235                 240

Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala
                245                 250                 255

Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly
            260                 265                 270

Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala
        275                 280                 285

Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala
    290                 295                 300

Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala
305                 310                 315                 320

Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val
```

325 330 335

Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro
340 345 350

Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val
355 360 365

Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly
370 375 380

Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly
385 390 395 400

Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly Gly Ile Pro Gly
405 410 415

Val Ala Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly Gly Val
420 425 430

Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala Ala Ala Ala Ala Lys
435 440 445

Ala Ala Lys Tyr Gly Val Gly Thr Pro Ala Ala Ala Ala Ala Lys Ala
450 455 460

Ala Ala Lys Ala Ala Gln Phe Ala Leu Leu Asn Leu Ala Gly Leu Val
465 470 475 480

Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly
485 490 495

Val Ala Pro Gly Val Gly Leu Ala Pro Gly Val Gly Val Ala Pro Gly
500 505 510

Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Ile Gly Pro Gly
515 520 525

Gly Val Ala Ala Ala Ala Lys Ser Ala Ala Lys Val Ala Ala Lys Ala
530 535 540

Gln Leu Arg Ala Ala Ala Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly
545 550 555 560

Val Gly Val Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly
565 570 575

Leu Gly Val Gly Ala Gly Val Pro Gly Phe Gly Ala Val Pro Gly Ala
580 585 590

Leu Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Val Pro Gly Val

595 600 605

Leu Gly Gly Leu Gly Ala Leu Gly Gly Val Gly Ile Pro Gly Gly Val
610 615 620

Val Gly Ala Gly Pro Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala
625 630 635 640

Lys Ala Ala Gln Phe Gly Leu Val Gly Ala Ala Gly Leu Gly Gly Leu
645 650 655

Gly Val Gly Gly Leu Gly Val Pro Gly Val Gly Gly Leu Gly Gly Ile
660 665 670

Pro Pro Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Gly Leu
675 680 685

Gly Gly Val Leu Gly Gly Ala Gly Gln Phe Pro Leu Gly Gly Val Ala
690 695 700

Ala Arg Pro Gly Phe Gly Leu Ser Pro Ile Phe Pro Gly Gly Ala Cys
705 710 715 720

Leu Gly Lys Ala Cys Gly Arg Lys Arg Lys
725 730

<210> 88
<211> 658
<212> PRT
<213> Homo sapiens

<400> 88

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1 5 10 15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
20 25 30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
35 40 45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
50 55 60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65 70 75 80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
85 90 95

Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
100 105 110

```
Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Gly Ala Val
        115                 120                 125

Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val
    130                 135                 140

Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe
145                 150                 155                 160

Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys
                165                 170                 175

Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val
            180                 185                 190

Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile
        195                 200                 205

Lys Ala Pro Lys Leu Pro Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala
    210                 215                 220

Ala Gly Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro Gln Ala
225                 230                 235                 240

Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala
                245                 250                 255

Ala Gly Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly Val Pro
            260                 265                 270

Gly Ala Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr Pro Ala
        275                 280                 285

Ala Ala Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala
    290                 295                 300

Ala Ala Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly Val Val
305                 310                 315                 320

Gly Val Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly Ala Gly
                325                 330                 335

Ile Pro Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val Pro Gly
            340                 345                 350

Val Val Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys
        355                 360                 365

Tyr Gly Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr Tyr Gly
    370                 375                 380
```

```
Val Gly Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly Gly Ile
385                 390                 395                 400

Pro Gly Val Ala Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly
                405                 410                 415

Gly Val Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala Ala Ala Ala
            420                 425                 430

Ala Lys Ala Ala Lys Tyr Gly Leu Val Pro Gly Val Gly Val Ala Pro
        435                 440                 445

Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Leu
    450                 455                 460

Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val
465                 470                 475                 480

Gly Val Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Gly Ala Ala Ala
                485                 490                 495

Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly Val Pro
            500                 505                 510

Gly Leu Gly Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly Ala Gly
        515                 520                 525

Val Pro Gly Phe Gly Ala Val Pro Gly Ala Leu Ala Ala Ala Lys Ala
    530                 535                 540

Ala Lys Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu Gly Ala
545                 550                 555                 560

Leu Gly Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly Pro Ala
                565                 570                 575

Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly
            580                 585                 590

Leu Val Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly Leu Gly
        595                 600                 605

Val Pro Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala Ala Ala
    610                 615                 620

Lys Ala Ala Lys Tyr Gly Val Ala Ala Arg Pro Gly Phe Gly Leu Ser
625                 630                 635                 640

Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly Arg Lys
                645                 650                 655
```

Arg Lys

<210> 89
<211> 714
<212> PRT
<213> Homo sapiens

<400> 89

```
Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Ala Leu Gly Pro
        35                  40                  45

Gly Gly Lys Pro Leu Lys Pro Val Pro Gly Gly Leu Ala Gly Ala Gly
    50                  55                  60

Leu Gly Ala Gly Leu Gly Ala Phe Pro Ala Val Thr Phe Pro Gly Ala
65                  70                  75                  80

Leu Val Pro Gly Gly Val Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala
                85                  90                  95

Lys Ala Gly Ala Gly Leu Gly Gly Val Pro Gly Val Gly Gly Leu Gly
            100                 105                 110

Val Ser Ala Gly Ala Val Val Pro Gln Pro Gly Ala Gly Val Lys Pro
        115                 120                 125

Gly Lys Val Pro Gly Val Gly Leu Pro Gly Val Tyr Pro Gly Gly Val
    130                 135                 140

Leu Pro Gly Ala Arg Phe Pro Gly Val Gly Val Leu Pro Gly Val Pro
145                 150                 155                 160

Thr Gly Ala Gly Val Lys Pro Lys Ala Pro Gly Val Gly Gly Ala Phe
                165                 170                 175

Ala Gly Ile Pro Gly Val Gly Pro Phe Gly Gly Pro Gln Pro Gly Val
            180                 185                 190

Pro Leu Gly Tyr Pro Ile Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly
        195                 200                 205

Leu Pro Tyr Thr Thr Gly Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly
    210                 215                 220
```

```
Val Ala Gly Ala Ala Gly Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val
225                 230                 235                 240

Gly Pro Gln Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe
                245                 250                 255

Gly Ala Gly Ala Ala Gly Val Leu Pro Gly Val Gly Gly Ala Gly Val
            260                 265                 270

Pro Gly Val Pro Gly Ala Ile Pro Gly Ile Gly Gly Ile Ala Gly Val
        275                 280                 285

Gly Thr Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala
    290                 295                 300

Lys Tyr Gly Ala Ala Ala Gly Leu Val Pro Gly Gly Pro Gly Phe Gly
305                 310                 315                 320

Pro Gly Val Val Gly Val Pro Gly Ala Gly Val Pro Gly Val Gly Val
                325                 330                 335

Pro Gly Ala Gly Ile Pro Val Val Pro Gly Ala Gly Ile Pro Gly Ala
            340                 345                 350

Ala Val Pro Gly Val Val Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala
        355                 360                 365

Lys Ala Ala Lys Tyr Gly Ala Arg Pro Gly Val Gly Val Gly Gly Ile
    370                 375                 380

Pro Thr Tyr Gly Val Gly Ala Gly Gly Phe Pro Gly Phe Gly Val Gly
385                 390                 395                 400

Val Gly Gly Ile Pro Gly Val Ala Gly Val Pro Gly Val Gly Gly Val
                405                 410                 415

Pro Gly Val Gly Gly Val Pro Gly Val Gly Ile Ser Pro Glu Ala Gln
            420                 425                 430

Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Val Gly Thr Pro Ala
        435                 440                 445

Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly Leu Val
    450                 455                 460

Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly
465                 470                 475                 480

Val Ala Pro Gly Val Gly Leu Ala Pro Gly Val Gly Val Ala Pro Gly
                485                 490                 495
```

```
Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Ile Gly Pro Gly
            500                 505                 510

Gly Val Ala Ala Ala Ala Lys Ser Ala Ala Lys Val Ala Ala Lys Ala
        515                 520                 525

Gln Leu Arg Ala Ala Ala Gly Leu Gly Ala Gly Ile Pro Gly Leu Gly
    530                 535                 540

Val Gly Val Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly
545                 550                 555                 560

Leu Gly Val Gly Ala Gly Val Pro Gly Phe Gly Ala Val Pro Gly Ala
                565                 570                 575

Leu Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Val Pro Gly Val
            580                 585                 590

Leu Gly Gly Leu Gly Ala Leu Gly Gly Val Gly Ile Pro Gly Gly Val
        595                 600                 605

Val Gly Ala Gly Pro Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala
    610                 615                 620

Lys Ala Ala Gln Phe Gly Leu Val Gly Ala Ala Gly Leu Gly Gly Leu
625                 630                 635                 640

Gly Val Gly Gly Leu Gly Val Pro Gly Val Gly Gly Leu Gly Gly Ile
                645                 650                 655

Pro Pro Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Gly Leu
            660                 665                 670

Gly Gly Val Leu Gly Gly Ala Gly Gln Phe Pro Leu Gly Gly Val Ala
        675                 680                 685

Ala Arg Pro Gly Phe Gly Leu Ser Pro Ile Phe Pro Gly Gly Ala Cys
    690                 695                 700

Leu Gly Lys Ala Cys Gly Arg Lys Arg Lys
705                 710


<210>  90
<211>  617
<212>  PRT
<213>  Homo sapiens

<400>  90

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1               5                   10                  15
```

```
Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
            20                  25                  30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Ala Leu Gly Pro
        35                  40                  45

Gly Gly Lys Pro Leu Lys Pro Val Pro Gly Gly Leu Ala Gly Ala Gly
    50                  55                  60

Leu Gly Ala Gly Leu Gly Ala Phe Pro Ala Val Thr Phe Pro Gly Ala
65                  70                  75                  80

Leu Val Pro Gly Gly Val Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala
                85                  90                  95

Lys Ala Gly Ala Gly Leu Gly Gly Val Pro Gly Val Gly Gly Leu Gly
            100                 105                 110

Val Ser Ala Gly Ala Val Val Pro Gln Pro Gly Ala Gly Val Lys Pro
        115                 120                 125

Gly Lys Val Pro Gly Val Gly Leu Pro Gly Val Tyr Pro Gly Gly Val
    130                 135                 140

Leu Pro Gly Val Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu
145                 150                 155                 160

Gly Tyr Pro Ile Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu Pro
                165                 170                 175

Tyr Thr Thr Gly Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val Ala
            180                 185                 190

Gly Ala Ala Gly Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro
        195                 200                 205

Gln Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala
    210                 215                 220

Gly Ala Ala Gly Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly
225                 230                 235                 240

Val Pro Gly Ala Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr
                245                 250                 255

Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr
            260                 265                 270

Gly Ala Ala Ala Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly
        275                 280                 285
```

```
Val Val Gly Val Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly
    290                 295                 300

Ala Gly Ile Pro Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val
305                 310                 315                 320

Pro Gly Val Val Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala
                325                 330                 335

Ala Lys Tyr Gly Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr
            340                 345                 350

Tyr Gly Val Gly Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly
        355                 360                 365

Ala Glu Ala Gln Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Leu
    370                 375                 380

Val Pro Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val
385                 390                 395                 400

Gly Val Ala Pro Gly Val Gly Leu Ala Pro Gly Val Gly Val Ala Pro
                405                 410                 415

Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Ile Gly Pro
            420                 425                 430

Gly Gly Val Ala Ala Ala Ala Lys Ser Ala Ala Lys Val Ala Ala Lys
        435                 440                 445

Ala Gln Leu Arg Ala Ala Ala Gly Leu Gly Ala Gly Ile Pro Gly Leu
    450                 455                 460

Gly Val Gly Val Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro
465                 470                 475                 480

Gly Leu Gly Val Gly Ala Gly Val Pro Gly Phe Gly Ala Val Pro Gly
                485                 490                 495

Ala Leu Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Val Pro Gly
            500                 505                 510

Val Leu Gly Gly Leu Gly Ala Leu Gly Gly Val Gly Ile Pro Gly Gly
        515                 520                 525

Val Val Gly Ala Gly Pro Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala
    530                 535                 540

Ala Lys Ala Ala Gln Phe Gly Leu Val Gly Ala Ala Gly Leu Gly Gly
545                 550                 555                 560
```

Leu Gly Val Gly Gly Leu Gly Val Pro Gly Val Gly Gly Leu Gly Gly
565 570 575

Ile Pro Pro Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Val Ala Ala
580 585 590

Arg Pro Gly Phe Gly Leu Ser Pro Ile Phe Pro Gly Gly Ala Cys Leu
595 600 605

Gly Lys Ala Cys Gly Arg Lys Arg Lys
610 615

<210> 91
<211> 786
<212> PRT
<213> Homo sapiens

<400> 91

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1 5 10 15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
20 25 30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
35 40 45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
50 55 60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65 70 75 80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
85 90 95

Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
100 105 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Gly Ala Val
115 120 125

Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val
130 135 140

Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe
145 150 155 160

Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys
165 170 175

Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val

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            180                 185                 190

Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile
        195                 200                 205

Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu Pro Tyr Thr Thr Gly
    210                 215                 220

Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly
225                 230                 235                 240

Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala
                245                 250                 255

Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly
            260                 265                 270

Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala
        275                 280                 285

Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala
    290                 295                 300

Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala
305                 310                 315                 320

Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val
                325                 330                 335

Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro
            340                 345                 350

Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val
        355                 360                 365

Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly
    370                 375                 380

Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly
385                 390                 395                 400

Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly Gly Ile Pro Gly
                405                 410                 415

Val Ala Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly Gly Val
            420                 425                 430

Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala Ala Ala Ala Ala Lys
        435                 440                 445

Ala Ala Lys Tyr Gly Ala Ala Gly Ala Gly Val Leu Gly Gly Leu Val
```

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    450                 455                 460

Pro Gly Ala Pro Gly Ala Val Pro Gly Val Pro Gly Thr Gly Gly Val
465                 470                 475                 480

Pro Gly Val Gly Thr Pro Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys
                485                 490                 495

Ala Ala Gln Phe Gly Leu Val Pro Gly Val Gly Val Ala Pro Gly Val
            500                 505                 510

Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Leu Ala Pro
        515                 520                 525

Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val
    530                 535                 540

Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Ala Ala Ala Lys Ser Ala
545                 550                 555                 560

Ala Lys Val Ala Ala Lys Ala Gln Leu Arg Ala Ala Ala Gly Leu Gly
                565                 570                 575

Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly Val Pro Gly Leu Gly
            580                 585                 590

Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly
        595                 600                 605

Phe Gly Ala Gly Ala Asp Glu Gly Val Arg Arg Ser Leu Ser Pro Glu
    610                 615                 620

Leu Arg Glu Gly Asp Pro Ser Ser Ser Gln His Leu Pro Ser Thr Pro
625                 630                 635                 640

Ser Ser Pro Arg Val Pro Gly Ala Leu Ala Ala Ala Lys Ala Ala Lys
                645                 650                 655

Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu Gly Ala Leu Gly
            660                 665                 670

Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly Pro Ala Ala Ala
        675                 680                 685

Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly Leu Val
    690                 695                 700

Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly Leu Gly Val Pro
705                 710                 715                 720

Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala Ala Ala Lys Ala
```

725 730 735

Ala Lys Tyr Gly Ala Ala Gly Leu Gly Gly Val Leu Gly Gly Ala Gly
740 745 750

Gln Phe Pro Leu Gly Gly Val Ala Ala Arg Pro Gly Phe Gly Leu Ser
755 760 765

Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly Arg Lys
770 775 780

Arg Lys
785

<210> 92
<211> 417
<212> PRT
<213> Homo sapiens

<400> 92

Met Arg Phe Ala Trp Thr Val Leu Leu Leu Gly Pro Leu Gln Leu Cys
1 5 10 15

Ala Leu Val His Cys Ala Pro Pro Ala Ala Gly Gln Gln Gln Pro Pro
20 25 30

Arg Glu Pro Pro Ala Ala Pro Gly Ala Trp Arg Gln Gln Ile Gln Trp
35 40 45

Glu Asn Asn Gly Gln Val Phe Ser Leu Leu Ser Leu Gly Ser Gln Tyr
50 55 60

Gln Pro Gln Arg Arg Arg Asp Pro Gly Ala Ala Val Pro Gly Ala Ala
65 70 75 80

Asn Ala Ser Ala Gln Gln Pro Arg Thr Pro Ile Leu Leu Ile Arg Asp
85 90 95

Asn Arg Thr Ala Ala Ala Arg Thr Arg Thr Ala Gly Ser Ser Gly Val
100 105 110

Thr Ala Gly Arg Pro Arg Pro Thr Ala Arg His Trp Phe Gln Ala Gly
115 120 125

Tyr Ser Thr Ser Arg Ala Arg Glu Ala Gly Ala Ser Arg Ala Glu Asn
130 135 140

Gln Thr Ala Pro Gly Glu Val Pro Ala Leu Ser Asn Leu Arg Pro Pro
145 150 155 160

Ser Arg Val Asp Gly Met Val Gly Asp Asp Pro Tyr Asn Pro Tyr Lys
165 170 175

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Tyr Ser Asp Asp Asn Pro Tyr Tyr Asn Tyr Tyr Asp Thr Tyr Glu Arg
            180                 185                 190

Pro Arg Pro Gly Gly Arg Tyr Arg Pro Gly Tyr Gly Thr Gly Tyr Phe
        195                 200                 205

Gln Tyr Gly Leu Pro Asp Leu Val Ala Asp Pro Tyr Tyr Ile Gln Ala
    210                 215                 220

Ser Thr Tyr Val Gln Lys Met Ser Met Tyr Asn Leu Arg Cys Ala Ala
225                 230                 235                 240

Glu Glu Asn Cys Leu Ala Ser Thr Ala Tyr Arg Ala Asp Val Arg Asp
                245                 250                 255

Tyr Asp His Arg Val Leu Leu Arg Phe Pro Gln Arg Val Lys Asn Gln
            260                 265                 270

Gly Thr Ser Asp Phe Leu Pro Ser Arg Pro Arg Tyr Ser Trp Glu Trp
        275                 280                 285

His Ser Cys His Gln His Tyr His Ser Met Asp Glu Phe Ser His Tyr
    290                 295                 300

Asp Leu Leu Asp Ala Asn Thr Gln Arg Arg Val Ala Glu Gly His Lys
305                 310                 315                 320

Ala Ser Phe Cys Leu Glu Asp Thr Ser Cys Asp Tyr Gly Tyr His Arg
                325                 330                 335

Arg Phe Ala Cys Thr Ala His Thr Gln Gly Leu Ser Pro Gly Cys Tyr
            340                 345                 350

Asp Thr Tyr Gly Ala Asp Ile Asp Cys Gln Trp Ile Asp Ile Thr Asp
        355                 360                 365

Val Lys Pro Gly Asn Tyr Ile Leu Lys Val Ser Val Asn Pro Ser Tyr
    370                 375                 380

Leu Val Pro Glu Ser Asp Tyr Thr Asn Asn Val Val Arg Cys Asp Ile
385                 390                 395                 400

Arg Tyr Thr Gly His His Ala Tyr Ala Ser Gly Cys Thr Ile Ser Pro
                405                 410                 415

Tyr
```

<210> 93
<211> 187

<212> PRT
<213> Homo sapiens

<400> 93

Met Ser Met Tyr Asn Leu Arg Cys Ala Ala Glu Glu Asn Cys Leu Ala
1 5 10 15

Ser Thr Ala Tyr Arg Ala Asp Val Arg Asp Tyr Asp His Arg Val Leu
20 25 30

Leu Arg Phe Pro Gln Arg Val Lys Asn Gln Gly Thr Ser Asp Phe Leu
35 40 45

Pro Ser Arg Pro Arg Tyr Ser Trp Glu Trp His Ser Cys His Gln His
50 55 60

Tyr His Ser Met Asp Glu Phe Ser His Tyr Asp Leu Leu Asp Ala Asn
65 70 75 80

Thr Gln Arg Arg Val Ala Glu Gly His Lys Ala Ser Phe Cys Leu Glu
85 90 95

Asp Thr Ser Cys Asp Tyr Gly Tyr His Arg Arg Phe Ala Cys Thr Ala
100 105 110

His Thr Gln Gly Leu Ser Pro Gly Cys Tyr Asp Thr Tyr Gly Ala Asp
115 120 125

Ile Asp Cys Gln Trp Ile Asp Ile Thr Asp Val Lys Pro Gly Asn Tyr
130 135 140

Ile Leu Lys Val Ser Val Asn Pro Ser Tyr Leu Val Pro Glu Ser Asp
145 150 155 160

Tyr Thr Asn Asn Val Val Arg Cys Asp Ile Arg Tyr Thr Gly His His
165 170 175

Ala Tyr Ala Ser Gly Cys Thr Ile Ser Pro Tyr
180 185

<210> 94
<211> 1132
<212> PRT
<213> Homo sapiens

<400> 94

Met Pro Arg Ala Pro Arg Cys Arg Ala Val Arg Ser Leu Leu Arg Ser
1 5 10 15

His Tyr Arg Glu Val Leu Pro Leu Ala Thr Phe Val Arg Arg Leu Gly
20 25 30

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Pro Gln Gly Trp Arg Leu Val Gln Arg Gly Asp Pro Ala Ala Phe Arg
        35                  40                  45

Ala Leu Val Ala Gln Cys Leu Val Cys Val Pro Trp Asp Ala Arg Pro
    50                  55                  60

Pro Pro Ala Ala Pro Ser Phe Arg Gln Val Ser Cys Leu Lys Glu Leu
65                  70                  75                  80

Val Ala Arg Val Leu Gln Arg Leu Cys Glu Arg Gly Ala Lys Asn Val
                85                  90                  95

Leu Ala Phe Gly Phe Ala Leu Leu Asp Gly Ala Arg Gly Gly Pro Pro
            100                 105                 110

Glu Ala Phe Thr Thr Ser Val Arg Ser Tyr Leu Pro Asn Thr Val Thr
        115                 120                 125

Asp Ala Leu Arg Gly Ser Gly Ala Trp Gly Leu Leu Leu Arg Arg Val
    130                 135                 140

Gly Asp Asp Val Leu Val His Leu Leu Ala Arg Cys Ala Leu Phe Val
145                 150                 155                 160

Leu Val Ala Pro Ser Cys Ala Tyr Gln Val Cys Gly Pro Pro Leu Tyr
                165                 170                 175

Gln Leu Gly Ala Ala Thr Gln Ala Arg Pro Pro Pro His Ala Ser Gly
            180                 185                 190

Pro Arg Arg Arg Leu Gly Cys Glu Arg Ala Trp Asn His Ser Val Arg
        195                 200                 205

Glu Ala Gly Val Pro Leu Gly Leu Pro Ala Pro Gly Ala Arg Arg Arg
    210                 215                 220

Gly Gly Ser Ala Ser Arg Ser Leu Pro Leu Pro Lys Arg Pro Arg Arg
225                 230                 235                 240

Gly Ala Ala Pro Glu Pro Glu Arg Thr Pro Val Gly Gln Gly Ser Trp
                245                 250                 255

Ala His Pro Gly Arg Thr Arg Gly Pro Ser Asp Arg Gly Phe Cys Val
            260                 265                 270

Val Ser Pro Ala Arg Pro Ala Glu Glu Ala Thr Ser Leu Glu Gly Ala
        275                 280                 285

Leu Ser Gly Thr Arg His Ser His Pro Ser Val Gly Arg Gln His His
    290                 295                 300
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```
Ala Gly Pro Pro Ser Thr Ser Arg Pro Pro Arg Pro Trp Asp Thr Pro
305                 310                 315                 320

Cys Pro Pro Val Tyr Ala Glu Thr Lys His Phe Leu Tyr Ser Ser Gly
                325                 330                 335

Asp Lys Glu Gln Leu Arg Pro Ser Phe Leu Leu Ser Ser Leu Arg Pro
            340                 345                 350

Ser Leu Thr Gly Ala Arg Arg Leu Val Glu Thr Ile Phe Leu Gly Ser
        355                 360                 365

Arg Pro Trp Met Pro Gly Thr Pro Arg Arg Leu Pro Arg Leu Pro Gln
    370                 375                 380

Arg Tyr Trp Gln Met Arg Pro Leu Phe Leu Glu Leu Leu Gly Asn His
385                 390                 395                 400

Ala Gln Cys Pro Tyr Gly Val Leu Leu Lys Thr His Cys Pro Leu Arg
                405                 410                 415

Ala Ala Val Thr Pro Ala Ala Gly Val Cys Ala Arg Glu Lys Pro Gln
            420                 425                 430

Gly Ser Val Ala Ala Pro Glu Glu Glu Asp Thr Asp Pro Arg Arg Leu
        435                 440                 445

Val Gln Leu Leu Arg Gln His Ser Ser Pro Trp Gln Val Tyr Gly Phe
    450                 455                 460

Val Arg Ala Cys Leu Arg Arg Leu Val Pro Pro Gly Leu Trp Gly Ser
465                 470                 475                 480

Arg His Asn Glu Arg Arg Phe Leu Arg Asn Thr Lys Lys Phe Ile Ser
                485                 490                 495

Leu Gly Lys His Ala Lys Leu Ser Leu Gln Glu Leu Thr Trp Lys Met
            500                 505                 510

Ser Val Arg Asp Cys Ala Trp Leu Arg Arg Ser Pro Gly Val Gly Cys
        515                 520                 525

Val Pro Ala Ala Glu His Arg Leu Arg Glu Glu Ile Leu Ala Lys Phe
    530                 535                 540

Leu His Trp Leu Met Ser Val Tyr Val Val Glu Leu Leu Arg Ser Phe
545                 550                 555                 560

Phe Tyr Val Thr Glu Thr Thr Phe Gln Lys Asn Arg Leu Phe Phe Tyr
                565                 570                 575
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Arg Lys Ser Val Trp Ser Lys Leu Gln Ser Ile Gly Ile Arg Gln His
            580                 585                 590

Leu Lys Arg Val Gln Leu Arg Glu Leu Ser Glu Ala Glu Val Arg Gln
        595                 600                 605

His Arg Glu Ala Arg Pro Ala Leu Leu Thr Ser Arg Leu Arg Phe Ile
    610                 615                 620

Pro Lys Pro Asp Gly Leu Arg Pro Ile Val Asn Met Asp Tyr Val Val
625                 630                 635                 640

Gly Ala Arg Thr Phe Arg Arg Glu Lys Arg Ala Glu Arg Leu Thr Ser
                645                 650                 655

Arg Val Lys Ala Leu Phe Ser Val Leu Asn Tyr Glu Arg Ala Arg Arg
            660                 665                 670

Pro Gly Leu Leu Gly Ala Ser Val Leu Gly Leu Asp Asp Ile His Arg
        675                 680                 685

Ala Trp Arg Thr Phe Val Leu Arg Val Arg Ala Gln Asp Pro Pro Pro
    690                 695                 700

Glu Leu Tyr Phe Val Lys Val Asp Val Thr Gly Ala Tyr Asp Thr Ile
705                 710                 715                 720

Pro Gln Asp Arg Leu Thr Glu Val Ile Ala Ser Ile Ile Lys Pro Gln
                725                 730                 735

Asn Thr Tyr Cys Val Arg Arg Tyr Ala Val Val Gln Lys Ala Ala His
            740                 745                 750

Gly His Val Arg Lys Ala Phe Lys Ser His Val Ser Thr Leu Thr Asp
        755                 760                 765

Leu Gln Pro Tyr Met Arg Gln Phe Val Ala His Leu Gln Glu Thr Ser
    770                 775                 780

Pro Leu Arg Asp Ala Val Val Ile Glu Gln Ser Ser Ser Leu Asn Glu
785                 790                 795                 800

Ala Ser Ser Gly Leu Phe Asp Val Phe Leu Arg Phe Met Cys His His
                805                 810                 815

Ala Val Arg Ile Arg Gly Lys Ser Tyr Val Gln Cys Gln Gly Ile Pro
            820                 825                 830

Gln Gly Ser Ile Leu Ser Thr Leu Leu Cys Ser Leu Cys Tyr Gly Asp
        835                 840                 845
```

```
Met Glu Asn Lys Leu Phe Ala Gly Ile Arg Arg Asp Gly Leu Leu Leu
    850                 855                 860

Arg Leu Val Asp Asp Phe Leu Leu Val Thr Pro His Leu Thr His Ala
865                 870                 875                 880

Lys Thr Phe Leu Arg Thr Leu Val Arg Gly Val Pro Glu Tyr Gly Cys
                885                 890                 895

Val Val Asn Leu Arg Lys Thr Val Val Asn Phe Pro Val Glu Asp Glu
            900                 905                 910

Ala Leu Gly Gly Thr Ala Phe Val Gln Met Pro Ala His Gly Leu Phe
        915                 920                 925

Pro Trp Cys Gly Leu Leu Leu Asp Thr Arg Thr Leu Glu Val Gln Ser
    930                 935                 940

Asp Tyr Ser Ser Tyr Ala Arg Thr Ser Ile Arg Ala Ser Leu Thr Phe
945                 950                 955                 960

Asn Arg Gly Phe Lys Ala Gly Arg Asn Met Arg Arg Lys Leu Phe Gly
                965                 970                 975

Val Leu Arg Leu Lys Cys His Ser Leu Phe Leu Asp Leu Gln Val Asn
            980                 985                 990

Ser Leu Gln Thr Val Cys Thr Asn  Ile Tyr Lys Ile Leu  Leu Leu Gln
        995                 1000                1005

Ala Tyr  Arg Phe His Ala Cys  Val Leu Gln Leu Pro  Phe His Gln
    1010                1015                1020

Gln Val  Trp Lys Asn Pro Thr  Phe Phe Leu Arg Val  Ile Ser Asp
    1025                1030                1035

Thr Ala  Ser Leu Cys Tyr Ser  Ile Leu Lys Ala Lys  Asn Ala Gly
    1040                1045                1050

Met Ser  Leu Gly Ala Lys Gly  Ala Ala Gly Pro Leu  Pro Ser Glu
    1055                1060                1065

Ala Val  Gln Trp Leu Cys His  Gln Ala Phe Leu Leu  Lys Leu Thr
    1070                1075                1080

Arg His  Arg Val Thr Tyr Val  Pro Leu Leu Gly Ser  Leu Arg Thr
    1085                1090                1095

Ala Gln  Thr Gln Leu Ser Arg  Lys Leu Pro Gly Thr  Thr Leu Thr
    1100                1105                1110
```

Ala Leu Glu Ala Ala Ala Asn Pro Ala Leu Pro Ser Asp Phe Lys
1115 1120 1125

Thr Ile Leu Asp
1130

<210> 95
<211> 1069
<212> PRT
<213> Homo sapiens

<400> 95

Met Pro Arg Ala Pro Arg Cys Arg Ala Val Arg Ser Leu Leu Arg Ser
1 5 10 15

His Tyr Arg Glu Val Leu Pro Leu Ala Thr Phe Val Arg Arg Leu Gly
20 25 30

Pro Gln Gly Trp Arg Leu Val Gln Arg Gly Asp Pro Ala Ala Phe Arg
35 40 45

Ala Leu Val Ala Gln Cys Leu Val Cys Val Pro Trp Asp Ala Arg Pro
50 55 60

Pro Pro Ala Ala Pro Ser Phe Arg Gln Val Ser Cys Leu Lys Glu Leu
65 70 75 80

Val Ala Arg Val Leu Gln Arg Leu Cys Glu Arg Gly Ala Lys Asn Val
85 90 95

Leu Ala Phe Gly Phe Ala Leu Leu Asp Gly Ala Arg Gly Gly Pro Pro
100 105 110

Glu Ala Phe Thr Thr Ser Val Arg Ser Tyr Leu Pro Asn Thr Val Thr
115 120 125

Asp Ala Leu Arg Gly Ser Gly Ala Trp Gly Leu Leu Leu Arg Arg Val
130 135 140

Gly Asp Asp Val Leu Val His Leu Leu Ala Arg Cys Ala Leu Phe Val
145 150 155 160

Leu Val Ala Pro Ser Cys Ala Tyr Gln Val Cys Gly Pro Pro Leu Tyr
165 170 175

Gln Leu Gly Ala Ala Thr Gln Ala Arg Pro Pro Pro His Ala Ser Gly
180 185 190

Pro Arg Arg Arg Leu Gly Cys Glu Arg Ala Trp Asn His Ser Val Arg
195 200 205

Glu Ala Gly Val Pro Leu Gly Leu Pro Ala Pro Gly Ala Arg Arg Arg

210 215 220

Gly Gly Ser Ala Ser Arg Ser Leu Pro Leu Pro Lys Arg Pro Arg Arg
225 230 235 240

Gly Ala Ala Pro Glu Pro Glu Arg Thr Pro Val Gly Gln Gly Ser Trp
245 250 255

Ala His Pro Gly Arg Thr Arg Gly Pro Ser Asp Arg Gly Phe Cys Val
260 265 270

Val Ser Pro Ala Arg Pro Ala Glu Glu Ala Thr Ser Leu Glu Gly Ala
275 280 285

Leu Ser Gly Thr Arg His Ser His Pro Ser Val Gly Arg Gln His His
290 295 300

Ala Gly Pro Pro Ser Thr Ser Arg Pro Pro Arg Pro Trp Asp Thr Pro
305 310 315 320

Cys Pro Pro Val Tyr Ala Glu Thr Lys His Phe Leu Tyr Ser Ser Gly
325 330 335

Asp Lys Glu Gln Leu Arg Pro Ser Phe Leu Leu Ser Ser Leu Arg Pro
340 345 350

Ser Leu Thr Gly Ala Arg Arg Leu Val Glu Thr Ile Phe Leu Gly Ser
355 360 365

Arg Pro Trp Met Pro Gly Thr Pro Arg Arg Leu Pro Arg Leu Pro Gln
370 375 380

Arg Tyr Trp Gln Met Arg Pro Leu Phe Leu Glu Leu Leu Gly Asn His
385 390 395 400

Ala Gln Cys Pro Tyr Gly Val Leu Leu Lys Thr His Cys Pro Leu Arg
405 410 415

Ala Ala Val Thr Pro Ala Ala Gly Val Cys Ala Arg Glu Lys Pro Gln
420 425 430

Gly Ser Val Ala Ala Pro Glu Glu Glu Asp Thr Asp Pro Arg Arg Leu
435 440 445

Val Gln Leu Leu Arg Gln His Ser Ser Pro Trp Gln Val Tyr Gly Phe
450 455 460

Val Arg Ala Cys Leu Arg Arg Leu Val Pro Pro Gly Leu Trp Gly Ser
465 470 475 480

Arg His Asn Glu Arg Arg Phe Leu Arg Asn Thr Lys Lys Phe Ile Ser

485 490 495

Leu Gly Lys His Ala Lys Leu Ser Leu Gln Glu Leu Thr Trp Lys Met
500 505 510

Ser Val Arg Asp Cys Ala Trp Leu Arg Arg Ser Pro Gly Val Gly Cys
515 520 525

Val Pro Ala Ala Glu His Arg Leu Arg Glu Glu Ile Leu Ala Lys Phe
530 535 540

Leu His Trp Leu Met Ser Val Tyr Val Val Glu Leu Leu Arg Ser Phe
545 550 555 560

Phe Tyr Val Thr Glu Thr Thr Phe Gln Lys Asn Arg Leu Phe Phe Tyr
565 570 575

Arg Lys Ser Val Trp Ser Lys Leu Gln Ser Ile Gly Ile Arg Gln His
580 585 590

Leu Lys Arg Val Gln Leu Arg Glu Leu Ser Glu Ala Glu Val Arg Gln
595 600 605

His Arg Glu Ala Arg Pro Ala Leu Leu Thr Ser Arg Leu Arg Phe Ile
610 615 620

Pro Lys Pro Asp Gly Leu Arg Pro Ile Val Asn Met Asp Tyr Val Val
625 630 635 640

Gly Ala Arg Thr Phe Arg Arg Glu Lys Arg Ala Glu Arg Leu Thr Ser
645 650 655

Arg Val Lys Ala Leu Phe Ser Val Leu Asn Tyr Glu Arg Ala Arg Arg
660 665 670

Pro Gly Leu Leu Gly Ala Ser Val Leu Gly Leu Asp Asp Ile His Arg
675 680 685

Ala Trp Arg Thr Phe Val Leu Arg Val Arg Ala Gln Asp Pro Pro Pro
690 695 700

Glu Leu Tyr Phe Val Lys Val Asp Val Thr Gly Ala Tyr Asp Thr Ile
705 710 715 720

Pro Gln Asp Arg Leu Thr Glu Val Ile Ala Ser Ile Ile Lys Pro Gln
725 730 735

Asn Thr Tyr Cys Val Arg Arg Tyr Ala Val Val Gln Lys Ala Ala His
740 745 750

Gly His Val Arg Lys Ala Phe Lys Ser His Val Ser Thr Leu Thr Asp

```
        755                 760                 765

Leu Gln Pro Tyr Met Arg Gln Phe Val Ala His Leu Gln Glu Thr Ser
    770                 775                 780

Pro Leu Arg Asp Ala Val Val Ile Glu Gln Ser Ser Ser Leu Asn Glu
785                 790                 795                 800

Ala Ser Ser Gly Leu Phe Asp Val Phe Leu Arg Phe Met Cys His His
                805                 810                 815

Ala Val Arg Ile Arg Gly Lys Ser Tyr Val Gln Cys Gln Gly Ile Pro
            820                 825                 830

Gln Gly Ser Ile Leu Ser Thr Leu Leu Cys Ser Leu Cys Tyr Gly Asp
        835                 840                 845

Met Glu Asn Lys Leu Phe Ala Gly Ile Arg Arg Asp Gly Leu Leu Leu
    850                 855                 860

Arg Leu Val Asp Asp Phe Leu Leu Val Thr Pro His Leu Thr His Ala
865                 870                 875                 880

Lys Thr Phe Leu Ser Tyr Ala Arg Thr Ser Ile Arg Ala Ser Leu Thr
                885                 890                 895

Phe Asn Arg Gly Phe Lys Ala Gly Arg Asn Met Arg Arg Lys Leu Phe
            900                 905                 910

Gly Val Leu Arg Leu Lys Cys His Ser Leu Phe Leu Asp Leu Gln Val
        915                 920                 925

Asn Ser Leu Gln Thr Val Cys Thr Asn Ile Tyr Lys Ile Leu Leu Leu
    930                 935                 940

Gln Ala Tyr Arg Phe His Ala Cys Val Leu Gln Leu Pro Phe His Gln
945                 950                 955                 960

Gln Val Trp Lys Asn Pro Thr Phe Phe Leu Arg Val Ile Ser Asp Thr
                965                 970                 975

Ala Ser Leu Cys Tyr Ser Ile Leu Lys Ala Lys Asn Ala Gly Met Ser
            980                 985                 990

Leu Gly Ala Lys Gly Ala Ala Gly  Pro Leu Pro Ser Glu  Ala Val Gln
        995                 1000                1005

Trp Leu  Cys His Gln Ala Phe  Leu Leu Lys Leu Thr  Arg His Arg
    1010                1015                1020

Val Thr  Tyr Val Pro Leu Leu  Gly Ser Leu Arg Thr  Ala Gln Thr
```

1025 1030 1035

Gln Leu Ser Arg Lys Leu Pro Gly Thr Thr Leu Thr Ala Leu Glu
1040 1045 1050

Ala Ala Ala Asn Pro Ala Leu Pro Ser Asp Phe Lys Thr Ile Leu
1055 1060 1065

Asp

<210> 96
<211> 2477
<212> PRT
<213> Homo sapiens

<400> 96

Met Leu Arg Gly Pro Gly Pro Gly Leu Leu Leu Leu Ala Val Gln Cys
1 5 10 15

Leu Gly Thr Ala Val Pro Ser Thr Gly Ala Ser Lys Ser Lys Arg Gln
20 25 30

Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val Ala Val Ser Gln Ser
35 40 45

Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr Gln Ile Asn Gln Gln
50 55 60

Trp Glu Arg Thr Tyr Leu Gly Asn Ala Leu Val Cys Thr Cys Tyr Gly
65 70 75 80

Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro Glu Ala Glu Glu Thr
85 90 95

Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg Val Gly Asp Thr Tyr
100 105 110

Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys Thr Cys Ile Gly Ala
115 120 125

Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn Arg Cys His Glu Gly
130 135 140

Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg Arg Pro His Glu Thr
145 150 155 160

Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly Asn Gly Lys Gly Glu
165 170 175

Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe Asp His Ala Ala Gly
180 185 190

```
Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys Pro Tyr Gln Gly Trp
        195                 200                 205

Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly Ser Gly Arg Ile Thr
    210                 215                 220

Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp Thr Arg Thr Ser Tyr
225                 230                 235                 240

Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn Arg Gly Asn Leu Leu
                245                 250                 255

Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu Trp Lys Cys Glu Arg
            260                 265                 270

His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser Gly Pro Phe Thr Asp
        275                 280                 285

Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His Pro Gln Pro Pro Pro
    290                 295                 300

Tyr Gly His Cys Val Thr Asp Ser Gly Val Val Tyr Ser Val Gly Met
305                 310                 315                 320

Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met Leu Cys Thr Cys Leu
                325                 330                 335

Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val Thr Gln Thr Tyr Gly
            340                 345                 350

Gly Asn Ser Asn Gly Glu Pro Cys Val Leu Pro Phe Thr Tyr Asn Gly
        355                 360                 365

Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg Gln Asp Gly His Leu
    370                 375                 380

Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp Gln Lys Tyr Ser Phe
385                 390                 395                 400

Cys Thr Asp His Thr Val Leu Val Gln Thr Arg Gly Gly Asn Ser Asn
                405                 410                 415

Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn Asn His Asn Tyr Thr
            420                 425                 430

Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met Lys Trp Cys Gly Thr
        435                 440                 445

Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly Phe Cys Pro Met Ala
    450                 455                 460
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```
Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly Val Met Tyr Arg Ile
465                 470                 475                 480

Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly His Met Met Arg Cys
                485                 490                 495

Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr Cys Ile Ala Tyr Ser
            500                 505                 510

Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile Thr Tyr Asn Val Asn
        515                 520                 525

Asp Thr Phe His Lys Arg His Glu Glu Gly His Met Leu Asn Cys Thr
    530                 535                 540

Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys Asp Pro Val Asp Gln
545                 550                 555                 560

Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln Ile Gly Asp Ser Trp
                565                 570                 575

Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys Tyr Cys Tyr Gly Arg
            580                 585                 590

Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln Thr Tyr Pro Ser Ser
        595                 600                 605

Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr Pro Ser Gln Pro Asn
    610                 615                 620

Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro Ser His Ile Ser Lys
625                 630                 635                 640

Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val Gly Arg Trp Lys Glu
                645                 650                 655

Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr Ile Lys Gly Leu Lys
            660                 665                 670

Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser Ile Gln Gln Tyr Gly
        675                 680                 685

His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr Thr Ser Thr Ser Thr
    690                 695                 700

Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr Thr Pro Phe Ser Pro
705                 710                 715                 720

Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile Thr Ala Ser Ser Phe
                725                 730                 735
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```
Val Val Ser Trp Val Ser Ala Ser Asp Thr Val Ser Gly Phe Arg Val
            740                 745                 750

Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro Gln Tyr Leu Asp Leu
        755                 760                 765

Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp Leu Leu Pro Gly Arg
    770                 775                 780

Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu Asp Gly Glu Gln Ser
785                 790                 795                 800

Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro Asp Ala Pro Pro Asp
                805                 810                 815

Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile Val Val Arg Trp Ser
            820                 825                 830

Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile Val Tyr Ser Pro Ser
        835                 840                 845

Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro Glu Thr Ala Asn Ser
    850                 855                 860

Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln Tyr Asn Ile Thr Ile
865                 870                 875                 880

Tyr Ala Val Glu Glu Asn Gln Glu Ser Thr Pro Val Val Ile Gln Gln
                885                 890                 895

Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val Pro Ser Pro Arg Asp
            900                 905                 910

Leu Gln Phe Val Glu Val Thr Asp Val Lys Val Thr Ile Met Trp Thr
        915                 920                 925

Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val Asp Val Ile Pro Val
    930                 935                 940

Asn Leu Pro Gly Glu His Gly Gln Arg Leu Pro Ile Ser Arg Asn Thr
945                 950                 955                 960

Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val Thr Tyr Tyr Phe Lys
                965                 970                 975

Val Phe Ala Val Ser His Gly Arg Glu Ser Lys Pro Leu Thr Ala Gln
            980                 985                 990

Gln Thr Thr Lys Leu Asp Ala Pro  Thr Asn Leu Gln Phe  Val Asn Glu
        995                 1000                1005
```

```
Thr Asp  Ser Thr Val Leu Val  Arg Trp Thr Pro Pro  Arg Ala Gln
    1010                 1015                 1020

Ile Thr  Gly Tyr Arg Leu Thr  Val Gly Leu Thr Arg  Arg Gly Gln
    1025                 1030                 1035

Pro Arg  Gln Tyr Asn Val Gly  Pro Ser Val Ser Lys  Tyr Pro Leu
    1040                 1045                 1050

Arg Asn  Leu Gln Pro Ala Ser  Glu Tyr Thr Val Ser  Leu Val Ala
    1055                 1060                 1065

Ile Lys  Gly Asn Gln Glu Ser  Pro Lys Ala Thr Gly  Val Phe Thr
    1070                 1075                 1080

Thr Leu  Gln Pro Gly Ser Ser  Ile Pro Pro Tyr Asn  Thr Glu Val
    1085                 1090                 1095

Thr Glu  Thr Thr Ile Val Ile  Thr Trp Thr Pro Ala  Pro Arg Ile
    1100                 1105                 1110

Gly Phe  Lys Leu Gly Val Arg  Pro Ser Gln Gly Gly  Glu Ala Pro
    1115                 1120                 1125

Arg Glu  Val Thr Ser Asp Ser  Gly Ser Ile Val Val  Ser Gly Leu
    1130                 1135                 1140

Thr Pro  Gly Val Glu Tyr Val  Tyr Thr Ile Gln Val  Leu Arg Asp
    1145                 1150                 1155

Gly Gln  Glu Arg Asp Ala Pro  Ile Val Asn Lys Val  Val Thr Pro
    1160                 1165                 1170

Leu Ser  Pro Pro Thr Asn Leu  His Leu Glu Ala Asn  Pro Asp Thr
    1175                 1180                 1185

Gly Val  Leu Thr Val Ser Trp  Glu Arg Ser Thr Thr  Pro Asp Ile
    1190                 1195                 1200

Thr Gly  Tyr Arg Ile Thr Thr  Thr Pro Thr Asn Gly  Gln Gln Gly
    1205                 1210                 1215

Asn Ser  Leu Glu Glu Val Val  His Ala Asp Gln Ser  Ser Cys Thr
    1220                 1225                 1230

Phe Asp  Asn Leu Ser Pro Gly  Leu Glu Tyr Asn Val  Ser Val Tyr
    1235                 1240                 1245

Thr Val  Lys Asp Asp Lys Glu  Ser Val Pro Ile Ser  Asp Thr Ile
    1250                 1255                 1260
```

```
Ile Pro  Glu Val Pro Gln Leu  Thr Asp Leu Ser Phe  Val Asp Ile
    1265                1270                1275

Thr Asp  Ser Ser Ile Gly Leu  Arg Trp Thr Pro Leu  Asn Ser Ser
    1280                1285                1290

Thr Ile  Ile Gly Tyr Arg Ile  Thr Val Val Ala Ala  Gly Glu Gly
    1295                1300                1305

Ile Pro  Ile Phe Glu Asp Phe  Val Asp Ser Ser Val  Gly Tyr Tyr
    1310                1315                1320

Thr Val  Thr Gly Leu Glu Pro  Gly Ile Asp Tyr Asp  Ile Ser Val
    1325                1330                1335

Ile Thr  Leu Ile Asn Gly Gly  Glu Ser Ala Pro Thr  Thr Leu Thr
    1340                1345                1350

Gln Gln  Thr Ala Val Pro Pro  Pro Thr Asp Leu Arg  Phe Thr Asn
    1355                1360                1365

Ile Gly  Pro Asp Thr Met Arg  Val Thr Trp Ala Pro  Pro Pro Ser
    1370                1375                1380

Ile Asp  Leu Thr Asn Phe Leu  Val Arg Tyr Ser Pro  Val Lys Asn
    1385                1390                1395

Glu Glu  Asp Val Ala Glu Leu  Ser Ile Ser Pro Ser  Asp Asn Ala
    1400                1405                1410

Val Val  Leu Thr Asn Leu Leu  Pro Gly Thr Glu Tyr  Val Val Ser
    1415                1420                1425

Val Ser  Ser Val Tyr Glu Gln  His Glu Ser Thr Pro  Leu Arg Gly
    1430                1435                1440

Arg Gln  Lys Thr Gly Leu Asp  Ser Pro Thr Gly Ile  Asp Phe Ser
    1445                1450                1455

Asp Ile  Thr Ala Asn Ser Phe  Thr Val His Trp Ile  Ala Pro Arg
    1460                1465                1470

Ala Thr  Ile Thr Gly Tyr Arg  Ile Arg His His Pro  Glu His Phe
    1475                1480                1485

Ser Gly  Arg Pro Arg Glu Asp  Arg Val Pro His Ser  Arg Asn Ser
    1490                1495                1500

Ile Thr  Leu Thr Asn Leu Thr  Pro Gly Thr Glu Tyr  Val Val Ser
    1505                1510                1515
```

```
Ile Val  Ala Leu Asn Gly Arg  Glu Glu Ser Pro Leu  Leu Ile Gly
    1520                1525                1530

Gln Gln  Ser Thr Val Ser Asp  Val Pro Arg Asp Leu  Glu Val Val
    1535                1540                1545

Ala Ala  Thr Pro Thr Ser Leu  Leu Ile Ser Trp Asp  Ala Pro Ala
    1550                1555                1560

Val Thr  Val Arg Tyr Tyr Arg  Ile Thr Tyr Gly Glu  Thr Gly Gly
    1565                1570                1575

Asn Ser  Pro Val Gln Glu Phe  Thr Val Pro Gly Ser  Lys Ser Thr
    1580                1585                1590

Ala Thr  Ile Ser Gly Leu Lys  Pro Gly Val Asp Tyr  Thr Ile Thr
    1595                1600                1605

Val Tyr  Ala Val Thr Gly Arg  Gly Asp Ser Pro Ala  Ser Ser Lys
    1610                1615                1620

Pro Ile  Ser Ile Asn Tyr Arg  Thr Glu Ile Asp Lys  Pro Ser Gln
    1625                1630                1635

Met Gln  Val Thr Asp Val Gln  Asp Asn Ser Ile Ser  Val Lys Trp
    1640                1645                1650

Leu Pro  Ser Ser Ser Pro Val  Thr Gly Tyr Arg Val  Thr Thr Thr
    1655                1660                1665

Pro Lys  Asn Gly Pro Gly Pro  Thr Lys Thr Lys Thr  Ala Gly Pro
    1670                1675                1680

Asp Gln  Thr Glu Met Thr Ile  Glu Gly Leu Gln Pro  Thr Val Glu
    1685                1690                1695

Tyr Val  Val Ser Val Tyr Ala  Gln Asn Pro Ser Gly  Glu Ser Gln
    1700                1705                1710

Pro Leu  Val Gln Thr Ala Val  Thr Asn Ile Asp Arg  Pro Lys Gly
    1715                1720                1725

Leu Ala  Phe Thr Asp Val Asp  Val Asp Ser Ile Lys  Ile Ala Trp
    1730                1735                1740

Glu Ser  Pro Gln Gly Gln Val  Ser Arg Tyr Arg Val  Thr Tyr Ser
    1745                1750                1755

Ser Pro  Glu Asp Gly Ile His  Glu Leu Phe Pro Ala  Pro Asp Gly
    1760                1765                1770
```

```
Glu Glu  Asp Thr Ala Glu Leu  Gln Gly Leu Arg Pro  Gly Ser Glu
    1775                1780                1785

Tyr Thr  Val Ser Val Val Ala  Leu His Asp Asp Met  Glu Ser Gln
    1790                1795                1800

Pro Leu  Ile Gly Thr Gln Ser  Thr Ala Ile Pro Ala  Pro Thr Asp
    1805                1810                1815

Leu Lys  Phe Thr Gln Val Thr  Pro Thr Ser Leu Ser  Ala Gln Trp
    1820                1825                1830

Thr Pro  Pro Asn Val Gln Leu  Thr Gly Tyr Arg Val  Arg Val Thr
    1835                1840                1845

Pro Lys  Glu Lys Thr Gly Pro  Met Lys Glu Ile Asn  Leu Ala Pro
    1850                1855                1860

Asp Ser  Ser Ser Val Val Val  Ser Gly Leu Met Val  Ala Thr Lys
    1865                1870                1875

Tyr Glu  Val Ser Val Tyr Ala  Leu Lys Asp Thr Leu  Thr Ser Arg
    1880                1885                1890

Pro Ala  Gln Gly Val Val Thr  Thr Leu Glu Asn Val  Ser Pro Pro
    1895                1900                1905

Arg Arg  Ala Arg Val Thr Asp  Ala Thr Glu Thr Thr  Ile Thr Ile
    1910                1915                1920

Ser Trp  Arg Thr Lys Thr Glu  Thr Ile Thr Gly Phe  Gln Val Asp
    1925                1930                1935

Ala Val  Pro Ala Asn Gly Gln  Thr Pro Ile Gln Arg  Thr Ile Lys
    1940                1945                1950

Pro Asp  Val Arg Ser Tyr Thr  Ile Thr Gly Leu Gln  Pro Gly Thr
    1955                1960                1965

Asp Tyr  Lys Ile Tyr Leu Tyr  Thr Leu Asn Asp Asn  Ala Arg Ser
    1970                1975                1980

Ser Pro  Val Val Ile Asp Ala  Ser Thr Ala Ile Asp  Ala Pro Ser
    1985                1990                1995

Asn Leu  Arg Phe Leu Ala Thr  Thr Pro Asn Ser Leu  Leu Val Ser
    2000                2005                2010

Trp Gln  Pro Pro Arg Ala Arg  Ile Thr Gly Tyr Ile  Ile Lys Tyr
    2015                2020                2025
```

```
Glu Lys  Pro Gly Ser Pro Pro  Arg Glu Val Val Pro  Arg Pro Arg
    2030                 2035                 2040

Pro Gly  Val Thr Glu Ala Thr  Ile Thr Gly Leu Glu  Pro Gly Thr
    2045                 2050                 2055

Glu Tyr  Thr Ile Tyr Val Ile  Ala Leu Lys Asn Asn  Gln Lys Ser
    2060                 2065                 2070

Glu Pro  Leu Ile Gly Arg Lys  Lys Thr Asp Glu Leu  Pro Gln Leu
    2075                 2080                 2085

Val Thr  Leu Pro His Pro Asn  Leu His Gly Pro Glu  Ile Leu Asp
    2090                 2095                 2100

Val Pro  Ser Thr Val Gln Lys  Thr Pro Phe Val Thr  His Pro Gly
    2105                 2110                 2115

Tyr Asp  Thr Gly Asn Gly Ile  Gln Leu Pro Gly Thr  Ser Gly Gln
    2120                 2125                 2130

Gln Pro  Ser Val Gly Gln Gln  Met Ile Phe Glu Glu  His Gly Phe
    2135                 2140                 2145

Arg Arg  Thr Thr Pro Pro Thr  Thr Ala Thr Pro Ile  Arg His Arg
    2150                 2155                 2160

Pro Arg  Pro Tyr Pro Pro Asn  Val Gly Glu Glu Ile  Gln Ile Gly
    2165                 2170                 2175

His Ile  Pro Arg Glu Asp Val  Asp Tyr His Leu Tyr  Pro His Gly
    2180                 2185                 2190

Pro Gly  Leu Asn Pro Asn Ala  Ser Thr Gly Gln Glu  Ala Leu Ser
    2195                 2200                 2205

Gln Thr  Thr Ile Ser Trp Ala  Pro Phe Gln Asp Thr  Ser Glu Tyr
    2210                 2215                 2220

Ile Ile  Ser Cys His Pro Val  Gly Thr Asp Glu Glu  Pro Leu Gln
    2225                 2230                 2235

Phe Arg  Val Pro Gly Thr Ser  Thr Ser Ala Thr Leu  Thr Gly Leu
    2240                 2245                 2250

Thr Arg  Gly Ala Thr Tyr Asn  Ile Ile Val Glu Ala  Leu Lys Asp
    2255                 2260                 2265

Gln Gln  Arg His Lys Val Arg  Glu Glu Val Val Thr  Val Gly Asn
    2270                 2275                 2280
```

```
Ser Val  Asn Glu Gly Leu Asn  Gln Pro Thr Asp Asp  Ser Cys Phe
    2285                 2290                 2295

Asp Pro  Tyr Thr Val Ser His  Tyr Ala Val Gly Asp  Glu Trp Glu
    2300                 2305                 2310

Arg Met  Ser Glu Ser Gly Phe  Lys Leu Leu Cys Gln  Cys Leu Gly
    2315                 2320                 2325

Phe Gly  Ser Gly His Phe Arg  Cys Asp Ser Ser Arg  Trp Cys His
    2330                 2335                 2340

Asp Asn  Gly Val Asn Tyr Lys  Ile Gly Glu Lys Trp  Asp Arg Gln
    2345                 2350                 2355

Gly Glu  Asn Gly Gln Met Met  Ser Cys Thr Cys Leu  Gly Asn Gly
    2360                 2365                 2370

Lys Gly  Glu Phe Lys Cys Asp  Pro His Glu Ala Thr  Cys Tyr Asp
    2375                 2380                 2385

Asp Gly  Lys Thr Tyr His Val  Gly Glu Gln Trp Gln  Lys Glu Tyr
    2390                 2395                 2400

Leu Gly  Ala Ile Cys Ser Cys  Thr Cys Phe Gly Gly  Gln Arg Gly
    2405                 2410                 2415

Trp Arg  Cys Asp Asn Cys Arg  Arg Pro Gly Gly Glu  Pro Ser Pro
    2420                 2425                 2430

Glu Gly  Thr Thr Gly Gln Ser  Tyr Asn Gln Tyr Ser  Gln Arg Tyr
    2435                 2440                 2445

His Gln  Arg Thr Asn Thr Asn  Val Asn Cys Pro Ile  Glu Cys Phe
    2450                 2455                 2460

Met Pro  Leu Asp Val Gln Ala  Asp Arg Glu Asp Ser  Arg Glu
    2465                 2470                 2475


<210>  97
<211>  2355
<212>  PRT
<213>  Homo sapiens

<400>  97

Met Leu Arg Gly Pro Gly Pro Gly Leu Leu Leu Leu Ala Val Gln Cys
1               5                  10                  15

Leu Gly Thr Ala Val Pro Ser Thr Gly Ala Ser Lys Ser Lys Arg Gln
            20                  25                  30
```

```
Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val Ala Val Ser Gln Ser
        35                  40                  45

Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr Gln Ile Asn Gln Gln
    50                  55                  60

Trp Glu Arg Thr Tyr Leu Gly Asn Ala Leu Val Cys Thr Cys Tyr Gly
65                  70                  75                  80

Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro Glu Ala Glu Glu Thr
                85                  90                  95

Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg Val Gly Asp Thr Tyr
            100                 105                 110

Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys Thr Cys Ile Gly Ala
        115                 120                 125

Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn Arg Cys His Glu Gly
    130                 135                 140

Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg Arg Pro His Glu Thr
145                 150                 155                 160

Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly Asn Gly Lys Gly Glu
                165                 170                 175

Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe Asp His Ala Ala Gly
            180                 185                 190

Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys Pro Tyr Gln Gly Trp
        195                 200                 205

Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly Ser Gly Arg Ile Thr
    210                 215                 220

Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp Thr Arg Thr Ser Tyr
225                 230                 235                 240

Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn Arg Gly Asn Leu Leu
                245                 250                 255

Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu Trp Lys Cys Glu Arg
            260                 265                 270

His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser Gly Pro Phe Thr Asp
        275                 280                 285

Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His Pro Gln Pro Pro Pro
    290                 295                 300
```

```
Tyr Gly His Cys Val Thr Asp Ser Gly Val Val Tyr Ser Val Gly Met
305                 310                 315                 320

Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met Leu Cys Thr Cys Leu
                325                 330                 335

Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val Thr Gln Thr Tyr Gly
            340                 345                 350

Gly Asn Ser Asn Gly Glu Pro Cys Val Leu Pro Phe Thr Tyr Asn Gly
        355                 360                 365

Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg Gln Asp Gly His Leu
    370                 375                 380

Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp Gln Lys Tyr Ser Phe
385                 390                 395                 400

Cys Thr Asp His Thr Val Leu Val Gln Thr Arg Gly Gly Asn Ser Asn
                405                 410                 415

Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn Asn His Asn Tyr Thr
            420                 425                 430

Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met Lys Trp Cys Gly Thr
        435                 440                 445

Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly Phe Cys Pro Met Ala
    450                 455                 460

Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly Val Met Tyr Arg Ile
465                 470                 475                 480

Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly His Met Met Arg Cys
                485                 490                 495

Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr Cys Ile Ala Tyr Ser
            500                 505                 510

Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile Thr Tyr Asn Val Asn
        515                 520                 525

Asp Thr Phe His Lys Arg His Glu Glu Gly His Met Leu Asn Cys Thr
    530                 535                 540

Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys Asp Pro Val Asp Gln
545                 550                 555                 560

Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln Ile Gly Asp Ser Trp
                565                 570                 575
```

```
Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys Tyr Cys Tyr Gly Arg
            580                 585                 590

Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln Thr Tyr Pro Ser Ser
        595                 600                 605

Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr Pro Ser Gln Pro Asn
    610                 615                 620

Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro Ser His Ile Ser Lys
625                 630                 635                 640

Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val Gly Arg Trp Lys Glu
                645                 650                 655

Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr Ile Lys Gly Leu Lys
            660                 665                 670

Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser Ile Gln Gln Tyr Gly
        675                 680                 685

His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr Thr Ser Thr Ser Thr
    690                 695                 700

Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr Thr Pro Phe Ser Pro
705                 710                 715                 720

Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile Thr Ala Ser Ser Phe
                725                 730                 735

Val Val Ser Trp Val Ser Ala Ser Asp Thr Val Ser Gly Phe Arg Val
            740                 745                 750

Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro Gln Tyr Leu Asp Leu
        755                 760                 765

Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp Leu Leu Pro Gly Arg
    770                 775                 780

Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu Asp Gly Glu Gln Ser
785                 790                 795                 800

Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro Asp Ala Pro Pro Asp
                805                 810                 815

Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile Val Val Arg Trp Ser
            820                 825                 830

Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile Val Tyr Ser Pro Ser
        835                 840                 845
```

```
Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro Glu Thr Ala Asn Ser
    850                 855                 860

Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln Tyr Asn Ile Thr Ile
865                 870                 875                 880

Tyr Ala Val Glu Glu Asn Gln Glu Ser Thr Pro Val Val Ile Gln Gln
                885                 890                 895

Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val Pro Ser Pro Arg Asp
            900                 905                 910

Leu Gln Phe Val Glu Val Thr Asp Val Lys Val Thr Ile Met Trp Thr
        915                 920                 925

Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val Asp Val Ile Pro Val
    930                 935                 940

Asn Leu Pro Gly Glu His Gly Gln Arg Leu Pro Ile Ser Arg Asn Thr
945                 950                 955                 960

Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val Thr Tyr Tyr Phe Lys
                965                 970                 975

Val Phe Ala Val Ser His Gly Arg Glu Ser Lys Pro Leu Thr Ala Gln
            980                 985                 990

Gln Thr Thr Lys Leu Asp Ala Pro  Thr Asn Leu Gln Phe  Val Asn Glu
        995                 1000                1005

Thr Asp  Ser Thr Val Leu Val  Arg Trp Thr Pro Pro  Arg Ala Gln
    1010                1015                1020

Ile Thr  Gly Tyr Arg Leu Thr  Val Gly Leu Thr Arg  Arg Gly Gln
    1025                1030                1035

Pro Arg  Gln Tyr Asn Val Gly  Pro Ser Val Ser Lys  Tyr Pro Leu
    1040                1045                1050

Arg Asn  Leu Gln Pro Ala Ser  Glu Tyr Thr Val Ser  Leu Val Ala
    1055                1060                1065

Ile Lys  Gly Asn Gln Glu Ser  Pro Lys Ala Thr Gly  Val Phe Thr
    1070                1075                1080

Thr Leu  Gln Pro Gly Ser Ser  Ile Pro Pro Tyr Asn  Thr Glu Val
    1085                1090                1095

Thr Glu  Thr Thr Ile Val Ile  Thr Trp Thr Pro Ala  Pro Arg Ile
    1100                1105                1110
```

```
Gly Phe  Lys Leu Gly Val Arg  Pro Ser Gln Gly Gly  Glu Ala Pro
    1115                1120                1125

Arg Glu  Val Thr Ser Asp Ser  Gly Ser Ile Val Val  Ser Gly Leu
    1130                1135                1140

Thr Pro  Gly Val Glu Tyr Val  Tyr Thr Ile Gln Val  Leu Arg Asp
    1145                1150                1155

Gly Gln  Glu Arg Asp Ala Pro  Ile Val Asn Lys Val  Val Thr Pro
    1160                1165                1170

Leu Ser  Pro Pro Thr Asn Leu  His Leu Glu Ala Asn  Pro Asp Thr
    1175                1180                1185

Gly Val  Leu Thr Val Ser Trp  Glu Arg Ser Thr Thr  Pro Asp Ile
    1190                1195                1200

Thr Gly  Tyr Arg Ile Thr Thr  Thr Pro Thr Asn Gly  Gln Gln Gly
    1205                1210                1215

Asn Ser  Leu Glu Glu Val Val  His Ala Asp Gln Ser  Ser Cys Thr
    1220                1225                1230

Phe Asp  Asn Leu Ser Pro Gly  Leu Glu Tyr Asn Val  Ser Val Tyr
    1235                1240                1245

Thr Val  Lys Asp Asp Lys Glu  Ser Val Pro Ile Ser  Asp Thr Ile
    1250                1255                1260

Ile Pro  Ala Val Pro Pro Pro  Thr Asp Leu Arg Phe  Thr Asn Ile
    1265                1270                1275

Gly Pro  Asp Thr Met Arg Val  Thr Trp Ala Pro Pro  Pro Ser Ile
    1280                1285                1290

Asp Leu  Thr Asn Phe Leu Val  Arg Tyr Ser Pro Val  Lys Asn Glu
    1295                1300                1305

Glu Asp  Val Ala Glu Leu Ser  Ile Ser Pro Ser Asp  Asn Ala Val
    1310                1315                1320

Val Leu  Thr Asn Leu Leu Pro  Gly Thr Glu Tyr Val  Val Ser Val
    1325                1330                1335

Ser Ser  Val Tyr Glu Gln His  Glu Ser Thr Pro Leu  Arg Gly Arg
    1340                1345                1350

Gln Lys  Thr Gly Leu Asp Ser  Pro Thr Gly Ile Asp  Phe Ser Asp
    1355                1360                1365
```

```
Ile Thr  Ala Asn Ser Phe Thr  Val His Trp Ile Ala  Pro Arg Ala
    1370                 1375                 1380

Thr Ile  Thr Gly Tyr Arg Ile  Arg His His Pro Glu  His Phe Ser
    1385                 1390                 1395

Gly Arg  Pro Arg Glu Asp Arg  Val Pro His Ser Arg  Asn Ser Ile
    1400                 1405                 1410

Thr Leu  Thr Asn Leu Thr Pro  Gly Thr Glu Tyr Val  Val Ser Ile
    1415                 1420                 1425

Val Ala  Leu Asn Gly Arg Glu  Glu Ser Pro Leu Leu  Ile Gly Gln
    1430                 1435                 1440

Gln Ser  Thr Val Ser Asp Val  Pro Arg Asp Leu Glu  Val Val Ala
    1445                 1450                 1455

Ala Thr  Pro Thr Ser Leu Leu  Ile Ser Trp Asp Ala  Pro Ala Val
    1460                 1465                 1470

Thr Val  Arg Tyr Tyr Arg Ile  Thr Tyr Gly Glu Thr  Gly Gly Asn
    1475                 1480                 1485

Ser Pro  Val Gln Glu Phe Thr  Val Pro Gly Ser Lys  Ser Thr Ala
    1490                 1495                 1500

Thr Ile  Ser Gly Leu Lys Pro  Gly Val Asp Tyr Thr  Ile Thr Val
    1505                 1510                 1515

Tyr Ala  Val Thr Gly Arg Gly  Asp Ser Pro Ala Ser  Ser Lys Pro
    1520                 1525                 1530

Ile Ser  Ile Asn Tyr Arg Thr  Glu Ile Asp Lys Pro  Ser Gln Met
    1535                 1540                 1545

Gln Val  Thr Asp Val Gln Asp  Asn Ser Ile Ser Val  Lys Trp Leu
    1550                 1555                 1560

Pro Ser  Ser Ser Pro Val Thr  Gly Tyr Arg Val Thr  Thr Thr Pro
    1565                 1570                 1575

Lys Asn  Gly Pro Gly Pro Thr  Lys Thr Lys Thr Ala  Gly Pro Asp
    1580                 1585                 1590

Gln Thr  Glu Met Thr Ile Glu  Gly Leu Gln Pro Thr  Val Glu Tyr
    1595                 1600                 1605

Val Val  Ser Val Tyr Ala Gln  Asn Pro Ser Gly Glu  Ser Gln Pro
    1610                 1615                 1620
```

```
Leu Val  Gln Thr Ala Val Thr  Asn Ile Asp Arg Pro  Lys Gly Leu
    1625                1630                1635

Ala Phe  Thr Asp Val Asp Val  Asp Ser Ile Lys Ile  Ala Trp Glu
    1640                1645                1650

Ser Pro  Gln Gly Gln Val Ser  Arg Tyr Arg Val Thr  Tyr Ser Ser
    1655                1660                1665

Pro Glu  Asp Gly Ile His Glu  Leu Phe Pro Ala Pro  Asp Gly Glu
    1670                1675                1680

Glu Asp  Thr Ala Glu Leu Gln  Gly Leu Arg Pro Gly  Ser Glu Tyr
    1685                1690                1695

Thr Val  Ser Val Val Ala Leu  His Asp Asp Met Glu  Ser Gln Pro
    1700                1705                1710

Leu Ile  Gly Thr Gln Ser Thr  Ala Ile Pro Ala Pro  Thr Asp Leu
    1715                1720                1725

Lys Phe  Thr Gln Val Thr Pro  Thr Ser Leu Ser Ala  Gln Trp Thr
    1730                1735                1740

Pro Pro  Asn Val Gln Leu Thr  Gly Tyr Arg Val Arg  Val Thr Pro
    1745                1750                1755

Lys Glu  Lys Thr Gly Pro Met  Lys Glu Ile Asn Leu  Ala Pro Asp
    1760                1765                1770

Ser Ser  Ser Val Val Val Ser  Gly Leu Met Val Ala  Thr Lys Tyr
    1775                1780                1785

Glu Val  Ser Val Tyr Ala Leu  Lys Asp Thr Leu Thr  Ser Arg Pro
    1790                1795                1800

Ala Gln  Gly Val Val Thr Thr  Leu Glu Asn Val Ser  Pro Pro Arg
    1805                1810                1815

Arg Ala  Arg Val Thr Asp Ala  Thr Glu Thr Thr Ile  Thr Ile Ser
    1820                1825                1830

Trp Arg  Thr Lys Thr Glu Thr  Ile Thr Gly Phe Gln  Val Asp Ala
    1835                1840                1845

Val Pro  Ala Asn Gly Gln Thr  Pro Ile Gln Arg Thr  Ile Lys Pro
    1850                1855                1860

Asp Val  Arg Ser Tyr Thr Ile  Thr Gly Leu Gln Pro  Gly Thr Asp
    1865                1870                1875
```

```
Tyr Lys  Ile Tyr Leu Tyr Thr  Leu Asn Asp Asn Ala  Arg Ser Ser
    1880                1885                1890

Pro Val  Val Ile Asp Ala Ser  Thr Ala Ile Asp Ala  Pro Ser Asn
    1895                1900                1905

Leu Arg  Phe Leu Ala Thr Thr  Pro Asn Ser Leu Leu  Val Ser Trp
    1910                1915                1920

Gln Pro  Pro Arg Ala Arg Ile  Thr Gly Tyr Ile Ile  Lys Tyr Glu
    1925                1930                1935

Lys Pro  Gly Ser Pro Pro Arg  Glu Val Val Pro Arg  Pro Arg Pro
    1940                1945                1950

Gly Val  Thr Glu Ala Thr Ile  Thr Gly Leu Glu Pro  Gly Thr Glu
    1955                1960                1965

Tyr Thr  Ile Tyr Val Ile Ala  Leu Lys Asn Asn Gln  Lys Ser Glu
    1970                1975                1980

Pro Leu  Ile Gly Arg Lys Lys  Thr Asp Glu Leu Pro  Gln Leu Val
    1985                1990                1995

Thr Leu  Pro His Pro Asn Leu  His Gly Pro Glu Ile  Leu Asp Val
    2000                2005                2010

Pro Ser  Thr Val Gln Lys Thr  Pro Phe Val Thr His  Pro Gly Tyr
    2015                2020                2025

Asp Thr  Gly Asn Gly Ile Gln  Leu Pro Gly Thr Ser  Gly Gln Gln
    2030                2035                2040

Pro Ser  Val Gly Gln Gln Met  Ile Phe Glu Glu His  Gly Phe Arg
    2045                2050                2055

Arg Thr  Thr Pro Pro Thr Thr  Ala Thr Pro Ile Arg  His Arg Pro
    2060                2065                2070

Arg Pro  Tyr Pro Pro Asn Val  Gly Gln Glu Ala Leu  Ser Gln Thr
    2075                2080                2085

Thr Ile  Ser Trp Ala Pro Phe  Gln Asp Thr Ser Glu  Tyr Ile Ile
    2090                2095                2100

Ser Cys  His Pro Val Gly Thr  Asp Glu Glu Pro Leu  Gln Phe Arg
    2105                2110                2115

Val Pro  Gly Thr Ser Thr Ser  Ala Thr Leu Thr Gly  Leu Thr Arg
    2120                2125                2130
```

```
Gly Ala  Thr Tyr Asn Ile Ile  Val Glu Ala Leu Lys  Asp Gln Gln
    2135                2140                2145

Arg His  Lys Val Arg Glu Glu  Val Val Thr Val Gly  Asn Ser Val
    2150                2155                2160

Asn Glu  Gly Leu Asn Gln Pro  Thr Asp Asp Ser Cys  Phe Asp Pro
    2165                2170                2175

Tyr Thr  Val Ser His Tyr Ala  Val Gly Asp Glu Trp  Glu Arg Met
    2180                2185                2190

Ser Glu  Ser Gly Phe Lys Leu  Leu Cys Gln Cys Leu  Gly Phe Gly
    2195                2200                2205

Ser Gly  His Phe Arg Cys Asp  Ser Ser Arg Trp Cys  His Asp Asn
    2210                2215                2220

Gly Val  Asn Tyr Lys Ile Gly  Glu Lys Trp Asp Arg  Gln Gly Glu
    2225                2230                2235

Asn Gly  Gln Met Met Ser Cys  Thr Cys Leu Gly Asn  Gly Lys Gly
    2240                2245                2250

Glu Phe  Lys Cys Asp Pro His  Glu Ala Thr Cys Tyr  Asp Asp Gly
    2255                2260                2265

Lys Thr  Tyr His Val Gly Glu  Gln Trp Gln Lys Glu  Tyr Leu Gly
    2270                2275                2280

Ala Ile  Cys Ser Cys Thr Cys  Phe Gly Gly Gln Arg  Gly Trp Arg
    2285                2290                2295

Cys Asp  Asn Cys Arg Arg Pro  Gly Gly Glu Pro Ser  Pro Glu Gly
    2300                2305                2310

Thr Thr  Gly Gln Ser Tyr Asn  Gln Tyr Ser Gln Arg  Tyr His Gln
    2315                2320                2325

Arg Thr  Asn Thr Asn Val Asn  Cys Pro Ile Glu Cys  Phe Met Pro
    2330                2335                2340

Leu Asp  Val Gln Ala Asp Arg  Glu Asp Ser Arg Glu
    2345                2350                2355


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<212>  PRT
<213>  Homo sapiens

<400>  98
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Met Leu Arg Gly Pro Gly Pro Gly Leu Leu Leu Ala Val Gln Cys
1               5                  10                  15

Leu Gly Thr Ala Val Pro Ser Thr Gly Ala Ser Lys Ser Lys Arg Gln
            20                  25                  30

Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val Ala Val Ser Gln Ser
        35                  40                  45

Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr Gln Ile Asn Gln Gln
    50                  55                  60

Trp Glu Arg Thr Tyr Leu Gly Asn Ala Leu Val Cys Thr Cys Tyr Gly
65                  70                  75                  80

Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro Glu Ala Glu Glu Thr
                85                  90                  95

Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg Val Gly Asp Thr Tyr
            100                 105                 110

Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys Thr Cys Ile Gly Ala
        115                 120                 125

Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn Arg Cys His Glu Gly
    130                 135                 140

Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg Arg Pro His Glu Thr
145                 150                 155                 160

Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly Asn Gly Lys Gly Glu
                165                 170                 175

Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe Asp His Ala Ala Gly
            180                 185                 190

Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys Pro Tyr Gln Gly Trp
        195                 200                 205

Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly Ser Gly Arg Ile Thr
    210                 215                 220

Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp Thr Arg Thr Ser Tyr
225                 230                 235                 240

Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn Arg Gly Asn Leu Leu
                245                 250                 255

Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu Trp Lys Cys Glu Arg
            260                 265                 270
```

```
His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser Gly Pro Phe Thr Asp
        275                 280                 285

Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His Pro Gln Pro Pro Pro
    290                 295                 300

Tyr Gly His Cys Val Thr Asp Ser Gly Val Val Tyr Ser Val Gly Met
305                 310                 315                 320

Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met Leu Cys Thr Cys Leu
                325                 330                 335

Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val Thr Gln Thr Tyr Gly
            340                 345                 350

Gly Asn Ser Asn Gly Glu Pro Cys Val Leu Pro Phe Thr Tyr Asn Gly
        355                 360                 365

Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg Gln Asp Gly His Leu
    370                 375                 380

Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp Gln Lys Tyr Ser Phe
385                 390                 395                 400

Cys Thr Asp His Thr Val Leu Val Gln Thr Arg Gly Gly Asn Ser Asn
                405                 410                 415

Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn Asn His Asn Tyr Thr
            420                 425                 430

Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met Lys Trp Cys Gly Thr
        435                 440                 445

Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly Phe Cys Pro Met Ala
    450                 455                 460

Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly Val Met Tyr Arg Ile
465                 470                 475                 480

Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly His Met Met Arg Cys
                485                 490                 495

Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr Cys Ile Ala Tyr Ser
            500                 505                 510

Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile Thr Tyr Asn Val Asn
        515                 520                 525

Asp Thr Phe His Lys Arg His Glu Glu Gly His Met Leu Asn Cys Thr
    530                 535                 540
```

```
Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys Asp Pro Val Asp Gln
545                 550                 555                 560

Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln Ile Gly Asp Ser Trp
                565                 570                 575

Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys Tyr Cys Tyr Gly Arg
            580                 585                 590

Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln Thr Tyr Pro Ser Ser
        595                 600                 605

Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr Pro Ser Gln Pro Asn
    610                 615                 620

Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro Ser His Ile Ser Lys
625                 630                 635                 640

Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val Gly Arg Trp Lys Glu
                645                 650                 655

Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr Ile Lys Gly Leu Lys
            660                 665                 670

Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser Ile Gln Gln Tyr Gly
        675                 680                 685

His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr Thr Ser Thr Ser Thr
    690                 695                 700

Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr Thr Pro Phe Ser Pro
705                 710                 715                 720

Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile Thr Ala Ser Ser Phe
                725                 730                 735

Val Val Ser Trp Val Ser Ala Ser Asp Thr Val Ser Gly Phe Arg Val
            740                 745                 750

Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro Gln Tyr Leu Asp Leu
        755                 760                 765

Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp Leu Leu Pro Gly Arg
    770                 775                 780

Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu Asp Gly Glu Gln Ser
785                 790                 795                 800

Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro Asp Ala Pro Pro Asp
                805                 810                 815
```

```
Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile Val Val Arg Trp Ser
            820                 825                 830

Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile Val Tyr Ser Pro Ser
        835                 840                 845

Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro Glu Thr Ala Asn Ser
    850                 855                 860

Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln Tyr Asn Ile Thr Ile
865                 870                 875                 880

Tyr Ala Val Glu Glu Asn Gln Glu Ser Thr Pro Val Val Ile Gln Gln
                885                 890                 895

Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val Pro Ser Pro Arg Asp
            900                 905                 910

Leu Gln Phe Val Glu Val Thr Asp Val Lys Val Thr Ile Met Trp Thr
        915                 920                 925

Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val Asp Val Ile Pro Val
    930                 935                 940

Asn Leu Pro Gly Glu His Gly Gln Arg Leu Pro Ile Ser Arg Asn Thr
945                 950                 955                 960

Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val Thr Tyr Tyr Phe Lys
                965                 970                 975

Val Phe Ala Val Ser His Gly Arg Glu Ser Lys Pro Leu Thr Ala Gln
            980                 985                 990

Gln Thr Thr Lys Leu Asp Ala Pro  Thr Asn Leu Gln Phe  Val Asn Glu
        995                 1000                1005

Thr Asp  Ser Thr Val Leu Val  Arg Trp Thr Pro Pro  Arg Ala Gln
    1010                1015                1020

Ile Thr  Gly Tyr Arg Leu Thr  Val Gly Leu Thr Arg  Arg Gly Gln
    1025                1030                1035

Pro Arg  Gln Tyr Asn Val Gly  Pro Ser Val Ser Lys  Tyr Pro Leu
    1040                1045                1050

Arg Asn  Leu Gln Pro Ala Ser  Glu Tyr Thr Val Ser  Leu Val Ala
    1055                1060                1065

Ile Lys  Gly Asn Gln Glu Ser  Pro Lys Ala Thr Gly  Val Phe Thr
    1070                1075                1080
```

```
Thr Leu  Gln Pro Gly Ser Ser  Ile Pro Pro Tyr Asn  Thr Glu Val
    1085                1090                1095

Thr Glu  Thr Thr Ile Val Ile  Thr Trp Thr Pro Ala  Pro Arg Ile
    1100                1105                1110

Gly Phe  Lys Leu Gly Val Arg  Pro Ser Gln Gly Gly  Glu Ala Pro
    1115                1120                1125

Arg Glu  Val Thr Ser Asp Ser  Gly Ser Ile Val Val  Ser Gly Leu
    1130                1135                1140

Thr Pro  Gly Val Glu Tyr Val  Tyr Thr Ile Gln Val  Leu Arg Asp
    1145                1150                1155

Gly Gln  Glu Arg Asp Ala Pro  Ile Val Asn Lys Val  Val Thr Pro
    1160                1165                1170

Leu Ser  Pro Pro Thr Asn Leu  His Leu Glu Ala Asn  Pro Asp Thr
    1175                1180                1185

Gly Val  Leu Thr Val Ser Trp  Glu Arg Ser Thr Thr  Pro Asp Ile
    1190                1195                1200

Thr Gly  Tyr Arg Ile Thr Thr  Thr Pro Thr Asn Gly  Gln Gln Gly
    1205                1210                1215

Asn Ser  Leu Glu Glu Val Val  His Ala Asp Gln Ser  Ser Cys Thr
    1220                1225                1230

Phe Asp  Asn Leu Ser Pro Gly  Leu Glu Tyr Asn Val  Ser Val Tyr
    1235                1240                1245

Thr Val  Lys Asp Asp Lys Glu  Ser Val Pro Ile Ser  Asp Thr Ile
    1250                1255                1260

Ile Pro  Ala Val Pro Pro Pro  Thr Asp Leu Arg Phe  Thr Asn Ile
    1265                1270                1275

Gly Pro  Asp Thr Met Arg Val  Thr Trp Ala Pro Pro  Pro Ser Ile
    1280                1285                1290

Asp Leu  Thr Asn Phe Leu Val  Arg Tyr Ser Pro Val  Lys Asn Glu
    1295                1300                1305

Glu Asp  Val Ala Glu Leu Ser  Ile Ser Pro Ser Asp  Asn Ala Val
    1310                1315                1320

Val Leu  Thr Asn Leu Leu Pro  Gly Thr Glu Tyr Val  Val Ser Val
    1325                1330                1335
```

```
Ser Ser  Val Tyr Glu Gln His  Glu Ser Thr Pro Leu  Arg Gly Arg
    1340                1345                1350

Gln Lys  Thr Gly Leu Asp Ser  Pro Thr Gly Ile Asp  Phe Ser Asp
    1355                1360                1365

Ile Thr  Ala Asn Ser Phe Thr  Val His Trp Ile Ala  Pro Arg Ala
    1370                1375                1380

Thr Ile  Thr Gly Tyr Arg Ile  Arg His His Pro Glu  His Phe Ser
    1385                1390                1395

Gly Arg  Pro Arg Glu Asp Arg  Val Pro His Ser Arg  Asn Ser Ile
    1400                1405                1410

Thr Leu  Thr Asn Leu Thr Pro  Gly Thr Glu Tyr Val  Val Ser Ile
    1415                1420                1425

Val Ala  Leu Asn Gly Arg Glu  Glu Ser Pro Leu Leu  Ile Gly Gln
    1430                1435                1440

Gln Ser  Thr Val Ser Asp Val  Pro Arg Asp Leu Glu  Val Val Ala
    1445                1450                1455

Ala Thr  Pro Thr Ser Leu Leu  Ile Ser Trp Asp Ala  Pro Ala Val
    1460                1465                1470

Thr Val  Arg Tyr Tyr Arg Ile  Thr Tyr Gly Glu Thr  Gly Gly Asn
    1475                1480                1485

Ser Pro  Val Gln Glu Phe Thr  Val Pro Gly Ser Lys  Ser Thr Ala
    1490                1495                1500

Thr Ile  Ser Gly Leu Lys Pro  Gly Val Asp Tyr Thr  Ile Thr Val
    1505                1510                1515

Tyr Ala  Val Thr Gly Arg Gly  Asp Ser Pro Ala Ser  Ser Lys Pro
    1520                1525                1530

Ile Ser  Ile Asn Tyr Arg Thr  Glu Ile Asp Lys Pro  Ser Gln Met
    1535                1540                1545

Gln Val  Thr Asp Val Gln Asp  Asn Ser Ile Ser Val  Lys Trp Leu
    1550                1555                1560

Pro Ser  Ser Ser Pro Val Thr  Gly Tyr Arg Val Thr  Thr Thr Pro
    1565                1570                1575

Lys Asn  Gly Pro Gly Pro Thr  Lys Thr Lys Thr Ala  Gly Pro Asp
    1580                1585                1590
```

```
Gln Thr  Glu Met Thr Ile Glu  Gly Leu Gln Pro Thr  Val Glu Tyr
    1595                1600                1605

Val Val  Ser Val Tyr Ala Gln  Asn Pro Ser Gly Glu  Ser Gln Pro
    1610                1615                1620

Leu Val  Gln Thr Ala Val Thr  Asn Ile Asp Arg Pro  Lys Gly Leu
    1625                1630                1635

Ala Phe  Thr Asp Val Asp Val  Asp Ser Ile Lys Ile  Ala Trp Glu
    1640                1645                1650

Ser Pro  Gln Gly Gln Val Ser  Arg Tyr Arg Val Thr  Tyr Ser Ser
    1655                1660                1665

Pro Glu  Asp Gly Ile His Glu  Leu Phe Pro Ala Pro  Asp Gly Glu
    1670                1675                1680

Glu Asp  Thr Ala Glu Leu Gln  Gly Leu Arg Pro Gly  Ser Glu Tyr
    1685                1690                1695

Thr Val  Ser Val Val Ala Leu  His Asp Asp Met Glu  Ser Gln Pro
    1700                1705                1710

Leu Ile  Gly Thr Gln Ser Thr  Ala Ile Pro Ala Pro  Thr Asp Leu
    1715                1720                1725

Lys Phe  Thr Gln Val Thr Pro  Thr Ser Leu Ser Ala  Gln Trp Thr
    1730                1735                1740

Pro Pro  Asn Val Gln Leu Thr  Gly Tyr Arg Val Arg  Val Thr Pro
    1745                1750                1755

Lys Glu  Lys Thr Gly Pro Met  Lys Glu Ile Asn Leu  Ala Pro Asp
    1760                1765                1770

Ser Ser  Ser Val Val Val Ser  Gly Leu Met Val Ala  Thr Lys Tyr
    1775                1780                1785

Glu Val  Ser Val Tyr Ala Leu  Lys Asp Thr Leu Thr  Ser Arg Pro
    1790                1795                1800

Ala Gln  Gly Val Val Thr Thr  Leu Glu Asn Val Ser  Pro Pro Arg
    1805                1810                1815

Arg Ala  Arg Val Thr Asp Ala  Thr Glu Thr Thr Ile  Thr Ile Ser
    1820                1825                1830

Trp Arg  Thr Lys Thr Glu Thr  Ile Thr Gly Phe Gln  Val Asp Ala
    1835                1840                1845
```

```
Val Pro  Ala Asn Gly Gln Thr  Pro Ile Gln Arg Thr  Ile Lys Pro
    1850                 1855                 1860

Asp Val  Arg Ser Tyr Thr Ile  Thr Gly Leu Gln Pro  Gly Thr Asp
    1865                 1870                 1875

Tyr Lys  Ile Tyr Leu Tyr Thr  Leu Asn Asp Asn Ala  Arg Ser Ser
    1880                 1885                 1890

Pro Val  Val Ile Asp Ala Ser  Thr Ala Ile Asp Ala  Pro Ser Asn
    1895                 1900                 1905

Leu Arg  Phe Leu Ala Thr Thr  Pro Asn Ser Leu Leu  Val Ser Trp
    1910                 1915                 1920

Gln Pro  Pro Arg Ala Arg Ile  Thr Gly Tyr Ile Ile  Lys Tyr Glu
    1925                 1930                 1935

Lys Pro  Gly Ser Pro Pro Arg  Glu Val Val Pro Arg  Pro Arg Pro
    1940                 1945                 1950

Gly Val  Thr Glu Ala Thr Ile  Thr Gly Leu Glu Pro  Gly Thr Glu
    1955                 1960                 1965

Tyr Thr  Ile Tyr Val Ile Ala  Leu Lys Asn Asn Gln  Lys Ser Glu
    1970                 1975                 1980

Pro Leu  Ile Gly Arg Lys Lys  Thr Val Gln Lys Thr  Pro Phe Val
    1985                 1990                 1995

Thr His  Pro Gly Tyr Asp Thr  Gly Asn Gly Ile Gln  Leu Pro Gly
    2000                 2005                 2010

Thr Ser  Gly Gln Gln Pro Ser  Val Gly Gln Gln Met  Ile Phe Glu
    2015                 2020                 2025

Glu His  Gly Phe Arg Arg Thr  Thr Pro Pro Thr Thr  Ala Thr Pro
    2030                 2035                 2040

Ile Arg  His Arg Pro Arg Pro  Tyr Pro Pro Asn Val  Gly Gln Glu
    2045                 2050                 2055

Ala Leu  Ser Gln Thr Thr Ile  Ser Trp Ala Pro Phe  Gln Asp Thr
    2060                 2065                 2070

Ser Glu  Tyr Ile Ile Ser Cys  His Pro Val Gly Thr  Asp Glu Glu
    2075                 2080                 2085

Pro Leu  Gln Phe Arg Val Pro  Gly Thr Ser Thr Ser  Ala Thr Leu
    2090                 2095                 2100
```

```
Thr Gly  Leu Thr Arg Gly Ala  Thr Tyr Asn Ile Ile  Val Glu Ala
    2105                 2110                 2115

Leu Lys  Asp Gln Gln Arg His  Lys Val Arg Glu Glu  Val Val Thr
    2120                 2125                 2130

Val Gly  Asn Ser Val Asn Glu  Gly Leu Asn Gln Pro  Thr Asp Asp
    2135                 2140                 2145

Ser Cys  Phe Asp Pro Tyr Thr  Val Ser His Tyr Ala  Val Gly Asp
    2150                 2155                 2160

Glu Trp  Glu Arg Met Ser Glu  Ser Gly Phe Lys Leu  Leu Cys Gln
    2165                 2170                 2175

Cys Leu  Gly Phe Gly Ser Gly  His Phe Arg Cys Asp  Ser Ser Arg
    2180                 2185                 2190

Trp Cys  His Asp Asn Gly Val  Asn Tyr Lys Ile Gly  Glu Lys Trp
    2195                 2200                 2205

Asp Arg  Gln Gly Glu Asn Gly  Gln Met Met Ser Cys  Thr Cys Leu
    2210                 2215                 2220

Gly Asn  Gly Lys Gly Glu Phe  Lys Cys Asp Pro His  Glu Ala Thr
    2225                 2230                 2235

Cys Tyr  Asp Asp Gly Lys Thr  Tyr His Val Gly Glu  Gln Trp Gln
    2240                 2245                 2250

Lys Glu  Tyr Leu Gly Ala Ile  Cys Ser Cys Thr Cys  Phe Gly Gly
    2255                 2260                 2265

Gln Arg  Gly Trp Arg Cys Asp  Asn Cys Arg Arg Pro  Gly Gly Glu
    2270                 2275                 2280

Pro Ser  Pro Glu Gly Thr Thr  Gly Gln Ser Tyr Asn  Gln Tyr Ser
    2285                 2290                 2295

Gln Arg  Tyr His Gln Arg Thr  Asn Thr Asn Val Asn  Cys Pro Ile
    2300                 2305                 2310

Glu Cys  Phe Met Pro Leu Asp  Val Gln Ala Asp Arg  Glu Asp Ser
    2315                 2320                 2325

Arg Glu
    2330


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<211>  2296
<212>  PRT
<213>  Homo sapiens
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<400> 99

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Met Leu Arg Gly Pro Gly Pro Gly Leu Leu Leu Leu Ala Val Gln Cys
1               5                  10                  15

Leu Gly Thr Ala Val Pro Ser Thr Gly Ala Ser Lys Ser Lys Arg Gln
            20                  25                  30

Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val Ala Val Ser Gln Ser
        35                  40                  45

Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr Gln Ile Asn Gln Gln
    50                  55                  60

Trp Glu Arg Thr Tyr Leu Gly Asn Ala Leu Val Cys Thr Cys Tyr Gly
65                  70                  75                  80

Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro Glu Ala Glu Glu Thr
                85                  90                  95

Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg Val Gly Asp Thr Tyr
            100                 105                 110

Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys Thr Cys Ile Gly Ala
        115                 120                 125

Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn Arg Cys His Glu Gly
    130                 135                 140

Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg Arg Pro His Glu Thr
145                 150                 155                 160

Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly Asn Gly Lys Gly Glu
                165                 170                 175

Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe Asp His Ala Ala Gly
            180                 185                 190

Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys Pro Tyr Gln Gly Trp
        195                 200                 205

Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly Ser Gly Arg Ile Thr
    210                 215                 220

Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp Thr Arg Thr Ser Tyr
225                 230                 235                 240

Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn Arg Gly Asn Leu Leu
                245                 250                 255

Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu Trp Lys Cys Glu Arg
```

```
            260                 265                 270

His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser Gly Pro Phe Thr Asp
        275                 280                 285

Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His Pro Gln Pro Pro Pro
    290                 295                 300

Tyr Gly His Cys Val Thr Asp Ser Gly Val Val Tyr Ser Val Gly Met
305                 310                 315                 320

Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met Leu Cys Thr Cys Leu
                325                 330                 335

Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val Thr Gln Thr Tyr Gly
            340                 345                 350

Gly Asn Ser Asn Gly Glu Pro Cys Val Leu Pro Phe Thr Tyr Asn Gly
        355                 360                 365

Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg Gln Asp Gly His Leu
    370                 375                 380

Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp Gln Lys Tyr Ser Phe
385                 390                 395                 400

Cys Thr Asp His Thr Val Leu Val Gln Thr Arg Gly Gly Asn Ser Asn
                405                 410                 415

Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn Asn His Asn Tyr Thr
            420                 425                 430

Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met Lys Trp Cys Gly Thr
        435                 440                 445

Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly Phe Cys Pro Met Ala
    450                 455                 460

Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly Val Met Tyr Arg Ile
465                 470                 475                 480

Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly His Met Met Arg Cys
                485                 490                 495

Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr Cys Ile Ala Tyr Ser
            500                 505                 510

Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile Thr Tyr Asn Val Asn
        515                 520                 525

Asp Thr Phe His Lys Arg His Glu Glu Gly His Met Leu Asn Cys Thr
```

```
    530                 535                 540

Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys Asp Pro Val Asp Gln
545                 550                 555                 560

Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln Ile Gly Asp Ser Trp
                565                 570                 575

Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys Tyr Cys Tyr Gly Arg
            580                 585                 590

Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln Thr Tyr Pro Ser Ser
        595                 600                 605

Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr Pro Ser Gln Pro Asn
    610                 615                 620

Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro Ser His Ile Ser Lys
625                 630                 635                 640

Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val Gly Arg Trp Lys Glu
                645                 650                 655

Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr Ile Lys Gly Leu Lys
            660                 665                 670

Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser Ile Gln Gln Tyr Gly
        675                 680                 685

His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr Thr Ser Thr Ser Thr
    690                 695                 700

Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr Thr Pro Phe Ser Pro
705                 710                 715                 720

Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile Thr Ala Ser Ser Phe
                725                 730                 735

Val Val Ser Trp Val Ser Ala Ser Asp Thr Val Ser Gly Phe Arg Val
            740                 745                 750

Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro Gln Tyr Leu Asp Leu
        755                 760                 765

Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp Leu Leu Pro Gly Arg
    770                 775                 780

Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu Asp Gly Glu Gln Ser
785                 790                 795                 800

Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro Asp Ala Pro Pro Asp
```

805 810 815

Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile Val Val Arg Trp Ser
820 825 830

Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile Val Tyr Ser Pro Ser
835 840 845

Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro Glu Thr Ala Asn Ser
850 855 860

Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln Tyr Asn Ile Thr Ile
865 870 875 880

Tyr Ala Val Glu Glu Asn Gln Glu Ser Thr Pro Val Val Ile Gln Gln
885 890 895

Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val Pro Ser Pro Arg Asp
900 905 910

Leu Gln Phe Val Glu Val Thr Asp Val Lys Val Thr Ile Met Trp Thr
915 920 925

Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val Asp Val Ile Pro Val
930 935 940

Asn Leu Pro Gly Glu His Gly Gln Arg Leu Pro Ile Ser Arg Asn Thr
945 950 955 960

Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val Thr Tyr Tyr Phe Lys
965 970 975

Val Phe Ala Val Ser His Gly Arg Glu Ser Lys Pro Leu Thr Ala Gln
980 985 990

Gln Thr Thr Lys Leu Asp Ala Pro Thr Asn Leu Gln Phe Val Asn Glu
995 1000 1005

Thr Asp Ser Thr Val Leu Val Arg Trp Thr Pro Pro Arg Ala Gln
1010 1015 1020

Ile Thr Gly Tyr Arg Leu Thr Val Gly Leu Thr Arg Arg Gly Gln
1025 1030 1035

Pro Arg Gln Tyr Asn Val Gly Pro Ser Val Ser Lys Tyr Pro Leu
1040 1045 1050

Arg Asn Leu Gln Pro Ala Ser Glu Tyr Thr Val Ser Leu Val Ala
1055 1060 1065

Ile Lys Gly Asn Gln Glu Ser Pro Lys Ala Thr Gly Val Phe Thr

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    1070                1075                1080

Thr Leu  Gln Pro Gly Ser Ser  Ile Pro Pro Tyr Asn  Thr Glu Val
    1085                1090                1095

Thr Glu  Thr Thr Ile Val Ile  Thr Trp Thr Pro Ala  Pro Arg Ile
    1100                1105                1110

Gly Phe  Lys Leu Gly Val Arg  Pro Ser Gln Gly Gly  Glu Ala Pro
    1115                1120                1125

Arg Glu  Val Thr Ser Asp Ser  Gly Ser Ile Val Val  Ser Gly Leu
    1130                1135                1140

Thr Pro  Gly Val Glu Tyr Val  Tyr Thr Ile Gln Val  Leu Arg Asp
    1145                1150                1155

Gly Gln  Glu Arg Asp Ala Pro  Ile Val Asn Lys Val  Val Thr Pro
    1160                1165                1170

Leu Ser  Pro Pro Thr Asn Leu  His Leu Glu Ala Asn  Pro Asp Thr
    1175                1180                1185

Gly Val  Leu Thr Val Ser Trp  Glu Arg Ser Thr Thr  Pro Asp Ile
    1190                1195                1200

Thr Gly  Tyr Arg Ile Thr Thr  Thr Pro Thr Asn Gly  Gln Gln Gly
    1205                1210                1215

Asn Ser  Leu Glu Glu Val Val  His Ala Asp Gln Ser  Ser Cys Thr
    1220                1225                1230

Phe Asp  Asn Leu Ser Pro Gly  Leu Glu Tyr Asn Val  Ser Val Tyr
    1235                1240                1245

Thr Val  Lys Asp Asp Lys Glu  Ser Val Pro Ile Ser  Asp Thr Ile
    1250                1255                1260

Ile Pro  Ala Val Pro Pro Pro  Thr Asp Leu Arg Phe  Thr Asn Ile
    1265                1270                1275

Gly Pro  Asp Thr Met Arg Val  Thr Trp Ala Pro Pro  Pro Ser Ile
    1280                1285                1290

Asp Leu  Thr Asn Phe Leu Val  Arg Tyr Ser Pro Val  Lys Asn Glu
    1295                1300                1305

Glu Asp  Val Ala Glu Leu Ser  Ile Ser Pro Ser Asp  Asn Ala Val
    1310                1315                1320

Val Leu  Thr Asn Leu Leu Pro  Gly Thr Glu Tyr Val  Val Ser Val
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1325 1330 1335

Ser Ser Val Tyr Glu Gln His Glu Ser Thr Pro Leu Arg Gly Arg
1340 1345 1350

Gln Lys Thr Gly Leu Asp Ser Pro Thr Gly Ile Asp Phe Ser Asp
1355 1360 1365

Ile Thr Ala Asn Ser Phe Thr Val His Trp Ile Ala Pro Arg Ala
1370 1375 1380

Thr Ile Thr Gly Tyr Arg Ile Arg His His Pro Glu His Phe Ser
1385 1390 1395

Gly Arg Pro Arg Glu Asp Arg Val Pro His Ser Arg Asn Ser Ile
1400 1405 1410

Thr Leu Thr Asn Leu Thr Pro Gly Thr Glu Tyr Val Val Ser Ile
1415 1420 1425

Val Ala Leu Asn Gly Arg Glu Glu Ser Pro Leu Leu Ile Gly Gln
1430 1435 1440

Gln Ser Thr Val Ser Asp Val Pro Arg Asp Leu Glu Val Val Ala
1445 1450 1455

Ala Thr Pro Thr Ser Leu Leu Ile Ser Trp Asp Ala Pro Ala Val
1460 1465 1470

Thr Val Arg Tyr Tyr Arg Ile Thr Tyr Gly Glu Thr Gly Gly Asn
1475 1480 1485

Ser Pro Val Gln Glu Phe Thr Val Pro Gly Ser Lys Ser Thr Ala
1490 1495 1500

Thr Ile Ser Gly Leu Lys Pro Gly Val Asp Tyr Thr Ile Thr Val
1505 1510 1515

Tyr Ala Val Thr Gly Arg Gly Asp Ser Pro Ala Ser Ser Lys Pro
1520 1525 1530

Ile Ser Ile Asn Tyr Arg Thr Glu Ile Asp Lys Pro Ser Gln Met
1535 1540 1545

Gln Val Thr Asp Val Gln Asp Asn Ser Ile Ser Val Lys Trp Leu
1550 1555 1560

Pro Ser Ser Ser Pro Val Thr Gly Tyr Arg Val Thr Thr Thr Pro
1565 1570 1575

Lys Asn Gly Pro Gly Pro Thr Lys Thr Lys Thr Ala Gly Pro Asp

1580 1585 1590

Gln Thr Glu Met Thr Ile Glu Gly Leu Gln Pro Thr Val Glu Tyr
1595 1600 1605

Val Val Ser Val Tyr Ala Gln Asn Pro Ser Gly Glu Ser Gln Pro
1610 1615 1620

Leu Val Gln Thr Ala Val Thr Thr Ile Pro Ala Pro Thr Asp Leu
1625 1630 1635

Lys Phe Thr Gln Val Thr Pro Thr Ser Leu Ser Ala Gln Trp Thr
1640 1645 1650

Pro Pro Asn Val Gln Leu Thr Gly Tyr Arg Val Arg Val Thr Pro
1655 1660 1665

Lys Glu Lys Thr Gly Pro Met Lys Glu Ile Asn Leu Ala Pro Asp
1670 1675 1680

Ser Ser Ser Val Val Val Ser Gly Leu Met Val Ala Thr Lys Tyr
1685 1690 1695

Glu Val Ser Val Tyr Ala Leu Lys Asp Thr Leu Thr Ser Arg Pro
1700 1705 1710

Ala Gln Gly Val Val Thr Thr Leu Glu Asn Val Ser Pro Pro Arg
1715 1720 1725

Arg Ala Arg Val Thr Asp Ala Thr Glu Thr Thr Ile Thr Ile Ser
1730 1735 1740

Trp Arg Thr Lys Thr Glu Thr Ile Thr Gly Phe Gln Val Asp Ala
1745 1750 1755

Val Pro Ala Asn Gly Gln Thr Pro Ile Gln Arg Thr Ile Lys Pro
1760 1765 1770

Asp Val Arg Ser Tyr Thr Ile Thr Gly Leu Gln Pro Gly Thr Asp
1775 1780 1785

Tyr Lys Ile Tyr Leu Tyr Thr Leu Asn Asp Asn Ala Arg Ser Ser
1790 1795 1800

Pro Val Val Ile Asp Ala Ser Thr Ala Ile Asp Ala Pro Ser Asn
1805 1810 1815

Leu Arg Phe Leu Ala Thr Thr Pro Asn Ser Leu Leu Val Ser Trp
1820 1825 1830

Gln Pro Pro Arg Ala Arg Ile Thr Gly Tyr Ile Ile Lys Tyr Glu

1835 1840 1845

Lys Pro Gly Ser Pro Pro Arg Glu Val Val Pro Arg Pro Arg Pro
1850 1855 1860

Gly Val Thr Glu Ala Thr Ile Thr Gly Leu Glu Pro Gly Thr Glu
1865 1870 1875

Tyr Thr Ile Tyr Val Ile Ala Leu Lys Asn Asn Gln Lys Ser Glu
1880 1885 1890

Pro Leu Ile Gly Arg Lys Lys Thr Asp Glu Leu Pro Gln Leu Val
1895 1900 1905

Thr Leu Pro His Pro Asn Leu His Gly Pro Glu Ile Leu Asp Val
1910 1915 1920

Pro Ser Thr Val Gln Lys Thr Pro Phe Val Thr His Pro Gly Tyr
1925 1930 1935

Asp Thr Gly Asn Gly Ile Gln Leu Pro Gly Thr Ser Gly Gln Gln
1940 1945 1950

Pro Ser Val Gly Gln Gln Met Ile Phe Glu Glu His Gly Phe Arg
1955 1960 1965

Arg Thr Thr Pro Pro Thr Thr Ala Thr Pro Ile Arg His Arg Pro
1970 1975 1980

Arg Pro Tyr Pro Pro Asn Val Gly Glu Glu Ile Gln Ile Gly His
1985 1990 1995

Ile Pro Arg Glu Asp Val Asp Tyr His Leu Tyr Pro His Gly Pro
2000 2005 2010

Gly Leu Asn Pro Asn Ala Ser Thr Gly Gln Glu Ala Leu Ser Gln
2015 2020 2025

Thr Thr Ile Ser Trp Ala Pro Phe Gln Asp Thr Ser Glu Tyr Ile
2030 2035 2040

Ile Ser Cys His Pro Val Gly Thr Asp Glu Glu Pro Leu Gln Phe
2045 2050 2055

Arg Val Pro Gly Thr Ser Thr Ser Ala Thr Leu Thr Gly Leu Thr
2060 2065 2070

Arg Gly Ala Thr Tyr Asn Ile Ile Val Glu Ala Leu Lys Asp Gln
2075 2080 2085

Gln Arg His Lys Val Arg Glu Glu Val Val Thr Val Gly Asn Ser

2090 2095 2100

Val Asn Glu Gly Leu Asn Gln Pro Thr Asp Asp Ser Cys Phe Asp
2105 2110 2115

Pro Tyr Thr Val Ser His Tyr Ala Val Gly Asp Glu Trp Glu Arg
2120 2125 2130

Met Ser Glu Ser Gly Phe Lys Leu Leu Cys Gln Cys Leu Gly Phe
2135 2140 2145

Gly Ser Gly His Phe Arg Cys Asp Ser Ser Arg Trp Cys His Asp
2150 2155 2160

Asn Gly Val Asn Tyr Lys Ile Gly Glu Lys Trp Asp Arg Gln Gly
2165 2170 2175

Glu Asn Gly Gln Met Met Ser Cys Thr Cys Leu Gly Asn Gly Lys
2180 2185 2190

Gly Glu Phe Lys Cys Asp Pro His Glu Ala Thr Cys Tyr Asp Asp
2195 2200 2205

Gly Lys Thr Tyr His Val Gly Glu Gln Trp Gln Lys Glu Tyr Leu
2210 2215 2220

Gly Ala Ile Cys Ser Cys Thr Cys Phe Gly Gly Gln Arg Gly Trp
2225 2230 2235

Arg Cys Asp Asn Cys Arg Arg Pro Gly Gly Glu Pro Ser Pro Glu
2240 2245 2250

Gly Thr Thr Gly Gln Ser Tyr Asn Gln Tyr Ser Gln Arg Tyr His
2255 2260 2265

Gln Arg Thr Asn Thr Asn Val Asn Cys Pro Ile Glu Cys Phe Met
2270 2275 2280

Pro Leu Asp Val Gln Ala Asp Arg Glu Asp Ser Arg Glu
2285 2290 2295

<210> 100
<211> 2176
<212> PRT
<213> Homo sapiens

<400> 100

Met Leu Arg Gly Pro Gly Pro Gly Leu Leu Leu Leu Ala Val Gln Cys
1 5 10 15

Leu Gly Thr Ala Val Pro Ser Thr Gly Ala Ser Lys Ser Lys Arg Gln
20 25 30

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Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val Ala Val Ser Gln Ser
        35                  40                  45

Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr Gln Ile Asn Gln Gln
    50                  55                  60

Trp Glu Arg Thr Tyr Leu Gly Asn Ala Leu Val Cys Thr Cys Tyr Gly
65                  70                  75                  80

Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro Glu Ala Glu Glu Thr
                85                  90                  95

Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg Val Gly Asp Thr Tyr
            100                 105                 110

Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys Thr Cys Ile Gly Ala
        115                 120                 125

Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn Arg Cys His Glu Gly
    130                 135                 140

Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg Arg Pro His Glu Thr
145                 150                 155                 160

Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly Asn Gly Lys Gly Glu
                165                 170                 175

Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe Asp His Ala Ala Gly
            180                 185                 190

Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys Pro Tyr Gln Gly Trp
        195                 200                 205

Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly Ser Gly Arg Ile Thr
    210                 215                 220

Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp Thr Arg Thr Ser Tyr
225                 230                 235                 240

Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn Arg Gly Asn Leu Leu
                245                 250                 255

Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu Trp Lys Cys Glu Arg
            260                 265                 270

His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser Gly Pro Phe Thr Asp
        275                 280                 285

Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His Pro Gln Pro Pro Pro
    290                 295                 300
```

```
Tyr Gly His Cys Val Thr Asp Ser Gly Val Val Tyr Ser Val Gly Met
305                 310                 315                 320

Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met Leu Cys Thr Cys Leu
                325                 330                 335

Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val Thr Gln Thr Tyr Gly
            340                 345                 350

Gly Asn Ser Asn Gly Glu Pro Cys Val Leu Pro Phe Thr Tyr Asn Gly
        355                 360                 365

Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg Gln Asp Gly His Leu
    370                 375                 380

Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp Gln Lys Tyr Ser Phe
385                 390                 395                 400

Cys Thr Asp His Thr Val Leu Val Gln Thr Arg Gly Gly Asn Ser Asn
                405                 410                 415

Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn Asn His Asn Tyr Thr
            420                 425                 430

Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met Lys Trp Cys Gly Thr
        435                 440                 445

Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly Phe Cys Pro Met Ala
    450                 455                 460

Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly Val Met Tyr Arg Ile
465                 470                 475                 480

Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly His Met Met Arg Cys
                485                 490                 495

Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr Cys Ile Ala Tyr Ser
            500                 505                 510

Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile Thr Tyr Asn Val Asn
        515                 520                 525

Asp Thr Phe His Lys Arg His Glu Glu Gly His Met Leu Asn Cys Thr
    530                 535                 540

Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys Asp Pro Val Asp Gln
545                 550                 555                 560

Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln Ile Gly Asp Ser Trp
                565                 570                 575
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Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys Tyr Cys Tyr Gly Arg
            580                 585                 590

Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln Thr Tyr Pro Ser Ser
        595                 600                 605

Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr Pro Ser Gln Pro Asn
    610                 615                 620

Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro Ser His Ile Ser Lys
625                 630                 635                 640

Tyr Ile Leu Arg Trp Arg Pro Lys Asn Ser Val Gly Arg Trp Lys Glu
                645                 650                 655

Ala Thr Ile Pro Gly His Leu Asn Ser Tyr Thr Ile Lys Gly Leu Lys
            660                 665                 670

Pro Gly Val Val Tyr Glu Gly Gln Leu Ile Ser Ile Gln Gln Tyr Gly
        675                 680                 685

His Gln Glu Val Thr Arg Phe Asp Phe Thr Thr Thr Ser Thr Ser Thr
    690                 695                 700

Pro Val Thr Ser Asn Thr Val Thr Gly Glu Thr Thr Pro Phe Ser Pro
705                 710                 715                 720

Leu Val Ala Thr Ser Glu Ser Val Thr Glu Ile Thr Ala Ser Ser Phe
                725                 730                 735

Val Val Ser Trp Val Ser Ala Ser Asp Thr Val Ser Gly Phe Arg Val
            740                 745                 750

Glu Tyr Glu Leu Ser Glu Glu Gly Asp Glu Pro Gln Tyr Leu Asp Leu
        755                 760                 765

Pro Ser Thr Ala Thr Ser Val Asn Ile Pro Asp Leu Leu Pro Gly Arg
    770                 775                 780

Lys Tyr Ile Val Asn Val Tyr Gln Ile Ser Glu Asp Gly Glu Gln Ser
785                 790                 795                 800

Leu Ile Leu Ser Thr Ser Gln Thr Thr Ala Pro Asp Ala Pro Pro Asp
                805                 810                 815

Pro Thr Val Asp Gln Val Asp Asp Thr Ser Ile Val Val Arg Trp Ser
            820                 825                 830

Arg Pro Gln Ala Pro Ile Thr Gly Tyr Arg Ile Val Tyr Ser Pro Ser
        835                 840                 845
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Val Glu Gly Ser Ser Thr Glu Leu Asn Leu Pro Glu Thr Ala Asn Ser
    850                 855                 860

Val Thr Leu Ser Asp Leu Gln Pro Gly Val Gln Tyr Asn Ile Thr Ile
865                 870                 875                 880

Tyr Ala Val Glu Glu Asn Gln Glu Ser Thr Pro Val Val Ile Gln Gln
                885                 890                 895

Glu Thr Thr Gly Thr Pro Arg Ser Asp Thr Val Pro Ser Pro Arg Asp
            900                 905                 910

Leu Gln Phe Val Glu Val Thr Asp Val Lys Val Thr Ile Met Trp Thr
        915                 920                 925

Pro Pro Glu Ser Ala Val Thr Gly Tyr Arg Val Asp Val Ile Pro Val
    930                 935                 940

Asn Leu Pro Gly Glu His Gly Gln Arg Leu Pro Ile Ser Arg Asn Thr
945                 950                 955                 960

Phe Ala Glu Val Thr Gly Leu Ser Pro Gly Val Thr Tyr Tyr Phe Lys
                965                 970                 975

Val Phe Ala Val Ser His Gly Arg Glu Ser Lys Pro Leu Thr Ala Gln
            980                 985                 990

Gln Thr Thr Lys Leu Asp Ala Pro  Thr Asn Leu Gln Phe  Val Asn Glu
        995                 1000                1005

Thr Asp  Ser Thr Val Leu Val  Arg Trp Thr Pro Pro  Arg Ala Gln
    1010                1015                1020

Ile Thr  Gly Tyr Arg Leu Thr  Val Gly Leu Thr Arg  Arg Gly Gln
    1025                1030                1035

Pro Arg  Gln Tyr Asn Val Gly  Pro Ser Val Ser Lys  Tyr Pro Leu
    1040                1045                1050

Arg Asn  Leu Gln Pro Ala Ser  Glu Tyr Thr Val Ser  Leu Val Ala
    1055                1060                1065

Ile Lys  Gly Asn Gln Glu Ser  Pro Lys Ala Thr Gly  Val Phe Thr
    1070                1075                1080

Thr Leu  Gln Pro Gly Ser Ser  Ile Pro Pro Tyr Asn  Thr Glu Val
    1085                1090                1095

Thr Glu  Thr Thr Ile Val Ile  Thr Trp Thr Pro Ala  Pro Arg Ile
    1100                1105                1110
```

```
Gly Phe  Lys Leu Gly Val Arg  Pro Ser Gln Gly Gly  Glu Ala Pro
    1115                1120                1125

Arg Glu  Val Thr Ser Asp Ser  Gly Ser Ile Val Val  Ser Gly Leu
    1130                1135                1140

Thr Pro  Gly Val Glu Tyr Val  Tyr Thr Ile Gln Val  Leu Arg Asp
    1145                1150                1155

Gly Gln  Glu Arg Asp Ala Pro  Ile Val Asn Lys Val  Val Thr Pro
    1160                1165                1170

Leu Ser  Pro Pro Thr Asn Leu  His Leu Glu Ala Asn  Pro Asp Thr
    1175                1180                1185

Gly Val  Leu Thr Val Ser Trp  Glu Arg Ser Thr Thr  Pro Asp Ile
    1190                1195                1200

Thr Gly  Tyr Arg Ile Thr Thr  Thr Pro Thr Asn Gly  Gln Gln Gly
    1205                1210                1215

Asn Ser  Leu Glu Glu Val Val  His Ala Asp Gln Ser  Ser Cys Thr
    1220                1225                1230

Phe Asp  Asn Leu Ser Pro Gly  Leu Glu Tyr Asn Val  Ser Val Tyr
    1235                1240                1245

Thr Val  Lys Asp Asp Lys Glu  Ser Val Pro Ile Ser  Asp Thr Ile
    1250                1255                1260

Ile Pro  Ala Val Pro Pro Pro  Thr Asp Leu Arg Phe  Thr Asn Ile
    1265                1270                1275

Gly Pro  Asp Thr Met Arg Val  Thr Trp Ala Pro Pro  Pro Ser Ile
    1280                1285                1290

Asp Leu  Thr Asn Phe Leu Val  Arg Tyr Ser Pro Val  Lys Asn Glu
    1295                1300                1305

Glu Asp  Val Ala Glu Leu Ser  Ile Ser Pro Ser Asp  Asn Ala Val
    1310                1315                1320

Val Leu  Thr Asn Leu Leu Pro  Gly Thr Glu Tyr Val  Val Ser Val
    1325                1330                1335

Ser Ser  Val Tyr Glu Gln His  Glu Ser Thr Pro Leu  Arg Gly Arg
    1340                1345                1350

Gln Lys  Thr Gly Leu Asp Ser  Pro Thr Gly Ile Asp  Phe Ser Asp
    1355                1360                1365
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```
Ile Thr  Ala Asn Ser Phe Thr  Val His Trp Ile Ala  Pro Arg Ala
    1370                1375                1380

Thr Ile  Thr Gly Tyr Arg Ile  Arg His His Pro Glu  His Phe Ser
    1385                1390                1395

Gly Arg  Pro Arg Glu Asp Arg  Val Pro His Ser Arg  Asn Ser Ile
    1400                1405                1410

Thr Leu  Thr Asn Leu Thr Pro  Gly Thr Glu Tyr Val  Val Ser Ile
    1415                1420                1425

Val Ala  Leu Asn Gly Arg Glu  Glu Ser Pro Leu Leu  Ile Gly Gln
    1430                1435                1440

Gln Ser  Thr Val Ser Asp Val  Pro Arg Asp Leu Glu  Val Val Ala
    1445                1450                1455

Ala Thr  Pro Thr Ser Leu Leu  Ile Ser Trp Asp Ala  Pro Ala Val
    1460                1465                1470

Thr Val  Arg Tyr Tyr Arg Ile  Thr Tyr Gly Glu Thr  Gly Gly Asn
    1475                1480                1485

Ser Pro  Val Gln Glu Phe Thr  Val Pro Gly Ser Lys  Ser Thr Ala
    1490                1495                1500

Thr Ile  Ser Gly Leu Lys Pro  Gly Val Asp Tyr Thr  Ile Thr Val
    1505                1510                1515

Tyr Ala  Val Thr Gly Arg Gly  Asp Ser Pro Ala Ser  Ser Lys Pro
    1520                1525                1530

Ile Ser  Ile Asn Tyr Arg Thr  Glu Ile Asp Lys Pro  Ser Gln Met
    1535                1540                1545

Gln Val  Thr Asp Val Gln Asp  Asn Ser Ile Ser Val  Lys Trp Leu
    1550                1555                1560

Pro Ser  Ser Ser Pro Val Thr  Gly Tyr Arg Val Thr  Thr Thr Pro
    1565                1570                1575

Lys Asn  Gly Pro Gly Pro Thr  Lys Thr Lys Thr Ala  Gly Pro Asp
    1580                1585                1590

Gln Thr  Glu Met Thr Ile Glu  Gly Leu Gln Pro Thr  Val Glu Tyr
    1595                1600                1605

Val Val  Ser Val Tyr Ala Gln  Asn Pro Ser Gly Glu  Ser Gln Pro
    1610                1615                1620
```

```
Leu Val  Gln Thr Ala Val Thr  Thr Ile Pro Ala Pro  Thr Asp Leu
    1625                1630                1635

Lys Phe  Thr Gln Val Thr Pro  Thr Ser Leu Ser Ala  Gln Trp Thr
    1640                1645                1650

Pro Pro  Asn Val Gln Leu Thr  Gly Tyr Arg Val Arg  Val Thr Pro
    1655                1660                1665

Lys Glu  Lys Thr Gly Pro Met  Lys Glu Ile Asn Leu  Ala Pro Asp
    1670                1675                1680

Ser Ser  Ser Val Val Val Ser  Gly Leu Met Val Ala  Thr Lys Tyr
    1685                1690                1695

Glu Val  Ser Val Tyr Ala Leu  Lys Asp Thr Leu Thr  Ser Arg Pro
    1700                1705                1710

Ala Gln  Gly Val Val Thr Thr  Leu Glu Asn Val Ser  Pro Pro Arg
    1715                1720                1725

Arg Ala  Arg Val Thr Asp Ala  Thr Glu Thr Thr Ile  Thr Ile Ser
    1730                1735                1740

Trp Arg  Thr Lys Thr Glu Thr  Ile Thr Gly Phe Gln  Val Asp Ala
    1745                1750                1755

Val Pro  Ala Asn Gly Gln Thr  Pro Ile Gln Arg Thr  Ile Lys Pro
    1760                1765                1770

Asp Val  Arg Ser Tyr Thr Ile  Thr Gly Leu Gln Pro  Gly Thr Asp
    1775                1780                1785

Tyr Lys  Ile Tyr Leu Tyr Thr  Leu Asn Asp Asn Ala  Arg Ser Ser
    1790                1795                1800

Pro Val  Val Ile Asp Ala Ser  Thr Ala Ile Asp Ala  Pro Ser Asn
    1805                1810                1815

Leu Arg  Phe Leu Ala Thr Thr  Pro Asn Ser Leu Leu  Val Ser Trp
    1820                1825                1830

Gln Pro  Pro Arg Ala Arg Ile  Thr Gly Tyr Ile Ile  Lys Tyr Glu
    1835                1840                1845

Lys Pro  Gly Ser Pro Pro Arg  Glu Val Val Pro Arg  Pro Arg Pro
    1850                1855                1860

Gly Val  Thr Glu Ala Thr Ile  Thr Gly Leu Glu Pro  Gly Thr Glu
    1865                1870                1875
```

```
Tyr Thr  Ile Tyr Val Ile Ala  Leu Lys Asn Asn Gln  Lys Ser Glu
    1880                1885                1890

Pro Leu  Ile Gly Arg Lys Lys  Thr Gly Gln Glu Ala  Leu Ser Gln
    1895                1900                1905

Thr Thr  Ile Ser Trp Ala Pro  Phe Gln Asp Thr Ser  Glu Tyr Ile
    1910                1915                1920

Ile Ser  Cys His Pro Val Gly  Thr Asp Glu Glu Pro  Leu Gln Phe
    1925                1930                1935

Arg Val  Pro Gly Thr Ser Thr  Ser Ala Thr Leu Thr  Gly Leu Thr
    1940                1945                1950

Arg Gly  Ala Thr Tyr Asn Ile  Ile Val Glu Ala Leu  Lys Asp Gln
    1955                1960                1965

Gln Arg  His Lys Val Arg Glu  Glu Val Val Thr Val  Gly Asn Ser
    1970                1975                1980

Val Asn  Glu Gly Leu Asn Gln  Pro Thr Asp Asp Ser  Cys Phe Asp
    1985                1990                1995

Pro Tyr  Thr Val Ser His Tyr  Ala Val Gly Asp Glu  Trp Glu Arg
    2000                2005                2010

Met Ser  Glu Ser Gly Phe Lys  Leu Leu Cys Gln Cys  Leu Gly Phe
    2015                2020                2025

Gly Ser  Gly His Phe Arg Cys  Asp Ser Ser Arg Trp  Cys His Asp
    2030                2035                2040

Asn Gly  Val Asn Tyr Lys Ile  Gly Glu Lys Trp Asp  Arg Gln Gly
    2045                2050                2055

Glu Asn  Gly Gln Met Met Ser  Cys Thr Cys Leu Gly  Asn Gly Lys
    2060                2065                2070

Gly Glu  Phe Lys Cys Asp Pro  His Glu Ala Thr Cys  Tyr Asp Asp
    2075                2080                2085

Gly Lys  Thr Tyr His Val Gly  Glu Gln Trp Gln Lys  Glu Tyr Leu
    2090                2095                2100

Gly Ala  Ile Cys Ser Cys Thr  Cys Phe Gly Gly Gln  Arg Gly Trp
    2105                2110                2115

Arg Cys  Asp Asn Cys Arg Arg  Pro Gly Gly Glu Pro  Ser Pro Glu
    2120                2125                2130
```

```
Gly Thr  Thr Gly Gln Ser Tyr  Asn Gln Tyr Ser Gln  Arg Tyr His
    2135                 2140                 2145


Gln Arg  Thr Asn Thr Asn Val  Asn Cys Pro Ile Glu  Cys Phe Met
    2150                 2155                 2160


Pro Leu  Asp Val Gln Ala Asp  Arg Glu Asp Ser Arg  Glu
    2165                 2170                 2175


<210>  101
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<212>  PRT
<213>  Homo sapiens

<400>  101

Met Leu Arg Gly Pro Gly Pro Gly Leu Leu Leu Leu Ala Val Gln Cys
1               5                   10                  15


Leu Gly Thr Ala Val Pro Ser Thr Gly Ala Ser Lys Ser Lys Arg Gln
            20                  25                  30


Ala Gln Gln Met Val Gln Pro Gln Ser Pro Val Ala Val Ser Gln Ser
        35                  40                  45


Lys Pro Gly Cys Tyr Asp Asn Gly Lys His Tyr Gln Ile Asn Gln Gln
    50                  55                  60


Trp Glu Arg Thr Tyr Leu Gly Asn Ala Leu Val Cys Thr Cys Tyr Gly
65                  70                  75                  80


Gly Ser Arg Gly Phe Asn Cys Glu Ser Lys Pro Glu Ala Glu Glu Thr
                85                  90                  95


Cys Phe Asp Lys Tyr Thr Gly Asn Thr Tyr Arg Val Gly Asp Thr Tyr
            100                 105                 110


Glu Arg Pro Lys Asp Ser Met Ile Trp Asp Cys Thr Cys Ile Gly Ala
        115                 120                 125


Gly Arg Gly Arg Ile Ser Cys Thr Ile Ala Asn Arg Cys His Glu Gly
    130                 135                 140


Gly Gln Ser Tyr Lys Ile Gly Asp Thr Trp Arg Arg Pro His Glu Thr
145                 150                 155                 160


Gly Gly Tyr Met Leu Glu Cys Val Cys Leu Gly Asn Gly Lys Gly Glu
                165                 170                 175


Trp Thr Cys Lys Pro Ile Ala Glu Lys Cys Phe Asp His Ala Ala Gly
            180                 185                 190
```

```
Thr Ser Tyr Val Val Gly Glu Thr Trp Glu Lys Pro Tyr Gln Gly Trp
        195                 200                 205

Met Met Val Asp Cys Thr Cys Leu Gly Glu Gly Ser Gly Arg Ile Thr
    210                 215                 220

Cys Thr Ser Arg Asn Arg Cys Asn Asp Gln Asp Thr Arg Thr Ser Tyr
225                 230                 235                 240

Arg Ile Gly Asp Thr Trp Ser Lys Lys Asp Asn Arg Gly Asn Leu Leu
                245                 250                 255

Gln Cys Ile Cys Thr Gly Asn Gly Arg Gly Glu Trp Lys Cys Glu Arg
            260                 265                 270

His Thr Ser Val Gln Thr Thr Ser Ser Gly Ser Gly Pro Phe Thr Asp
        275                 280                 285

Val Arg Ala Ala Val Tyr Gln Pro Gln Pro His Pro Gln Pro Pro Pro
    290                 295                 300

Tyr Gly His Cys Val Thr Asp Ser Gly Val Val Tyr Ser Val Gly Met
305                 310                 315                 320

Gln Trp Leu Lys Thr Gln Gly Asn Lys Gln Met Leu Cys Thr Cys Leu
                325                 330                 335

Gly Asn Gly Val Ser Cys Gln Glu Thr Ala Val Thr Gln Thr Tyr Gly
            340                 345                 350

Gly Asn Ser Asn Gly Glu Pro Cys Val Leu Pro Phe Thr Tyr Asn Gly
        355                 360                 365

Arg Thr Phe Tyr Ser Cys Thr Thr Glu Gly Arg Gln Asp Gly His Leu
    370                 375                 380

Trp Cys Ser Thr Thr Ser Asn Tyr Glu Gln Asp Gln Lys Tyr Ser Phe
385                 390                 395                 400

Cys Thr Asp His Thr Val Leu Val Gln Thr Arg Gly Gly Asn Ser Asn
                405                 410                 415

Gly Ala Leu Cys His Phe Pro Phe Leu Tyr Asn Asn His Asn Tyr Thr
            420                 425                 430

Asp Cys Thr Ser Glu Gly Arg Arg Asp Asn Met Lys Trp Cys Gly Thr
        435                 440                 445

Thr Gln Asn Tyr Asp Ala Asp Gln Lys Phe Gly Phe Cys Pro Met Ala
    450                 455                 460
```

```
Ala His Glu Glu Ile Cys Thr Thr Asn Glu Gly Val Met Tyr Arg Ile
465                 470                 475                 480


Gly Asp Gln Trp Asp Lys Gln His Asp Met Gly His Met Met Arg Cys
                485                 490                 495


Thr Cys Val Gly Asn Gly Arg Gly Glu Trp Thr Cys Ile Ala Tyr Ser
            500                 505                 510


Gln Leu Arg Asp Gln Cys Ile Val Asp Asp Ile Thr Tyr Asn Val Asn
        515                 520                 525


Asp Thr Phe His Lys Arg His Glu Glu Gly His Met Leu Asn Cys Thr
    530                 535                 540


Cys Phe Gly Gln Gly Arg Gly Arg Trp Lys Cys Asp Pro Val Asp Gln
545                 550                 555                 560


Cys Gln Asp Ser Glu Thr Gly Thr Phe Tyr Gln Ile Gly Asp Ser Trp
                565                 570                 575


Glu Lys Tyr Val His Gly Val Arg Tyr Gln Cys Tyr Cys Tyr Gly Arg
            580                 585                 590


Gly Ile Gly Glu Trp His Cys Gln Pro Leu Gln Thr Tyr Pro Ser Ser
        595                 600                 605


Ser Gly Pro Val Glu Val Phe Ile Thr Glu Thr Pro Ser Gln Pro Asn
    610                 615                 620


Ser His Pro Ile Gln Trp Asn Ala Pro Gln Pro Ser His Ile Ser Lys
625                 630                 635                 640


Tyr Ile Leu Arg Trp Arg Pro Val Ser Ile Pro Pro Arg Asn Leu Gly
                645                 650                 655


Tyr



<210>  102
<211>  478
<212>  PRT
<213>  Homo sapiens

<400>  102

Met Ala Pro Leu Arg Pro Leu Leu Ile Leu Ala Leu Leu Ala Trp Val
1               5                   10                  15


Ala Leu Ala Asp Gln Glu Ser Cys Lys Gly Arg Cys Thr Glu Gly Phe
            20                  25                  30
```

```
Asn Val Asp Lys Lys Cys Gln Cys Asp Glu Leu Cys Ser Tyr Tyr Gln
        35                  40                  45

Ser Cys Cys Thr Asp Tyr Thr Ala Glu Cys Lys Pro Gln Val Thr Arg
    50                  55                  60

Gly Asp Val Phe Thr Met Pro Glu Asp Glu Tyr Thr Val Tyr Asp Asp
65                  70                  75                  80

Gly Glu Glu Lys Asn Asn Ala Thr Val His Glu Gln Val Gly Gly Pro
                85                  90                  95

Ser Leu Thr Ser Asp Leu Gln Ala Gln Ser Lys Gly Asn Pro Glu Gln
            100                 105                 110

Thr Pro Val Leu Lys Pro Glu Glu Glu Ala Pro Ala Pro Glu Val Gly
        115                 120                 125

Ala Ser Lys Pro Glu Gly Ile Asp Ser Arg Pro Glu Thr Leu His Pro
    130                 135                 140

Gly Arg Pro Gln Pro Pro Ala Glu Glu Glu Leu Cys Ser Gly Lys Pro
145                 150                 155                 160

Phe Asp Ala Phe Thr Asp Leu Lys Asn Gly Ser Leu Phe Ala Phe Arg
                165                 170                 175

Gly Gln Tyr Cys Tyr Glu Leu Asp Glu Lys Ala Val Arg Pro Gly Tyr
            180                 185                 190

Pro Lys Leu Ile Arg Asp Val Trp Gly Ile Glu Gly Pro Ile Asp Ala
        195                 200                 205

Ala Phe Thr Arg Ile Asn Cys Gln Gly Lys Thr Tyr Leu Phe Lys Gly
    210                 215                 220

Ser Gln Tyr Trp Arg Phe Glu Asp Gly Val Leu Asp Pro Asp Tyr Pro
225                 230                 235                 240

Arg Asn Ile Ser Asp Gly Phe Asp Gly Ile Pro Asp Asn Val Asp Ala
                245                 250                 255

Ala Leu Ala Leu Pro Ala His Ser Tyr Ser Gly Arg Glu Arg Val Tyr
            260                 265                 270

Phe Phe Lys Gly Lys Gln Tyr Trp Glu Tyr Gln Phe Gln His Gln Pro
        275                 280                 285

Ser Gln Glu Glu Cys Glu Gly Ser Ser Leu Ser Ala Val Phe Glu His
    290                 295                 300
```

```
Phe Ala Met Met Gln Arg Asp Ser Trp Glu Asp Ile Phe Glu Leu Leu
305                 310                 315                 320

Phe Trp Gly Arg Thr Ser Ala Gly Thr Arg Gln Pro Gln Phe Ile Ser
                325                 330                 335

Arg Asp Trp His Gly Val Pro Gly Gln Val Asp Ala Ala Met Ala Gly
            340                 345                 350

Arg Ile Tyr Ile Ser Gly Met Ala Pro Arg Pro Ser Leu Ala Lys Lys
        355                 360                 365

Gln Arg Phe Arg His Arg Asn Arg Lys Gly Tyr Arg Ser Gln Arg Gly
    370                 375                 380

His Ser Arg Gly Arg Asn Gln Asn Ser Arg Arg Pro Ser Arg Ala Thr
385                 390                 395                 400

Trp Leu Ser Leu Phe Ser Ser Glu Glu Ser Asn Leu Gly Ala Asn Asn
                405                 410                 415

Tyr Asp Asp Tyr Arg Met Asp Trp Leu Val Pro Ala Thr Cys Glu Pro
            420                 425                 430

Ile Gln Ser Val Phe Phe Phe Ser Gly Asp Lys Tyr Tyr Arg Val Asn
        435                 440                 445

Leu Arg Thr Arg Arg Val Asp Thr Val Asp Pro Pro Tyr Pro Arg Ser
    450                 455                 460

Ile Ala Gln Tyr Trp Leu Gly Cys Pro Ala Pro Gly His Leu
465                 470                 475


<210>  103
<211>  1247
<212>  PRT
<213>  Homo sapiens

<400>  103

Met Leu Ala Ser Ser Ser Arg Ile Arg Ala Ala Trp Thr Arg Ala Leu
1               5                   10                  15

Leu Leu Pro Leu Leu Leu Ala Gly Pro Val Gly Cys Leu Ser Arg Gln
            20                  25                  30

Glu Leu Phe Pro Phe Gly Pro Gly Gln Gly Asp Leu Glu Leu Glu Asp
        35                  40                  45

Gly Asp Asp Phe Val Ser Pro Ala Leu Glu Leu Ser Gly Ala Leu Arg
    50                  55                  60

Phe Tyr Asp Arg Ser Asp Ile Asp Ala Val Tyr Val Thr Thr Asn Gly
```

65 70 75 80

Ile Ile Ala Thr Ser Glu Pro Pro Ala Lys Glu Ser His Pro Gly Leu
85 90 95

Phe Pro Pro Thr Phe Gly Ala Val Ala Pro Phe Leu Ala Asp Leu Asp
100 105 110

Thr Thr Asp Gly Leu Gly Lys Val Tyr Tyr Arg Glu Asp Leu Ser Pro
115 120 125

Ser Ile Thr Gln Arg Ala Ala Glu Cys Val His Arg Gly Phe Pro Glu
130 135 140

Ile Ser Phe Gln Pro Ser Ser Ala Val Val Val Thr Trp Glu Ser Val
145 150 155 160

Ala Pro Tyr Gln Gly Pro Ser Arg Asp Pro Asp Gln Lys Gly Lys Arg
165 170 175

Asn Thr Phe Gln Ala Val Leu Ala Ser Ser Asp Ser Ser Ser Tyr Ala
180 185 190

Ile Phe Leu Tyr Pro Glu Asp Gly Leu Gln Phe His Thr Thr Phe Ser
195 200 205

Lys Lys Glu Asn Asn Gln Val Pro Ala Val Val Ala Phe Ser Gln Gly
210 215 220

Ser Val Gly Phe Leu Trp Lys Ser Asn Gly Ala Tyr Asn Ile Phe Ala
225 230 235 240

Asn Asp Arg Glu Ser Val Glu Asn Leu Ala Lys Ser Ser Asn Ser Gly
245 250 255

Gln Gln Gly Val Trp Val Phe Glu Ile Gly Ser Pro Ala Thr Thr Asn
260 265 270

Gly Val Val Pro Ala Asp Val Ile Leu Gly Thr Glu Asp Gly Ala Glu
275 280 285

Tyr Asp Asp Glu Asp Glu Asp Tyr Asp Leu Ala Thr Thr Arg Leu Gly
290 295 300

Leu Glu Asp Val Gly Thr Thr Pro Phe Ser Tyr Lys Ala Leu Arg Arg
305 310 315 320

Gly Gly Ala Asp Thr Tyr Ser Val Pro Ser Val Leu Ser Pro Arg Arg
325 330 335

Ala Ala Thr Glu Arg Pro Leu Gly Pro Pro Thr Glu Arg Thr Arg Ser

```
            340                 345                 350

Phe Gln Leu Ala Val Glu Thr Phe His Gln Gln His Pro Gln Val Ile
        355                 360                 365

Asp Val Asp Glu Val Glu Glu Thr Gly Val Val Phe Ser Tyr Asn Thr
    370                 375                 380

Asp Ser Arg Gln Thr Cys Ala Asn Asn Arg His Gln Cys Ser Val His
385                 390                 395                 400

Ala Glu Cys Arg Asp Tyr Ala Thr Gly Phe Cys Cys Ser Cys Val Ala
                405                 410                 415

Gly Tyr Thr Gly Asn Gly Arg Gln Cys Val Ala Glu Gly Ser Pro Gln
            420                 425                 430

Arg Val Asn Gly Lys Val Lys Gly Arg Ile Phe Val Gly Ser Ser Gln
        435                 440                 445

Val Pro Ile Val Phe Glu Asn Thr Asp Leu His Ser Tyr Val Val Met
    450                 455                 460

Asn His Gly Arg Ser Tyr Thr Ala Ile Ser Thr Ile Pro Glu Thr Val
465                 470                 475                 480

Gly Tyr Ser Leu Leu Pro Leu Ala Pro Val Gly Gly Ile Ile Gly Trp
                485                 490                 495

Met Phe Ala Val Glu Gln Asp Gly Phe Lys Asn Gly Phe Ser Ile Thr
            500                 505                 510

Gly Gly Glu Phe Thr Arg Gln Ala Glu Val Thr Phe Val Gly His Pro
        515                 520                 525

Gly Asn Leu Val Ile Lys Gln Arg Phe Ser Gly Ile Asp Glu His Gly
    530                 535                 540

His Leu Thr Ile Asp Thr Glu Leu Glu Gly Arg Val Pro Gln Ile Pro
545                 550                 555                 560

Phe Gly Ser Ser Val His Ile Glu Pro Tyr Thr Glu Leu Tyr His Tyr
                565                 570                 575

Ser Thr Ser Val Ile Thr Ser Ser Ser Thr Arg Glu Tyr Thr Val Thr
            580                 585                 590

Glu Pro Glu Arg Asp Gly Ala Ser Pro Ser Arg Ile Tyr Thr Tyr Gln
        595                 600                 605

Trp Arg Gln Thr Ile Thr Phe Gln Glu Cys Val His Asp Asp Ser Arg
```

610 615 620

Pro Ala Leu Pro Ser Thr Gln Gln Leu Ser Val Asp Ser Val Phe Val
625 630 635 640

Leu Tyr Asn Gln Glu Glu Lys Ile Leu Arg Tyr Ala Leu Ser Asn Ser
645 650 655

Ile Gly Pro Val Arg Glu Gly Ser Pro Asp Ala Leu Gln Asn Pro Cys
660 665 670

Tyr Ile Gly Thr His Gly Cys Asp Thr Asn Ala Ala Cys Arg Pro Gly
675 680 685

Pro Arg Thr Gln Phe Thr Cys Glu Cys Ser Ile Gly Phe Arg Gly Asp
690 695 700

Gly Arg Thr Cys Tyr Asp Ile Asp Glu Cys Ser Glu Gln Pro Ser Val
705 710 715 720

Cys Gly Ser His Thr Ile Cys Asn Asn His Pro Gly Thr Phe Arg Cys
725 730 735

Glu Cys Val Glu Gly Tyr Gln Phe Ser Asp Glu Gly Thr Cys Val Ala
740 745 750

Val Val Asp Gln Arg Pro Ile Asn Tyr Cys Glu Thr Gly Leu His Asn
755 760 765

Cys Asp Ile Pro Gln Arg Ala Gln Cys Ile Tyr Thr Gly Gly Ser Ser
770 775 780

Tyr Thr Cys Ser Cys Leu Pro Gly Phe Ser Gly Asp Gly Gln Ala Cys
785 790 795 800

Gln Asp Val Asp Glu Cys Gln Pro Ser Arg Cys His Pro Asp Ala Phe
805 810 815

Cys Tyr Asn Thr Pro Gly Ser Phe Thr Cys Gln Cys Lys Pro Gly Tyr
820 825 830

Gln Gly Asp Gly Phe Arg Cys Val Pro Gly Glu Val Glu Lys Thr Arg
835 840 845

Cys Gln His Glu Arg Glu His Ile Leu Gly Ala Ala Gly Ala Thr Asp
850 855 860

Pro Gln Arg Pro Ile Pro Pro Gly Leu Phe Val Pro Glu Cys Asp Ala
865 870 875 880

His Gly His Tyr Ala Pro Thr Gln Cys His Gly Ser Thr Gly Tyr Cys

885 890 895

Trp Cys Val Asp Arg Asp Gly Arg Glu Val Glu Gly Thr Arg Thr Arg
900 905 910

Pro Gly Met Thr Pro Pro Cys Leu Ser Thr Val Ala Pro Pro Ile His
915 920 925

Gln Gly Pro Ala Val Pro Thr Ala Val Ile Pro Leu Pro Pro Gly Thr
930 935 940

His Leu Leu Phe Ala Gln Thr Gly Lys Ile Glu Arg Leu Pro Leu Glu
945 950 955 960

Gly Asn Thr Met Arg Lys Thr Glu Ala Lys Ala Phe Leu His Val Pro
965 970 975

Ala Lys Val Ile Ile Gly Leu Ala Phe Asp Cys Val Asp Lys Met Val
980 985 990

Tyr Trp Thr Asp Ile Thr Glu Pro Ser Ile Gly Arg Ala Ser Leu His
995 1000 1005

Gly Gly Glu Pro Thr Thr Ile Ile Arg Gln Asp Leu Gly Ser Pro
1010 1015 1020

Glu Gly Ile Ala Val Asp His Leu Gly Arg Asn Ile Phe Trp Thr
1025 1030 1035

Asp Ser Asn Leu Asp Arg Ile Glu Val Ala Lys Leu Asp Gly Thr
1040 1045 1050

Gln Arg Arg Val Leu Phe Glu Thr Asp Leu Val Asn Pro Arg Gly
1055 1060 1065

Ile Val Thr Asp Ser Val Arg Gly Asn Leu Tyr Trp Thr Asp Trp
1070 1075 1080

Asn Arg Asp Asn Pro Lys Ile Glu Thr Ser Tyr Met Asp Gly Thr
1085 1090 1095

Asn Arg Arg Ile Leu Val Gln Asp Asp Leu Gly Leu Pro Asn Gly
1100 1105 1110

Leu Thr Phe Asp Ala Phe Ser Ser Gln Leu Cys Trp Val Asp Ala
1115 1120 1125

Gly Thr Asn Arg Ala Glu Cys Leu Asn Pro Ser Gln Pro Ser Arg
1130 1135 1140

Arg Lys Ala Leu Glu Gly Leu Gln Tyr Pro Phe Ala Val Thr Ser

1145 1150 1155

Tyr Gly Lys Asn Leu Tyr Phe Thr Asp Trp Lys Met Asn Ser Val
1160 1165 1170

Val Ala Leu Asp Leu Ala Ile Ser Lys Glu Thr Asp Ala Phe Gln
1175 1180 1185

Pro His Lys Gln Thr Arg Leu Tyr Gly Ile Thr Thr Ala Leu Ser
1190 1195 1200

Gln Cys Pro Gln Gly His Asn Tyr Cys Ser Val Asn Asn Gly Gly
1205 1210 1215

Cys Thr His Leu Cys Leu Ala Thr Pro Gly Ser Arg Thr Cys Arg
1220 1225 1230

Cys Pro Asp Asn Thr Leu Gly Val Asp Cys Ile Glu Gln Lys
1235 1240 1245

<210> 104
<211> 3075
<212> PRT
<213> Homo sapiens

<400> 104

Met Arg Gly Gly Val Leu Leu Val Leu Leu Leu Cys Val Ala Ala Gln
1 5 10 15

Cys Arg Gln Arg Gly Leu Phe Pro Ala Ile Leu Asn Leu Ala Ser Asn
20 25 30

Ala His Ile Ser Thr Asn Ala Thr Cys Gly Glu Lys Gly Pro Glu Met
35 40 45

Phe Cys Lys Leu Val Glu His Val Pro Gly Arg Pro Val Arg Asn Pro
50 55 60

Gln Cys Arg Ile Cys Asp Gly Asn Ser Ala Asn Pro Arg Glu Arg His
65 70 75 80

Pro Ile Ser His Ala Ile Asp Gly Thr Asn Asn Trp Trp Gln Ser Pro
85 90 95

Ser Ile Gln Asn Gly Arg Glu Tyr His Trp Val Thr Ile Thr Leu Asp
100 105 110

Leu Arg Gln Val Phe Gln Val Ala Tyr Val Ile Ile Lys Ala Ala Asn
115 120 125

Ala Pro Arg Pro Gly Asn Trp Ile Leu Glu Arg Ser Leu Asp Gly Thr
130 135 140

```
Thr Phe Ser Pro Trp Gln Tyr Tyr Ala Val Ser Asp Ser Glu Cys Leu
145                 150                 155                 160

Ser Arg Tyr Asn Ile Thr Pro Arg Arg Gly Pro Pro Thr Tyr Arg Ala
                165                 170                 175

Asp Asp Glu Val Ile Cys Thr Ser Tyr Tyr Ser Arg Leu Val Pro Leu
            180                 185                 190

Glu His Gly Glu Ile His Thr Ser Leu Ile Asn Gly Arg Pro Ser Ala
        195                 200                 205

Asp Asp Leu Ser Pro Lys Leu Leu Glu Phe Thr Ser Ala Arg Tyr Ile
    210                 215                 220

Arg Leu Arg Leu Gln Arg Ile Arg Thr Leu Asn Ala Asp Leu Met Thr
225                 230                 235                 240

Leu Ser His Arg Glu Pro Lys Glu Leu Asp Pro Ile Val Thr Arg Arg
                245                 250                 255

Tyr Tyr Tyr Ser Ile Lys Asp Ile Ser Val Gly Gly Met Cys Ile Cys
            260                 265                 270

Tyr Gly His Ala Ser Ser Cys Pro Trp Asp Glu Thr Thr Lys Lys Leu
        275                 280                 285

Gln Cys Gln Cys Glu His Asn Thr Cys Gly Glu Ser Cys Asn Arg Cys
    290                 295                 300

Cys Pro Gly Tyr His Gln Gln Pro Trp Arg Pro Gly Thr Val Ser Ser
305                 310                 315                 320

Gly Asn Thr Cys Glu Ala Cys Asn Cys His Asn Lys Ala Lys Asp Cys
                325                 330                 335

Tyr Tyr Asp Glu Ser Val Ala Lys Gln Lys Lys Ser Leu Asn Thr Ala
            340                 345                 350

Gly Gln Phe Arg Gly Gly Gly Val Cys Ile Asn Cys Leu Gln Asn Thr
        355                 360                 365

Met Gly Ile Asn Cys Glu Thr Cys Ile Asp Gly Tyr Tyr Arg Pro His
    370                 375                 380

Lys Val Ser Pro Tyr Glu Asp Glu Pro Cys Arg Pro Cys Asn Cys Asp
385                 390                 395                 400

Pro Val Gly Ser Leu Ser Ser Val Cys Ile Lys Asp Asp Leu His Ser
                405                 410                 415
```

```
Asp Leu His Asn Gly Lys Gln Pro Gly Gln Cys Pro Cys Lys Glu Gly
            420                 425                 430

Tyr Thr Gly Glu Lys Cys Asp Arg Cys Gln Leu Gly Tyr Lys Asp Tyr
        435                 440                 445

Pro Thr Cys Val Ser Cys Gly Cys Asn Pro Val Gly Ser Ala Ser Asp
    450                 455                 460

Glu Pro Cys Thr Gly Pro Cys Val Cys Lys Glu Asn Val Glu Gly Lys
465                 470                 475                 480

Ala Cys Asp Arg Cys Lys Pro Gly Phe Tyr Asn Leu Lys Glu Lys Asn
                485                 490                 495

Pro Arg Gly Cys Ser Glu Cys Phe Cys Phe Gly Val Ser Asp Val Cys
            500                 505                 510

Ser Ser Leu Ser Trp Pro Val Gly Gln Val Asn Ser Met Ser Gly Trp
        515                 520                 525

Leu Val Thr Asp Leu Ile Ser Pro Arg Lys Ile Pro Ser Gln Gln Asp
    530                 535                 540

Ala Leu Gly Gly Arg His Gln Val Ser Ile Asn Asn Thr Ala Val Met
545                 550                 555                 560

Gln Arg Leu Ala Pro Lys Tyr Tyr Trp Ala Ala Pro Glu Ala Tyr Leu
                565                 570                 575

Gly Asn Lys Leu Thr Ala Phe Gly Gly Phe Leu Lys Tyr Thr Val Ser
            580                 585                 590

Tyr Asp Ile Pro Val Glu Thr Val Asp Ser Asn Leu Met Ser His Ala
        595                 600                 605

Asp Val Ile Ile Lys Gly Asn Gly Leu Thr Leu Ser Thr Gln Ala Glu
    610                 615                 620

Gly Leu Ser Leu Gln Pro Tyr Glu Glu Tyr Leu Asn Val Val Arg Leu
625                 630                 635                 640

Val Pro Glu Asn Phe Gln Asp Phe His Ser Lys Arg Gln Ile Asp Arg
                645                 650                 655

Asp Gln Leu Met Thr Val Leu Ala Asn Val Thr His Leu Leu Ile Arg
            660                 665                 670

Ala Asn Tyr Asn Ser Ala Lys Met Ala Leu Tyr Arg Leu Glu Ser Val
        675                 680                 685
```

```
Ser Leu Asp Ile Ala Ser Ser Asn Ala Ile Asp Leu Val Val Ala Ala
    690                 695                 700

Asp Val Glu His Cys Glu Cys Pro Gln Gly Tyr Thr Gly Thr Ser Cys
705                 710                 715                 720

Glu Ser Cys Leu Ser Gly Tyr Tyr Arg Val Asp Gly Ile Leu Phe Gly
                725                 730                 735

Gly Ile Cys Gln Pro Cys Glu Cys His Gly His Ala Ala Glu Cys Asn
            740                 745                 750

Val His Gly Val Cys Ile Ala Cys Ala His Asn Thr Thr Gly Val His
        755                 760                 765

Cys Glu Gln Cys Leu Pro Gly Phe Tyr Gly Glu Pro Ser Arg Gly Thr
    770                 775                 780

Pro Gly Asp Cys Gln Pro Cys Ala Cys Pro Leu Thr Ile Ala Ser Asn
785                 790                 795                 800

Asn Phe Ser Pro Thr Cys His Leu Asn Asp Gly Asp Glu Val Val Cys
                805                 810                 815

Asp Trp Cys Ala Pro Gly Tyr Ser Gly Ala Trp Cys Glu Arg Cys Ala
            820                 825                 830

Asp Gly Tyr Tyr Gly Asn Pro Thr Val Pro Gly Glu Ser Cys Val Pro
        835                 840                 845

Cys Asp Cys Ser Gly Asn Val Asp Pro Ser Glu Ala Gly His Cys Asp
    850                 855                 860

Ser Val Thr Gly Glu Cys Leu Lys Cys Leu Gly Asn Thr Asp Gly Ala
865                 870                 875                 880

His Cys Glu Arg Cys Ala Asp Gly Phe Tyr Gly Asp Ala Val Thr Ala
                885                 890                 895

Lys Asn Cys Arg Ala Cys Glu Cys His Val Lys Gly Ser His Ser Ala
            900                 905                 910

Val Cys His Leu Glu Thr Gly Leu Cys Asp Cys Lys Pro Asn Val Thr
        915                 920                 925

Gly Gln Gln Cys Asp Gln Cys Leu His Gly Tyr Tyr Gly Leu Asp Ser
    930                 935                 940

Gly His Gly Cys Arg Pro Cys Asn Cys Ser Val Ala Gly Ser Val Ser
945                 950                 955                 960
```

```
Asp Gly Cys Thr Asp Glu Gly Gln Cys His Cys Val Pro Gly Val Ala
               965                 970                 975

Gly Lys Arg Cys Asp Arg Cys Ala His Gly Phe Tyr Ala Tyr Gln Asp
           980                 985                 990

Gly Ser Cys Thr Pro Cys Asp Cys  Pro His Thr Gln Asn  Thr Cys Asp
       995                1000                1005

Pro Glu  Thr Gly Glu Cys Val  Cys Pro Pro His Thr  Gln Gly Val
   1010                1015                1020

Lys Cys  Glu Glu Cys Glu Asp  Gly His Trp Gly Tyr  Asp Ala Glu
   1025                1030                1035

Val Gly  Cys Gln Ala Cys Asn  Cys Ser Leu Val Gly  Ser Thr His
   1040                1045                1050

His Arg  Cys Asp Val Val Thr  Gly His Cys Gln Cys  Lys Ser Lys
   1055                1060                1065

Phe Gly  Gly Arg Ala Cys Asp  Gln Cys Ser Leu Gly  Tyr Arg Asp
   1070                1075                1080

Phe Pro  Asp Cys Val Pro Cys  Asp Cys Asp Leu Arg  Gly Thr Ser
   1085                1090                1095

Gly Asp  Ala Cys Asn Leu Glu  Gln Gly Leu Cys Gly  Cys Val Glu
   1100                1105                1110

Glu Thr  Gly Ala Cys Pro Cys  Lys Glu Asn Val Phe  Gly Pro Gln
   1115                1120                1125

Cys Asn  Glu Cys Arg Glu Gly  Thr Phe Ala Leu Arg  Ala Asp Asn
   1130                1135                1140

Pro Leu  Gly Cys Ser Pro Cys  Phe Cys Ser Gly Leu  Ser His Leu
   1145                1150                1155

Cys Ser  Glu Leu Glu Asp Tyr  Val Arg Thr Pro Val  Thr Leu Gly
   1160                1165                1170

Ser Asp  Gln Pro Leu Leu Arg  Val Val Ser Gln Ser  Asn Leu Arg
   1175                1180                1185

Gly Thr  Thr Glu Gly Val Tyr  Tyr Gln Ala Pro Asp  Phe Leu Leu
   1190                1195                1200

Asp Ala  Ala Thr Val Arg Gln  His Ile Arg Ala Glu  Pro Phe Tyr
   1205                1210                1215
```

```
Trp Arg  Leu Pro Gln Gln Phe  Gln Gly Asp Gln Leu  Met Ala Tyr
    1220                 1225                 1230

Gly Gly  Lys Leu Lys Tyr Ser  Val Ala Phe Tyr Ser  Leu Asp Gly
    1235                 1240                 1245

Val Gly  Thr Ser Asn Phe Glu  Pro Gln Val Leu Ile  Lys Gly Gly
    1250                 1255                 1260

Arg Ile  Arg Lys Gln Val Ile  Tyr Met Asp Ala Pro  Ala Pro Glu
    1265                 1270                 1275

Asn Gly  Val Arg Gln Glu Gln  Glu Val Ala Met Arg  Glu Asn Phe
    1280                 1285                 1290

Trp Lys  Tyr Phe Asn Ser Val  Ser Glu Lys Pro Val  Thr Arg Glu
    1295                 1300                 1305

Asp Phe  Met Ser Val Leu Ser  Asp Ile Glu Tyr Ile  Leu Ile Lys
    1310                 1315                 1320

Ala Ser  Tyr Gly Gln Gly Leu  Gln Gln Ser Arg Ile  Ser Asp Ile
    1325                 1330                 1335

Ser Met  Glu Val Gly Arg Lys  Ala Glu Lys Leu His  Pro Glu Glu
    1340                 1345                 1350

Glu Val  Ala Ser Leu Leu Glu  Asn Cys Val Cys Pro  Pro Gly Thr
    1355                 1360                 1365

Val Gly  Phe Ser Cys Gln Asp  Cys Ala Pro Gly Tyr  His Arg Gly
    1370                 1375                 1380

Lys Leu  Pro Ala Gly Ser Asp  Arg Gly Pro Arg Pro  Leu Val Ala
    1385                 1390                 1395

Pro Cys  Val Pro Cys Ser Cys  Asn Asn His Ser Asp  Thr Cys Asp
    1400                 1405                 1410

Pro Asn  Thr Gly Lys Cys Leu  Asn Cys Gly Asp Asn  Thr Ala Gly
    1415                 1420                 1425

Asp His  Cys Asp Val Cys Thr  Ser Gly Tyr Tyr Gly  Lys Val Thr
    1430                 1435                 1440

Gly Ser  Ala Ser Asp Cys Ala  Leu Cys Ala Cys Pro  His Ser Pro
    1445                 1450                 1455

Pro Ala  Ser Phe Ser Pro Thr  Cys Val Leu Glu Gly  Asp His Asp
    1460                 1465                 1470
```

```
Phe Arg  Cys Asp Ala Cys Leu  Leu Gly Tyr Glu Gly  Lys His Cys
    1475                 1480                 1485

Glu Arg  Cys Ser Ser Ser Tyr  Tyr Gly Asn Pro Gln  Thr Pro Gly
    1490                 1495                 1500

Gly Ser  Cys Gln Lys Cys Asp  Cys Asn Pro His Gly  Ser Val His
    1505                 1510                 1515

Gly Asp  Cys Asp Arg Thr Ser  Gly Gln Cys Val Cys  Arg Leu Gly
    1520                 1525                 1530

Ala Ser  Gly Leu Arg Cys Asp  Glu Cys Glu Pro Arg  His Ile Leu
    1535                 1540                 1545

Met Glu  Thr Asp Cys Val Ser  Cys Asp Asp Glu Cys  Val Gly Val
    1550                 1555                 1560

Leu Leu  Asn Asp Leu Asp Glu  Ile Gly Asp Ala Val  Leu Ser Leu
    1565                 1570                 1575

Asn Leu  Thr Gly Ile Ile Pro  Val Pro Tyr Gly Ile  Leu Ser Asn
    1580                 1585                 1590

Leu Glu  Asn Thr Thr Lys Tyr  Leu Gln Glu Ser Leu  Leu Lys Glu
    1595                 1600                 1605

Asn Met  Gln Lys Asp Leu Gly  Lys Ile Lys Leu Glu  Gly Val Ala
    1610                 1615                 1620

Glu Glu  Thr Asp Asn Leu Gln  Lys Lys Leu Thr Arg  Met Leu Ala
    1625                 1630                 1635

Ser Thr  Gln Lys Val Asn Arg  Ala Thr Glu Arg Ile  Phe Lys Glu
    1640                 1645                 1650

Ser Gln  Asp Leu Ala Ile Ala  Ile Glu Arg Leu Gln  Met Ser Ile
    1655                 1660                 1665

Thr Glu  Ile Met Glu Lys Thr  Thr Leu Asn Gln Thr  Leu Asp Glu
    1670                 1675                 1680

Asp Phe  Leu Leu Pro Asn Ser  Thr Leu Gln Asn Met  Gln Gln Asn
    1685                 1690                 1695

Gly Thr  Ser Leu Leu Glu Ile  Met Gln Ile Arg Asp  Phe Thr Gln
    1700                 1705                 1710

Leu His  Gln Asn Ala Thr Leu  Glu Leu Lys Ala Ala  Glu Asp Leu
    1715                 1720                 1725
```

```
Leu Ser  Gln Ile Gln Glu Asn  Tyr Gln Lys Pro Leu  Glu Glu Leu
    1730                1735                1740

Glu Val  Leu Lys Glu Ala Ala  Ser His Val Leu Ser  Lys His Asn
    1745                1750                1755

Asn Glu  Leu Lys Ala Ala Glu  Ala Leu Val Arg Glu  Ala Glu Ala
    1760                1765                1770

Lys Met  Gln Glu Ser Asn His  Leu Leu Leu Met Val  Asn Ala Asn
    1775                1780                1785

Leu Arg  Glu Phe Ser Asp Lys  Lys Leu His Val Gln  Glu Glu Gln
    1790                1795                1800

Asn Leu  Thr Ser Glu Leu Ile  Val Gln Gly Arg Gly  Leu Ile Asp
    1805                1810                1815

Ala Ala  Ala Ala Gln Thr Asp  Ala Val Gln Asp Ala  Leu Glu His
    1820                1825                1830

Leu Glu  Asp His Gln Asp Lys  Leu Leu Leu Trp Ser  Ala Lys Ile
    1835                1840                1845

Arg His  His Ile Asp Asp Leu  Val Met His Met Ser  Gln Arg Asn
    1850                1855                1860

Ala Val  Asp Leu Val Tyr Arg  Ala Glu Asp His Ala  Ala Glu Phe
    1865                1870                1875

Gln Arg  Leu Ala Asp Val Leu  Tyr Ser Gly Leu Glu  Asn Ile Arg
    1880                1885                1890

Asn Val  Ser Leu Asn Ala Thr  Ser Ala Ala Tyr Val  His Tyr Asn
    1895                1900                1905

Ile Gln  Ser Leu Ile Glu Glu  Ser Glu Glu Leu Ala  Arg Asp Ala
    1910                1915                1920

His Arg  Thr Val Thr Glu Thr  Ser Leu Leu Ser Glu  Ser Leu Val
    1925                1930                1935

Ser Asn  Gly Lys Ala Ala Val  Gln Arg Ser Ser Arg  Phe Leu Lys
    1940                1945                1950

Glu Gly  Asn Asn Leu Ser Arg  Lys Leu Pro Gly Ile  Ala Leu Glu
    1955                1960                1965

Leu Ser  Glu Leu Arg Asn Lys  Thr Asn Arg Phe Gln  Glu Asn Ala
    1970                1975                1980
```

```
Val Glu  Ile Thr Arg Gln Thr  Asn Glu Ser Leu Leu  Ile Leu Arg
    1985                 1990                 1995

Ala Ile  Pro Lys Gly Ile Arg  Asp Lys Gly Ala Lys  Thr Lys Glu
    2000                 2005                 2010

Leu Ala  Thr Ser Ala Ser Gln  Ser Ala Val Ser Thr  Leu Arg Asp
    2015                 2020                 2025

Val Ala  Gly Leu Ser Gln Glu  Leu Leu Asn Thr Ser  Ala Ser Leu
    2030                 2035                 2040

Ser Arg  Val Asn Thr Thr Leu  Arg Glu Thr His Gln  Leu Leu Gln
    2045                 2050                 2055

Asp Ser  Thr Met Ala Thr Leu  Leu Ala Gly Arg Lys  Val Lys Asp
    2060                 2065                 2070

Val Glu  Ile Gln Ala Asn Leu  Leu Phe Asp Arg Leu  Lys Pro Leu
    2075                 2080                 2085

Lys Met  Leu Glu Glu Asn Leu  Ser Arg Asn Leu Ser  Glu Ile Lys
    2090                 2095                 2100

Leu Leu  Ile Ser Gln Ala Arg  Lys Gln Ala Ala Ser  Ile Lys Val
    2105                 2110                 2115

Ala Val  Ser Ala Asp Arg Asp  Cys Ile Arg Ala Tyr  Gln Pro Gln
    2120                 2125                 2130

Ile Ser  Ser Thr Asn Tyr Asn  Thr Leu Thr Leu Asn  Val Lys Thr
    2135                 2140                 2145

Gln Glu  Pro Asp Asn Leu Leu  Phe Tyr Leu Gly Ser  Ser Thr Ala
    2150                 2155                 2160

Ser Asp  Phe Leu Ala Val Glu  Met Arg Arg Gly Arg  Val Ala Phe
    2165                 2170                 2175

Leu Trp  Asp Leu Gly Ser Gly  Ser Thr Arg Leu Glu  Phe Pro Asp
    2180                 2185                 2190

Phe Pro  Ile Asp Asp Asn Arg  Trp His Ser Ile His  Val Ala Arg
    2195                 2200                 2205

Phe Gly  Asn Ile Gly Ser Leu  Ser Val Lys Glu Met  Ser Ser Asn
    2210                 2215                 2220

Gln Lys  Ser Pro Thr Lys Thr  Ser Lys Ser Pro Gly  Thr Ala Asn
    2225                 2230                 2235
```

```
Val Leu  Asp Val Asn Asn Ser  Thr Leu Met Phe Val  Gly Gly Leu
    2240                 2245                 2250

Gly Gly  Gln Ile Lys Lys Ser  Pro Ala Val Lys Val  Thr His Phe
    2255                 2260                 2265

Lys Gly  Cys Leu Gly Glu Ala  Phe Leu Asn Gly Lys  Ser Ile Gly
    2270                 2275                 2280

Leu Trp  Asn Tyr Ile Glu Arg  Glu Gly Lys Cys Arg  Gly Cys Phe
    2285                 2290                 2295

Gly Ser  Ser Gln Asn Glu Asp  Pro Ser Phe His Phe  Asp Gly Ser
    2300                 2305                 2310

Gly Tyr  Ser Val Val Glu Lys  Ser Leu Pro Ala Thr  Val Thr Gln
    2315                 2320                 2325

Ile Ile  Met Leu Phe Asn Thr  Phe Ser Pro Asn Gly  Leu Leu Leu
    2330                 2335                 2340

Tyr Leu  Gly Ser Tyr Gly Thr  Lys Asp Phe Leu Ser  Ile Glu Leu
    2345                 2350                 2355

Phe Arg  Gly Arg Val Lys Val  Met Thr Asp Leu Gly  Ser Gly Pro
    2360                 2365                 2370

Ile Thr  Leu Leu Thr Asp Arg  Arg Tyr Asn Asn Gly  Thr Trp Tyr
    2375                 2380                 2385

Lys Ile  Ala Phe Gln Arg Asn  Arg Lys Gln Gly Val  Leu Ala Val
    2390                 2395                 2400

Ile Asp  Ala Tyr Asn Thr Ser  Asn Lys Glu Thr Lys  Gln Gly Glu
    2405                 2410                 2415

Thr Pro  Gly Ala Ser Ser Asp  Leu Asn Arg Leu Asp  Lys Asp Pro
    2420                 2425                 2430

Ile Tyr  Val Gly Gly Leu Pro  Arg Ser Arg Val Val  Arg Arg Gly
    2435                 2440                 2445

Val Thr  Thr Lys Ser Phe Val  Gly Cys Ile Lys Asn  Leu Glu Ile
    2450                 2455                 2460

Ser Arg  Ser Thr Phe Asp Leu  Leu Arg Asn Ser Tyr  Gly Val Arg
    2465                 2470                 2475

Lys Gly  Cys Leu Leu Glu Pro  Ile Arg Ser Val Ser  Phe Leu Lys
    2480                 2485                 2490
```

```
Gly Gly  Tyr Ile Glu Leu Pro  Pro Lys Ser Leu Ser  Pro Glu Ser
    2495                 2500                 2505

Glu Trp  Leu Val Thr Phe Ala  Thr Thr Asn Ser Ser  Gly Ile Ile
    2510                 2515                 2520

Leu Ala  Ala Leu Gly Gly Asp  Val Glu Lys Arg Gly  Asp Arg Glu
    2525                 2530                 2535

Glu Ala  His Val Pro Phe Phe  Ser Val Met Leu Ile  Gly Gly Asn
    2540                 2545                 2550

Ile Glu  Val His Val Asn Pro  Gly Asp Gly Thr Gly  Leu Arg Lys
    2555                 2560                 2565

Ala Leu  Leu His Ala Pro Thr  Gly Thr Cys Ser Asp  Gly Gln Ala
    2570                 2575                 2580

His Ser  Ile Ser Leu Val Arg  Asn Arg Arg Ile Ile  Thr Val Gln
    2585                 2590                 2595

Leu Asp  Glu Asn Asn Pro Val  Glu Met Lys Leu Gly  Thr Leu Val
    2600                 2605                 2610

Glu Ser  Arg Thr Ile Asn Val  Ser Asn Leu Tyr Val  Gly Gly Ile
    2615                 2620                 2625

Pro Glu  Gly Glu Gly Thr Ser  Leu Leu Thr Met Arg  Arg Ser Phe
    2630                 2635                 2640

His Gly  Cys Ile Lys Asn Leu  Ile Phe Asn Leu Glu  Leu Leu Asp
    2645                 2650                 2655

Phe Asn  Ser Ala Val Gly His  Glu Gln Val Asp Leu  Asp Thr Cys
    2660                 2665                 2670

Trp Leu  Ser Glu Arg Pro Lys  Leu Ala Pro Asp Ala  Glu Asp Ser
    2675                 2680                 2685

Lys Leu  Leu Pro Glu Pro Arg  Ala Phe Pro Glu Gln  Cys Val Val
    2690                 2695                 2700

Asp Ala  Ala Leu Glu Tyr Val  Pro Gly Ala His Gln  Phe Gly Leu
    2705                 2710                 2715

Thr Gln  Asn Ser His Phe Ile  Leu Pro Phe Asn Gln  Ser Ala Val
    2720                 2725                 2730

Arg Lys  Lys Leu Ser Val Glu  Leu Ser Ile Arg Thr  Phe Ala Ser
    2735                 2740                 2745
```

```
Ser Gly  Leu Ile Tyr Tyr Met  Ala His Gln Asn Gln  Ala Asp Tyr
    2750                 2755                 2760

Ala Val  Leu Gln Leu His Gly  Gly Arg Leu His Phe  Met Phe Asp
    2765                 2770                 2775

Leu Gly  Lys Gly Arg Thr Lys  Val Ser His Pro Ala  Leu Leu Ser
    2780                 2785                 2790

Asp Gly  Lys Trp His Thr Val  Lys Thr Asp Tyr Val  Lys Arg Lys
    2795                 2800                 2805

Gly Phe  Ile Thr Val Asp Gly  Arg Glu Ser Pro Met  Val Thr Val
    2810                 2815                 2820

Val Gly  Asp Gly Thr Met Leu  Asp Val Glu Gly Leu  Phe Tyr Leu
    2825                 2830                 2835

Gly Gly  Leu Pro Ser Gln Tyr  Gln Ala Arg Lys Ile  Gly Asn Ile
    2840                 2845                 2850

Thr His  Ser Ile Pro Ala Cys  Ile Gly Asp Val Thr  Val Asn Ser
    2855                 2860                 2865

Lys Gln  Leu Asp Lys Asp Ser  Pro Val Ser Ala Phe  Thr Val Asn
    2870                 2875                 2880

Arg Cys  Tyr Ala Val Ala Gln  Glu Gly Thr Tyr Phe  Asp Gly Ser
    2885                 2890                 2895

Gly Tyr  Ala Ala Leu Val Lys  Glu Gly Tyr Lys Val  Gln Ser Asp
    2900                 2905                 2910

Val Asn  Ile Thr Leu Glu Phe  Arg Thr Ser Ser Gln  Asn Gly Val
    2915                 2920                 2925

Leu Leu  Gly Ile Ser Thr Ala  Lys Val Asp Ala Ile  Gly Leu Glu
    2930                 2935                 2940

Leu Val  Asp Gly Lys Val Leu  Phe His Val Asn Asn  Gly Ala Gly
    2945                 2950                 2955

Arg Ile  Thr Ala Ala Tyr Glu  Pro Lys Thr Ala Thr  Val Leu Cys
    2960                 2965                 2970

Asp Gly  Lys Trp His Thr Leu  Gln Ala Asn Lys Ser  Lys His Arg
    2975                 2980                 2985

Ile Thr  Leu Ile Val Asp Gly  Asn Ala Val Gly Ala  Glu Ser Pro
    2990                 2995                 3000
```

```
His Thr  Gln Ser Thr Ser Val  Asp Thr Asn Asn Pro  Ile Tyr Val
    3005                3010                3015

Gly Gly  Tyr Pro Ala Gly Val  Lys Gln Lys Cys Leu  Arg Ser Gln
    3020                3025                3030

Thr Ser  Phe Arg Gly Cys Leu  Arg Lys Leu Ala Leu  Ile Lys Ser
    3035                3040                3045

Pro Gln  Val Gln Ser Phe Asp  Phe Ser Arg Ala Phe  Glu Leu His
    3050                3055                3060

Gly Val  Phe Leu His Ser Cys  Pro Gly Thr Glu Ser
    3065                3070                3075


<210>  105
<211>  158
<212>  PRT
<213>  Homo sapiens

<400>  105

Met Gly Lys Ile Ser Ser Leu Pro Thr Gln Leu Phe Lys Cys Cys Phe
1               5                   10                  15

Cys Asp Phe Leu Lys Val Lys Met His Thr Met Ser Ser Ser His Leu
            20                  25                  30

Phe Tyr Leu Ala Leu Cys Leu Leu Thr Phe Thr Ser Ser Ala Thr Ala
        35                  40                  45

Gly Pro Glu Thr Leu Cys Gly Ala Glu Leu Val Asp Ala Leu Gln Phe
    50                  55                  60

Val Cys Gly Asp Arg Gly Phe Tyr Phe Asn Lys Pro Thr Gly Tyr Gly
65                  70                  75                  80

Ser Ser Ser Arg Arg Ala Pro Gln Thr Gly Ile Val Asp Glu Cys Cys
                85                  90                  95

Phe Arg Ser Cys Asp Leu Arg Arg Leu Glu Met Tyr Cys Ala Pro Leu
            100                 105                 110

Lys Pro Ala Lys Ser Ala Arg Ser Val Arg Ala Gln Arg His Thr Asp
        115                 120                 125

Met Pro Lys Thr Gln Lys Tyr Gln Pro Pro Ser Thr Asn Lys Asn Thr
    130                 135                 140

Lys Ser Gln Arg Arg Lys Gly Ser Thr Phe Glu Glu Arg Lys
145                 150                 155
```

<210> 106
<211> 155
<212> PRT
<213> Homo sapiens

<400> 106

Met Ala Glu Gly Glu Ile Thr Thr Phe Thr Ala Leu Thr Glu Lys Phe
1 5 10 15

Asn Leu Pro Pro Gly Asn Tyr Lys Lys Pro Lys Leu Leu Tyr Cys Ser
20 25 30

Asn Gly Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly
35 40 45

Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu
50 55 60

Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu
65 70 75 80

Ala Met Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu
85 90 95

Glu Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr
100 105 110

Ile Ser Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys
115 120 125

Asn Gly Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala
130 135 140

Ile Leu Phe Leu Pro Leu Pro Val Ser Ser Asp
145 150 155

<210> 107
<211> 288
<212> PRT
<213> Homo sapiens

<400> 107

Met Val Gly Val Gly Gly Gly Asp Val Glu Asp Val Thr Pro Arg Pro
1 5 10 15

Gly Gly Cys Gln Ile Ser Gly Arg Gly Ala Arg Gly Cys Asn Gly Ile
20 25 30

Pro Gly Ala Ala Ala Trp Glu Ala Ala Leu Pro Arg Arg Arg Pro Arg
35 40 45

Arg His Pro Ser Val Asn Pro Arg Ser Arg Ala Ala Gly Ser Pro Arg

50 55 60

Thr Arg Gly Arg Arg Thr Glu Glu Arg Pro Ser Gly Ser Arg Leu Gly
65 70 75 80

Asp Arg Gly Arg Gly Arg Ala Leu Pro Gly Gly Arg Leu Gly Gly Arg
85 90 95

Gly Arg Gly Arg Ala Pro Glu Arg Val Gly Gly Arg Gly Arg Gly Arg
100 105 110

Gly Thr Ala Ala Pro Arg Ala Ala Pro Ala Ala Arg Gly Ser Arg Pro
115 120 125

Gly Pro Ala Gly Thr Met Ala Ala Gly Ser Ile Thr Thr Leu Pro Ala
130 135 140

Leu Pro Glu Asp Gly Gly Ser Gly Ala Phe Pro Pro Gly His Phe Lys
145 150 155 160

Asp Pro Lys Arg Leu Tyr Cys Lys Asn Gly Gly Phe Phe Leu Arg Ile
165 170 175

His Pro Asp Gly Arg Val Asp Gly Val Arg Glu Lys Ser Asp Pro His
180 185 190

Ile Lys Leu Gln Leu Gln Ala Glu Glu Arg Gly Val Val Ser Ile Lys
195 200 205

Gly Val Cys Ala Asn Arg Tyr Leu Ala Met Lys Glu Asp Gly Arg Leu
210 215 220

Leu Ala Ser Lys Cys Val Thr Asp Glu Cys Phe Phe Phe Glu Arg Leu
225 230 235 240

Glu Ser Asn Asn Tyr Asn Thr Tyr Arg Ser Arg Lys Tyr Thr Ser Trp
245 250 255

Tyr Val Ala Leu Lys Arg Thr Gly Gln Tyr Lys Leu Gly Ser Lys Thr
260 265 270

Gly Pro Gly Gln Lys Ala Ile Leu Phe Leu Pro Met Ser Ala Lys Ser
275 280 285

<210> 108
<211> 390
<212> PRT
<213> Homo sapiens

<400> 108

Met Pro Pro Ser Gly Leu Arg Leu Leu Pro Leu Leu Leu Pro Leu Leu
1 5 10 15

```
Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr
            20                  25                  30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala
        35                  40                  45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
    50                  55                  60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu
65                  70                  75                  80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Glu Pro Glu
                85                  90                  95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu
            100                 105                 110

Met Val Glu Thr His Asn Glu Ile Tyr Asp Lys Phe Lys Gln Ser Thr
        115                 120                 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Glu Leu Arg Glu Ala Val
    130                 135                 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu
145                 150                 155                 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn
                165                 170                 175

Asn Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser
            180                 185                 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu
        195                 200                 205

Ser Arg Gly Gly Glu Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser
    210                 215                 220

Cys Asp Ser Arg Asp Asn Thr Leu Gln Val Asp Ile Asn Gly Phe Thr
225                 230                 235                 240

Thr Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro
                245                 250                 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu Gln
            260                 265                 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser
        275                 280                 285
```

```
Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys
    290                 295                 300

Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn
305                 310                 315                 320

Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr
                325                 330                 335

Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala
            340                 345                 350

Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr
        355                 360                 365

Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val
    370                 375                 380

Arg Ser Cys Lys Cys Ser
385                 390


<210>  109
<211>  442
<212>  PRT
<213>  Homo sapiens

<400>  109

Met His Tyr Cys Val Leu Ser Ala Phe Leu Ile Leu His Leu Val Thr
1               5                   10                  15

Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe
            20                  25                  30

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu
        35                  40                  45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Glu Glu Val Pro
    50                  55                  60

Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu
65                  70                  75                  80

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Asp Glu
                85                  90                  95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Pro Phe Phe
            100                 105                 110

Pro Ser Glu Thr Val Cys Pro Val Val Thr Thr Pro Ser Gly Ser Val
        115                 120                 125
```

```
Gly Ser Leu Cys Ser Arg Gln Ser Gln Val Leu Cys Gly Tyr Leu Asp
    130                 135                 140

Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg Ile Val Arg Phe
145                 150                 155                 160

Asp Val Ser Ala Met Glu Lys Asn Ala Ser Asn Leu Val Lys Ala Glu
                165                 170                 175

Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg Val Pro Glu Gln
            180                 185                 190

Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp Leu Thr Ser Pro
        195                 200                 205

Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr Arg Ala Glu Gly
    210                 215                 220

Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val His Glu Trp Leu His
225                 230                 235                 240

His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu His Cys Pro Cys
                245                 250                 255

Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro Asn Lys Ser Glu
            260                 265                 270

Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr Ser Thr Tyr Thr
        275                 280                 285

Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys Lys Asn Ser Gly
    290                 295                 300

Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser Tyr Arg Leu Glu
305                 310                 315                 320

Ser Gln Gln Thr Asn Arg Arg Lys Lys Arg Ala Leu Asp Ala Ala Tyr
                325                 330                 335

Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro Leu Tyr Ile
            340                 345                 350

Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly
        355                 360                 365

Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu Trp Ser Ser
    370                 375                 380

Asp Thr Gln His Ser Arg Val Leu Ser Leu Tyr Asn Thr Ile Asn Pro
385                 390                 395                 400
```

```
Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu Glu Pro Leu
                405                 410                 415


Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro Lys Ile Glu Gln Leu Ser
            420                 425                 430


Asn Met Ile Val Lys Ser Cys Lys Cys Ser
        435                 440


<210>  110
<211>  414
<212>  PRT
<213>  Homo sapiens

<400>  110

Met His Tyr Cys Val Leu Ser Ala Phe Leu Ile Leu His Leu Val Thr
1               5                   10                  15


Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe
            20                  25                  30


Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu
        35                  40                  45


Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Glu Glu Val Pro
    50                  55                  60


Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu
65                  70                  75                  80


Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Asp Glu
                85                  90                  95


Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Pro Phe Phe
            100                 105                 110


Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg
        115                 120                 125


Ile Val Arg Phe Asp Val Ser Ala Met Glu Lys Asn Ala Ser Asn Leu
    130                 135                 140


Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg
145                 150                 155                 160


Val Pro Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp
                165                 170                 175


Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr
            180                 185                 190
```

```
Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val His
        195                 200                 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu
    210                 215                 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro
225                 230                 235                 240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr
                245                 250                 255

Ser Thr Tyr Thr Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys
            260                 265                 270

Lys Asn Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser
        275                 280                 285

Tyr Arg Leu Glu Ser Gln Gln Thr Asn Arg Arg Lys Lys Arg Ala Leu
    290                 295                 300

Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg
305                 310                 315                 320

Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His
                325                 330                 335

Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr
            340                 345                 350

Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu Tyr Asn
        355                 360                 365

Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp
    370                 375                 380

Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro Lys Ile
385                 390                 395                 400

Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser
                405                 410
```

<210> 111
<211> 377
<212> PRT
<213> Homo sapiens

<400> 111

```
Met Cys Asp Glu Asp Glu Thr Thr Ala Leu Val Cys Asp Asn Gly Ser
1               5                   10                  15

Gly Leu Val Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val
```

20 25 30

Phe Pro Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly
35 40 45

Met Gly Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg
50 55 60

Gly Ile Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Ile Thr Asn
65 70 75 80

Trp Asp Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu
85 90 95

Arg Val Ala Pro Glu Glu His Pro Thr Leu Leu Thr Glu Ala Pro Leu
100 105 110

Asn Pro Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr
115 120 125

Phe Asn Val Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu
130 135 140

Tyr Ala Ser Gly Arg Thr Thr Gly Ile Val Leu Asp Ser Gly Asp Gly
145 150 155 160

Val Thr His Asn Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala
165 170 175

Ile Met Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met
180 185 190

Lys Ile Leu Thr Glu Arg Gly Tyr Ser Phe Val Thr Thr Ala Glu Arg
195 200 205

Glu Ile Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp
210 215 220

Phe Glu Asn Glu Met Ala Thr Ala Ala Ser Ser Ser Ser Leu Glu Lys
225 230 235 240

Ser Tyr Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg
245 250 255

Phe Arg Cys Pro Glu Thr Leu Phe Gln Pro Ser Phe Ile Gly Met Glu
260 265 270

Ser Ala Gly Ile His Glu Thr Thr Tyr Asn Ser Ile Met Lys Cys Asp
275 280 285

Ile Asp Ile Arg Lys Asp Leu Tyr Ala Asn Asn Val Met Ser Gly Gly

290 295 300

Thr Thr Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr
305 310 315 320

Ala Leu Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu
325 330 335

Arg Lys Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser
340 345 350

Thr Phe Gln Gln Met Trp Ile Thr Lys Gln Glu Tyr Asp Glu Ala Gly
355 360 365

Pro Ser Ile Val His Arg Lys Cys Phe
370 375

<210> 112
<211> 377
<212> PRT
<213> Homo sapiens

<400> 112

Met Cys Glu Glu Glu Asp Ser Thr Ala Leu Val Cys Asp Asn Gly Ser
1 5 10 15

Gly Leu Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val
20 25 30

Phe Pro Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly
35 40 45

Met Gly Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg
50 55 60

Gly Ile Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Ile Thr Asn
65 70 75 80

Trp Asp Asp Met Glu Lys Ile Trp His His Ser Phe Tyr Asn Glu Leu
85 90 95

Arg Val Ala Pro Glu Glu His Pro Thr Leu Leu Thr Glu Ala Pro Leu
100 105 110

Asn Pro Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr
115 120 125

Phe Asn Val Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu
130 135 140

Tyr Ala Ser Gly Arg Thr Thr Gly Ile Val Leu Asp Ser Gly Asp Gly
145 150 155 160

```
Val Thr His Asn Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala
                165                 170                 175

Ile Met Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met
            180                 185                 190

Lys Ile Leu Thr Glu Arg Gly Tyr Ser Phe Val Thr Thr Ala Glu Arg
        195                 200                 205

Glu Ile Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp
    210                 215                 220

Phe Glu Asn Glu Met Ala Thr Ala Ala Ser Ser Ser Leu Glu Lys
225                 230                 235                 240

Ser Tyr Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg
                245                 250                 255

Phe Arg Cys Pro Glu Thr Leu Phe Gln Pro Ser Phe Ile Gly Met Glu
            260                 265                 270

Ser Ala Gly Ile His Glu Thr Thr Tyr Asn Ser Ile Met Lys Cys Asp
        275                 280                 285

Ile Asp Ile Arg Lys Asp Leu Tyr Ala Asn Asn Val Leu Ser Gly Gly
    290                 295                 300

Thr Thr Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr
305                 310                 315                 320

Ala Leu Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu
                325                 330                 335

Arg Lys Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser
            340                 345                 350

Thr Phe Gln Gln Met Trp Ile Ser Lys Gln Glu Tyr Asp Glu Ala Gly
        355                 360                 365

Pro Ser Ile Val His Arg Lys Cys Phe
    370                 375


<210>  113
<211>  375
<212>  PRT
<213>  Homo sapiens

<400>  113

Met Asp Asp Asp Ile Ala Ala Leu Val Val Asp Asn Gly Ser Gly Met
1               5                   10                  15
```

```
Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe Pro
            20                  25                  30

Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly Met Gly
        35                  40                  45

Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg Gly Ile
    50                  55                  60

Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Val Thr Asn Trp Asp
65                  70                  75                  80

Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu Arg Val
                85                  90                  95

Ala Pro Glu Glu His Pro Val Leu Leu Thr Glu Ala Pro Leu Asn Pro
            100                 105                 110

Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe Asn
        115                 120                 125

Thr Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu Tyr Ala
    130                 135                 140

Ser Gly Arg Thr Thr Gly Ile Val Met Asp Ser Gly Asp Gly Val Thr
145                 150                 155                 160

His Thr Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala Ile Leu
                165                 170                 175

Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met Lys Ile
            180                 185                 190

Leu Thr Glu Arg Gly Tyr Ser Phe Thr Thr Thr Ala Glu Arg Glu Ile
        195                 200                 205

Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp Phe Glu
    210                 215                 220

Gln Glu Met Ala Thr Ala Ala Ser Ser Ser Ser Leu Glu Lys Ser Tyr
225                 230                 235                 240

Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg Phe Arg
                245                 250                 255

Cys Pro Glu Ala Leu Phe Gln Pro Ser Phe Leu Gly Met Glu Ser Cys
            260                 265                 270

Gly Ile His Glu Thr Thr Phe Asn Ser Ile Met Lys Cys Asp Val Asp
        275                 280                 285
```

```
Ile Arg Lys Asp Leu Tyr Ala Asn Thr Val Leu Ser Gly Gly Thr Thr
    290                 295                 300

Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr Ala Leu
305                 310                 315                 320

Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu Arg Lys
                325                 330                 335

Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser Thr Phe
            340                 345                 350

Gln Gln Met Trp Ile Ser Lys Gln Glu Tyr Asp Glu Ser Gly Pro Ser
        355                 360                 365

Ile Val His Arg Lys Cys Phe
    370                 375


<210>  114
<211>  377
<212>  PRT
<213>  Homo sapiens

<400>  114

Met Cys Asp Asp Glu Glu Thr Thr Ala Leu Val Cys Asp Asn Gly Ser
1               5                   10                  15

Gly Leu Val Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val
            20                  25                  30

Phe Pro Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly
        35                  40                  45

Met Gly Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg
    50                  55                  60

Gly Ile Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Ile Thr Asn
65                  70                  75                  80

Trp Asp Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu
                85                  90                  95

Arg Val Ala Pro Glu Glu His Pro Thr Leu Leu Thr Glu Ala Pro Leu
            100                 105                 110

Asn Pro Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr
        115                 120                 125

Phe Asn Val Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu
    130                 135                 140
```

```
Tyr Ala Ser Gly Arg Thr Thr Gly Ile Val Leu Asp Ser Gly Asp Gly
145                 150                 155                 160

Val Thr His Asn Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala
                165                 170                 175

Ile Met Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met
            180                 185                 190

Lys Ile Leu Thr Glu Arg Gly Tyr Ser Phe Val Thr Thr Ala Glu Arg
        195                 200                 205

Glu Ile Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp
    210                 215                 220

Phe Glu Asn Glu Met Ala Thr Ala Ala Ser Ser Ser Ser Leu Glu Lys
225                 230                 235                 240

Ser Tyr Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg
                245                 250                 255

Phe Arg Cys Pro Glu Thr Leu Phe Gln Pro Ser Phe Ile Gly Met Glu
            260                 265                 270

Ser Ala Gly Ile His Glu Thr Thr Tyr Asn Ser Ile Met Lys Cys Asp
        275                 280                 285

Ile Asp Ile Arg Lys Asp Leu Tyr Ala Asn Asn Val Leu Ser Gly Gly
    290                 295                 300

Thr Thr Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr
305                 310                 315                 320

Ala Leu Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu
                325                 330                 335

Arg Lys Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser
            340                 345                 350

Thr Phe Gln Gln Met Trp Ile Ser Lys Gln Glu Tyr Asp Glu Ala Gly
        355                 360                 365

Pro Ser Ile Val His Arg Lys Cys Phe
    370                 375


<210>  115
<211>  375
<212>  PRT
<213>  Homo sapiens

<400>  115

Met Glu Glu Glu Ile Ala Ala Leu Val Ile Asp Asn Gly Ser Gly Met
```

1 5 10 15

Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe Pro
20 25 30

Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly Met Gly
35 40 45

Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg Gly Ile
50 55 60

Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Val Thr Asn Trp Asp
65 70 75 80

Asp Met Glu Lys Ile Trp His His Thr Phe Tyr Asn Glu Leu Arg Val
85 90 95

Ala Pro Glu Glu His Pro Val Leu Leu Thr Glu Ala Pro Leu Asn Pro
100 105 110

Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe Asn
115 120 125

Thr Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu Tyr Ala
130 135 140

Ser Gly Arg Thr Thr Gly Ile Val Met Asp Ser Gly Asp Gly Val Thr
145 150 155 160

His Thr Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala Ile Leu
165 170 175

Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met Lys Ile
180 185 190

Leu Thr Glu Arg Gly Tyr Ser Phe Thr Thr Thr Ala Glu Arg Glu Ile
195 200 205

Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp Phe Glu
210 215 220

Gln Glu Met Ala Thr Ala Ala Ser Ser Ser Ser Leu Glu Lys Ser Tyr
225 230 235 240

Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg Phe Arg
245 250 255

Cys Pro Glu Ala Leu Phe Gln Pro Ser Phe Leu Gly Met Glu Ser Cys
260 265 270

Gly Ile His Glu Thr Thr Phe Asn Ser Ile Met Lys Cys Asp Val Asp

275 280 285

Ile Arg Lys Asp Leu Tyr Ala Asn Thr Val Leu Ser Gly Gly Thr Thr
290 295 300

Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr Ala Leu
305 310 315 320

Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu Arg Lys
325 330 335

Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser Thr Phe
340 345 350

Gln Gln Met Trp Ile Ser Lys Gln Glu Tyr Asp Glu Ser Gly Pro Ser
355 360 365

Ile Val His Arg Lys Cys Phe
370 375

<210> 116
<211> 376
<212> PRT
<213> Homo sapiens

<400> 116

Met Cys Glu Glu Glu Thr Thr Ala Leu Val Cys Asp Asn Gly Ser Gly
1 5 10 15

Leu Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe
20 25 30

Pro Ser Ile Val Gly Arg Pro Arg His Gln Gly Val Met Val Gly Met
35 40 45

Gly Gln Lys Asp Ser Tyr Val Gly Asp Glu Ala Gln Ser Lys Arg Gly
50 55 60

Ile Leu Thr Leu Lys Tyr Pro Ile Glu His Gly Ile Ile Thr Asn Trp
65 70 75 80

Asp Asp Met Glu Lys Ile Trp His His Ser Phe Tyr Asn Glu Leu Arg
85 90 95

Val Ala Pro Glu Glu His Pro Thr Leu Leu Thr Glu Ala Pro Leu Asn
100 105 110

Pro Lys Ala Asn Arg Glu Lys Met Thr Gln Ile Met Phe Glu Thr Phe
115 120 125

Asn Val Pro Ala Met Tyr Val Ala Ile Gln Ala Val Leu Ser Leu Tyr
130 135 140

```
Ala Ser Gly Arg Thr Thr Gly Ile Val Leu Asp Ser Gly Asp Gly Val
145                 150                 155                 160

Thr His Asn Val Pro Ile Tyr Glu Gly Tyr Ala Leu Pro His Ala Ile
                165                 170                 175

Met Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr Asp Tyr Leu Met Lys
            180                 185                 190

Ile Leu Thr Glu Arg Gly Tyr Ser Phe Val Thr Thr Ala Glu Arg Glu
        195                 200                 205

Ile Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr Val Ala Leu Asp Phe
    210                 215                 220

Glu Asn Glu Met Ala Thr Ala Ala Ser Ser Ser Ser Leu Glu Lys Ser
225                 230                 235                 240

Tyr Glu Leu Pro Asp Gly Gln Val Ile Thr Ile Gly Asn Glu Arg Phe
                245                 250                 255

Arg Cys Pro Glu Thr Leu Phe Gln Pro Ser Phe Ile Gly Met Glu Ser
            260                 265                 270

Ala Gly Ile His Glu Thr Thr Tyr Asn Ser Ile Met Lys Cys Asp Ile
        275                 280                 285

Asp Ile Arg Lys Asp Leu Tyr Ala Asn Asn Val Leu Ser Gly Gly Thr
    290                 295                 300

Thr Met Tyr Pro Gly Ile Ala Asp Arg Met Gln Lys Glu Ile Thr Ala
305                 310                 315                 320

Leu Ala Pro Ser Thr Met Lys Ile Lys Ile Ile Ala Pro Pro Glu Arg
                325                 330                 335

Lys Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu Ala Ser Leu Ser Thr
            340                 345                 350

Phe Gln Gln Met Trp Ile Ser Lys Pro Glu Tyr Asp Glu Ala Gly Pro
        355                 360                 365

Ser Ile Val His Arg Lys Cys Phe
    370                 375

<210>  117
<211>  333
<212>  PRT
<213>  Homo sapiens

<400>  117
```

```
Met Cys Glu Glu Glu Thr Thr Ala Leu Val Cys Asp Asn Gly Ser Gly
1               5                  10                  15

Leu Cys Lys Ala Gly Phe Ala Gly Asp Asp Ala Pro Arg Ala Val Phe
            20                  25                  30

Pro Ser Ile Val Gly Arg Pro Arg His Gln Ile Trp His His Ser Phe
        35                  40                  45

Tyr Asn Glu Leu Arg Val Ala Pro Glu Glu His Pro Thr Leu Leu Thr
    50                  55                  60

Glu Ala Pro Leu Asn Pro Lys Ala Asn Arg Glu Lys Met Thr Gln Ile
65                  70                  75                  80

Met Phe Glu Thr Phe Asn Val Pro Ala Met Tyr Val Ala Ile Gln Ala
                85                  90                  95

Val Leu Ser Leu Tyr Ala Ser Gly Arg Thr Thr Gly Ile Val Leu Asp
            100                 105                 110

Ser Gly Asp Gly Val Thr His Asn Val Pro Ile Tyr Glu Gly Tyr Ala
        115                 120                 125

Leu Pro His Ala Ile Met Arg Leu Asp Leu Ala Gly Arg Asp Leu Thr
    130                 135                 140

Asp Tyr Leu Met Lys Ile Leu Thr Glu Arg Gly Tyr Ser Phe Val Thr
145                 150                 155                 160

Thr Ala Glu Arg Glu Ile Val Arg Asp Ile Lys Glu Lys Leu Cys Tyr
                165                 170                 175

Val Ala Leu Asp Phe Glu Asn Glu Met Ala Thr Ala Ala Ser Ser Ser
            180                 185                 190

Ser Leu Glu Lys Ser Tyr Glu Leu Pro Asp Gly Gln Val Ile Thr Ile
        195                 200                 205

Gly Asn Glu Arg Phe Arg Cys Pro Glu Thr Leu Phe Gln Pro Ser Phe
    210                 215                 220

Ile Gly Met Glu Ser Ala Gly Ile His Glu Thr Thr Tyr Asn Ser Ile
225                 230                 235                 240

Met Lys Cys Asp Ile Asp Ile Arg Lys Asp Leu Tyr Ala Asn Asn Val
                245                 250                 255

Leu Ser Gly Gly Thr Thr Met Tyr Pro Gly Ile Ala Asp Arg Met Gln
            260                 265                 270
```

Lys Glu Ile Thr Ala Leu Ala Pro Ser Thr Met Lys Ile Lys Ile Ile
275 280 285

Ala Pro Pro Glu Arg Lys Tyr Ser Val Trp Ile Gly Gly Ser Ile Leu
290 295 300

Ala Ser Leu Ser Thr Phe Gln Gln Met Trp Ile Ser Lys Pro Glu Tyr
305 310 315 320

Asp Glu Ala Gly Pro Ser Ile Val His Arg Lys Cys Phe
325 330

<210> 118
<211> 207
<212> PRT
<213> Homo sapiens

<400> 118

Met Ala Gly Pro Ala Thr Gln Ser Pro Met Lys Leu Met Ala Leu Gln
1 5 10 15

Leu Leu Leu Trp His Ser Ala Leu Trp Thr Val Gln Glu Ala Thr Pro
20 25 30

Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
35 40 45

Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
50 55 60

Leu Val Ser Glu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
65 70 75 80

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
85 90 95

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
100 105 110

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
115 120 125

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
130 135 140

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
145 150 155 160

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
165 170 175

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
180 185 190

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
195 200 205

<210> 119
<211> 204
<212> PRT
<213> Homo sapiens

<400> 119

Met Ala Gly Pro Ala Thr Gln Ser Pro Met Lys Leu Met Ala Leu Gln
1 5 10 15

Leu Leu Leu Trp His Ser Ala Leu Trp Thr Val Gln Glu Ala Thr Pro
20 25 30

Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
35 40 45

Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
50 55 60

Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
65 70 75 80

Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
85 90 95

Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
100 105 110

Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
115 120 125

Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala
130 135 140

Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu
145 150 155 160

Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
165 170 175

Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
180 185 190

Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
195 200

<210> 120

<211> 171
<212> PRT
<213> Homo sapiens

<400> 120

```
Met Ala Gly Pro Ala Thr Gln Ser Pro Met Lys Leu Met Ala Leu Gln
1               5                   10                  15

Leu Leu Leu Trp His Ser Ala Leu Trp Thr Val Gln Glu Ala Thr Pro
            20                  25                  30

Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
        35                  40                  45

Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
    50                  55                  60

Leu Val Ser Glu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe
65                  70                  75                  80

Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu
                85                  90                  95

Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr
            100                 105                 110

Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln
        115                 120                 125

Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg
    130                 135                 140

Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val
145                 150                 155                 160

Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170
```

<210> 121
<211> 168
<212> PRT
<213> Homo sapiens

<400> 121

```
Met Ala Gly Pro Ala Thr Gln Ser Pro Met Lys Leu Met Ala Leu Gln
1               5                   10                  15

Leu Leu Leu Trp His Ser Ala Leu Trp Thr Val Gln Glu Ala Thr Pro
            20                  25                  30

Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
        35                  40                  45
```

```
Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
    50                  55                  60

Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln
65                  70                  75                  80

Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr
                85                  90                  95

Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
            100                 105                 110

Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln
        115                 120                 125

Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly
    130                 135                 140

Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg
145                 150                 155                 160

Val Leu Arg His Leu Ala Gln Pro
                165
```

<210> 122
<211> 211
<212> PRT
<213> Homo sapiens

<400> 122

```
Met Arg Thr Leu Ala Cys Leu Leu Leu Leu Gly Cys Gly Tyr Leu Ala
1               5                   10                  15

His Val Leu Ala Glu Glu Ala Glu Ile Pro Arg Glu Val Ile Glu Arg
            20                  25                  30

Leu Ala Arg Ser Gln Ile His Ser Ile Arg Asp Leu Gln Arg Leu Leu
        35                  40                  45

Glu Ile Asp Ser Val Gly Ser Glu Asp Ser Leu Asp Thr Ser Leu Arg
    50                  55                  60

Ala His Gly Val His Ala Thr Lys His Val Pro Glu Lys Arg Pro Leu
65                  70                  75                  80

Pro Ile Arg Arg Lys Arg Ser Ile Glu Glu Ala Val Pro Ala Val Cys
                85                  90                  95

Lys Thr Arg Thr Val Ile Tyr Glu Ile Pro Arg Ser Gln Val Asp Pro
            100                 105                 110
```

```
Thr Ser Ala Asn Phe Leu Ile Trp Pro Pro Cys Val Glu Val Lys Arg
        115                 120                 125

Cys Thr Gly Cys Cys Asn Thr Ser Ser Val Lys Cys Gln Pro Ser Arg
    130                 135                 140

Val His His Arg Ser Val Lys Val Ala Lys Val Glu Tyr Val Arg Lys
145                 150                 155                 160

Lys Pro Lys Leu Lys Glu Val Gln Val Arg Leu Glu Glu His Leu Glu
                165                 170                 175

Cys Ala Cys Ala Thr Thr Ser Leu Asn Pro Asp Tyr Arg Glu Glu Asp
            180                 185                 190

Thr Gly Arg Pro Arg Glu Ser Gly Lys Lys Arg Lys Arg Lys Arg Leu
        195                 200                 205

Lys Pro Thr
    210
```

<210> 123
<211> 196
<212> PRT
<213> Homo sapiens

<400> 123

```
Met Arg Thr Leu Ala Cys Leu Leu Leu Leu Gly Cys Gly Tyr Leu Ala
1               5                   10                  15

His Val Leu Ala Glu Glu Ala Glu Ile Pro Arg Glu Val Ile Glu Arg
            20                  25                  30

Leu Ala Arg Ser Gln Ile His Ser Ile Arg Asp Leu Gln Arg Leu Leu
        35                  40                  45

Glu Ile Asp Ser Val Gly Ser Glu Asp Ser Leu Asp Thr Ser Leu Arg
    50                  55                  60

Ala His Gly Val His Ala Thr Lys His Val Pro Glu Lys Arg Pro Leu
65                  70                  75                  80

Pro Ile Arg Arg Lys Arg Ser Ile Glu Glu Ala Val Pro Ala Val Cys
                85                  90                  95

Lys Thr Arg Thr Val Ile Tyr Glu Ile Pro Arg Ser Gln Val Asp Pro
            100                 105                 110

Thr Ser Ala Asn Phe Leu Ile Trp Pro Pro Cys Val Glu Val Lys Arg
        115                 120                 125

Cys Thr Gly Cys Cys Asn Thr Ser Ser Val Lys Cys Gln Pro Ser Arg
```

130 135 140

Val His His Arg Ser Val Lys Val Ala Lys Val Glu Tyr Val Arg Lys
145 150 155 160

Lys Pro Lys Leu Lys Glu Val Gln Val Arg Leu Glu Glu His Leu Glu
165 170 175

Cys Ala Cys Ala Thr Thr Ser Leu Asn Pro Asp Tyr Arg Glu Glu Asp
180 185 190

Thr Asp Val Arg
195

<210> 124
<211> 241
<212> PRT
<213> Homo sapiens

<400> 124

Met Asn Arg Cys Trp Ala Leu Phe Leu Ser Leu Cys Cys Tyr Leu Arg
1 5 10 15

Leu Val Ser Ala Glu Gly Asp Pro Ile Pro Glu Glu Leu Tyr Glu Met
20 25 30

Leu Ser Asp His Ser Ile Arg Ser Phe Asp Asp Leu Gln Arg Leu Leu
35 40 45

His Gly Asp Pro Gly Glu Glu Asp Gly Ala Glu Leu Asp Leu Asn Met
50 55 60

Thr Arg Ser His Ser Gly Gly Glu Leu Glu Ser Leu Ala Arg Gly Arg
65 70 75 80

Arg Ser Leu Gly Ser Leu Thr Ile Ala Glu Pro Ala Met Ile Ala Glu
85 90 95

Cys Lys Thr Arg Thr Glu Val Phe Glu Ile Ser Arg Arg Leu Ile Asp
100 105 110

Arg Thr Asn Ala Asn Phe Leu Val Trp Pro Pro Cys Val Glu Val Gln
115 120 125

Arg Cys Ser Gly Cys Cys Asn Asn Arg Asn Val Gln Cys Arg Pro Thr
130 135 140

Gln Val Gln Leu Arg Pro Val Gln Val Arg Lys Ile Glu Ile Val Arg
145 150 155 160

Lys Lys Pro Ile Phe Lys Lys Ala Thr Val Thr Leu Glu Asp His Leu
165 170 175

```
Ala Cys Lys Cys Glu Thr Val Ala Ala Ala Arg Pro Val Thr Arg Ser
            180                 185                 190

Pro Gly Gly Ser Gln Glu Gln Arg Ala Lys Thr Pro Gln Thr Arg Val
        195                 200                 205

Thr Ile Arg Thr Val Arg Val Arg Arg Pro Pro Lys Gly Lys His Arg
    210                 215                 220

Lys Phe Lys His Thr His Asp Lys Thr Ala Leu Lys Glu Thr Leu Gly
225                 230                 235                 240

Ala
```

<210> 125
<211> 226
<212> PRT
<213> Homo sapiens

<400> 125

```
Met Phe Ile Met Gly Leu Gly Asp Pro Ile Pro Glu Glu Leu Tyr Glu
1               5                   10                  15

Met Leu Ser Asp His Ser Ile Arg Ser Phe Asp Asp Leu Gln Arg Leu
            20                  25                  30

Leu His Gly Asp Pro Gly Glu Glu Asp Gly Ala Glu Leu Asp Leu Asn
        35                  40                  45

Met Thr Arg Ser His Ser Gly Gly Glu Leu Glu Ser Leu Ala Arg Gly
    50                  55                  60

Arg Arg Ser Leu Gly Ser Leu Thr Ile Ala Glu Pro Ala Met Ile Ala
65                  70                  75                  80

Glu Cys Lys Thr Arg Thr Glu Val Phe Glu Ile Ser Arg Arg Leu Ile
                85                  90                  95

Asp Arg Thr Asn Ala Asn Phe Leu Val Trp Pro Pro Cys Val Glu Val
            100                 105                 110

Gln Arg Cys Ser Gly Cys Cys Asn Asn Arg Asn Val Gln Cys Arg Pro
        115                 120                 125

Thr Gln Val Gln Leu Arg Pro Val Gln Val Arg Lys Ile Glu Ile Val
    130                 135                 140

Arg Lys Lys Pro Ile Phe Lys Lys Ala Thr Val Thr Leu Glu Asp His
145                 150                 155                 160
```

```
Leu Ala Cys Lys Cys Glu Thr Val Ala Ala Ala Arg Pro Val Thr Arg
                165                 170                 175


Ser Pro Gly Gly Ser Gln Glu Gln Arg Ala Lys Thr Pro Gln Thr Arg
            180                 185                 190


Val Thr Ile Arg Thr Val Arg Val Arg Arg Pro Pro Lys Gly Lys His
        195                 200                 205


Arg Lys Phe Lys His Thr His Asp Lys Thr Ala Leu Lys Glu Thr Leu
    210                 215                 220


Gly Ala
225


<210>  126
<211>  345
<212>  PRT
<213>  Homo sapiens

<400>  126

Met Ser Leu Phe Gly Leu Leu Leu Leu Thr Ser Ala Leu Ala Gly Gln
1               5                   10                  15


Arg Gln Gly Thr Gln Ala Glu Ser Asn Leu Ser Ser Lys Phe Gln Phe
            20                  25                  30


Ser Ser Asn Lys Glu Gln Asn Gly Val Gln Asp Pro Gln His Glu Arg
        35                  40                  45


Ile Ile Thr Val Ser Thr Asn Gly Ser Ile His Ser Pro Arg Phe Pro
    50                  55                  60


His Thr Tyr Pro Arg Asn Thr Val Leu Val Trp Arg Leu Val Ala Val
65                  70                  75                  80


Glu Glu Asn Val Trp Ile Gln Leu Thr Phe Asp Glu Arg Phe Gly Leu
                85                  90                  95


Glu Asp Pro Glu Asp Asp Ile Cys Lys Tyr Asp Phe Val Glu Val Glu
            100                 105                 110


Glu Pro Ser Asp Gly Thr Ile Leu Gly Arg Trp Cys Gly Ser Gly Thr
        115                 120                 125


Val Pro Gly Lys Gln Ile Ser Lys Gly Asn Gln Ile Arg Ile Arg Phe
    130                 135                 140


Val Ser Asp Glu Tyr Phe Pro Ser Glu Pro Gly Phe Cys Ile His Tyr
145                 150                 155                 160
```

```
Asn Ile Val Met Pro Gln Phe Thr Glu Ala Val Ser Pro Ser Val Leu
                165                 170                 175

Pro Pro Ser Ala Leu Pro Leu Asp Leu Leu Asn Asn Ala Ile Thr Ala
            180                 185                 190

Phe Ser Thr Leu Glu Asp Leu Ile Arg Tyr Leu Glu Pro Glu Arg Trp
        195                 200                 205

Gln Leu Asp Leu Glu Asp Leu Tyr Arg Pro Thr Trp Gln Leu Leu Gly
    210                 215                 220

Lys Ala Phe Val Phe Gly Arg Lys Ser Arg Val Val Asp Leu Asn Leu
225                 230                 235                 240

Leu Thr Glu Glu Val Arg Leu Tyr Ser Cys Thr Pro Arg Asn Phe Ser
                245                 250                 255

Val Ser Ile Arg Glu Glu Leu Lys Arg Thr Asp Thr Ile Phe Trp Pro
            260                 265                 270

Gly Cys Leu Leu Val Lys Arg Cys Gly Gly Asn Cys Ala Cys Cys Leu
        275                 280                 285

His Asn Cys Asn Glu Cys Gln Cys Val Pro Ser Lys Val Thr Lys Lys
    290                 295                 300

Tyr His Glu Val Leu Gln Leu Arg Pro Lys Thr Gly Val Arg Gly Leu
305                 310                 315                 320

His Lys Ser Leu Thr Asp Val Ala Leu Glu His His Glu Glu Cys Asp
                325                 330                 335

Cys Val Cys Arg Gly Ser Thr Gly Gly
            340                 345


<210>  127
<211>  370
<212>  PRT
<213>  Homo sapiens

<400>  127

Met His Arg Leu Ile Phe Val Tyr Thr Leu Ile Cys Ala Asn Phe Cys
1               5                   10                  15

Ser Cys Arg Asp Thr Ser Ala Thr Pro Gln Ser Ala Ser Ile Lys Ala
            20                  25                  30

Leu Arg Asn Ala Asn Leu Arg Arg Asp Glu Ser Asn His Leu Thr Asp
        35                  40                  45

Leu Tyr Arg Arg Asp Glu Thr Ile Gln Val Lys Gly Asn Gly Tyr Val
```

50 55 60

Gln Ser Pro Arg Phe Pro Asn Ser Tyr Pro Arg Asn Leu Leu Leu Thr
65 70 75 80

Trp Arg Leu His Ser Gln Glu Asn Thr Arg Ile Gln Leu Val Phe Asp
85 90 95

Asn Gln Phe Gly Leu Glu Glu Ala Glu Asn Asp Ile Cys Arg Tyr Asp
100 105 110

Phe Val Glu Val Glu Asp Ile Ser Glu Thr Ser Thr Ile Ile Arg Gly
115 120 125

Arg Trp Cys Gly His Lys Glu Val Pro Pro Arg Ile Lys Ser Arg Thr
130 135 140

Asn Gln Ile Lys Ile Thr Phe Lys Ser Asp Asp Tyr Phe Val Ala Lys
145 150 155 160

Pro Gly Phe Lys Ile Tyr Tyr Ser Leu Leu Glu Asp Phe Gln Pro Ala
165 170 175

Ala Ala Ser Glu Thr Asn Trp Glu Ser Val Thr Ser Ser Ile Ser Gly
180 185 190

Val Ser Tyr Asn Ser Pro Ser Val Thr Asp Pro Thr Leu Ile Ala Asp
195 200 205

Ala Leu Asp Lys Lys Ile Ala Glu Phe Asp Thr Val Glu Asp Leu Leu
210 215 220

Lys Tyr Phe Asn Pro Glu Ser Trp Gln Glu Asp Leu Glu Asn Met Tyr
225 230 235 240

Leu Asp Thr Pro Arg Tyr Arg Gly Arg Ser Tyr His Asp Arg Lys Ser
245 250 255

Lys Val Asp Leu Asp Arg Leu Asn Asp Asp Ala Lys Arg Tyr Ser Cys
260 265 270

Thr Pro Arg Asn Tyr Ser Val Asn Ile Arg Glu Glu Leu Lys Leu Ala
275 280 285

Asn Val Val Phe Phe Pro Arg Cys Leu Leu Val Gln Arg Cys Gly Gly
290 295 300

Asn Cys Gly Cys Gly Thr Val Asn Trp Arg Ser Cys Thr Cys Asn Ser
305 310 315 320

Gly Lys Thr Val Lys Lys Tyr His Glu Val Leu Gln Phe Glu Pro Gly

325 330 335

His Ile Lys Arg Arg Gly Arg Ala Lys Thr Met Ala Leu Val Asp Ile
340 345 350

Gln Leu Asp His His Glu Arg Cys Asp Cys Ile Cys Ser Ser Arg Pro
355 360 365

Pro Arg
370

<210> 128
<211> 364
<212> PRT
<213> Homo sapiens

<400> 128

Met His Arg Leu Ile Phe Val Tyr Thr Leu Ile Cys Ala Asn Phe Cys
1 5 10 15

Ser Cys Arg Asp Thr Ser Ala Thr Pro Gln Ser Ala Ser Ile Lys Ala
20 25 30

Leu Arg Asn Ala Asn Leu Arg Arg Asp Asp Leu Tyr Arg Arg Asp Glu
35 40 45

Thr Ile Gln Val Lys Gly Asn Gly Tyr Val Gln Ser Pro Arg Phe Pro
50 55 60

Asn Ser Tyr Pro Arg Asn Leu Leu Leu Thr Trp Arg Leu His Ser Gln
65 70 75 80

Glu Asn Thr Arg Ile Gln Leu Val Phe Asp Asn Gln Phe Gly Leu Glu
85 90 95

Glu Ala Glu Asn Asp Ile Cys Arg Tyr Asp Phe Val Glu Val Glu Asp
100 105 110

Ile Ser Glu Thr Ser Thr Ile Ile Arg Gly Arg Trp Cys Gly His Lys
115 120 125

Glu Val Pro Pro Arg Ile Lys Ser Arg Thr Asn Gln Ile Lys Ile Thr
130 135 140

Phe Lys Ser Asp Asp Tyr Phe Val Ala Lys Pro Gly Phe Lys Ile Tyr
145 150 155 160

Tyr Ser Leu Leu Glu Asp Phe Gln Pro Ala Ala Ala Ser Glu Thr Asn
165 170 175

Trp Glu Ser Val Thr Ser Ser Ile Ser Gly Val Ser Tyr Asn Ser Pro
180 185 190

```
Ser Val Thr Asp Pro Thr Leu Ile Ala Asp Ala Leu Asp Lys Lys Ile
        195                 200                 205

Ala Glu Phe Asp Thr Val Glu Asp Leu Leu Lys Tyr Phe Asn Pro Glu
    210                 215                 220

Ser Trp Gln Glu Asp Leu Glu Asn Met Tyr Leu Asp Thr Pro Arg Tyr
225                 230                 235                 240

Arg Gly Arg Ser Tyr His Asp Arg Lys Ser Lys Val Asp Leu Asp Arg
                245                 250                 255

Leu Asn Asp Asp Ala Lys Arg Tyr Ser Cys Thr Pro Arg Asn Tyr Ser
            260                 265                 270

Val Asn Ile Arg Glu Glu Leu Lys Leu Ala Asn Val Val Phe Phe Pro
        275                 280                 285

Arg Cys Leu Leu Val Gln Arg Cys Gly Gly Asn Cys Gly Cys Gly Thr
    290                 295                 300

Val Asn Trp Arg Ser Cys Thr Cys Asn Ser Gly Lys Thr Val Lys Lys
305                 310                 315                 320

Tyr His Glu Val Leu Gln Phe Glu Pro Gly His Ile Lys Arg Arg Gly
                325                 330                 335

Arg Ala Lys Thr Met Ala Leu Val Asp Ile Gln Leu Asp His His Glu
            340                 345                 350

Arg Cys Asp Cys Ile Cys Ser Ser Arg Pro Pro Arg
        355                 360


<210>  129
<211>  469
<212>  PRT
<213>  Homo sapiens

<400>  129

Met His Ser Phe Pro Pro Leu Leu Leu Leu Leu Phe Trp Gly Val Val
1               5                   10                  15

Ser His Ser Phe Pro Ala Thr Leu Glu Thr Gln Glu Gln Asp Val Asp
            20                  25                  30

Leu Val Gln Lys Tyr Leu Glu Lys Tyr Tyr Asn Leu Lys Asn Asp Gly
        35                  40                  45

Arg Gln Val Glu Lys Arg Arg Asn Ser Gly Pro Val Val Glu Lys Leu
    50                  55                  60
```

```
Lys Gln Met Gln Glu Phe Phe Gly Leu Lys Val Thr Gly Lys Pro Asp
65                  70                  75                  80

Ala Glu Thr Leu Lys Val Met Lys Gln Pro Arg Cys Gly Val Pro Asp
                85                  90                  95

Val Ala Gln Phe Val Leu Thr Glu Gly Asn Pro Arg Trp Glu Gln Thr
            100                 105                 110

His Leu Thr Tyr Arg Ile Glu Asn Tyr Thr Pro Asp Leu Pro Arg Ala
        115                 120                 125

Asp Val Asp His Ala Ile Glu Lys Ala Phe Gln Leu Trp Ser Asn Val
    130                 135                 140

Thr Pro Leu Thr Phe Thr Lys Val Ser Glu Gly Gln Ala Asp Ile Met
145                 150                 155                 160

Ile Ser Phe Val Arg Gly Asp His Arg Asp Asn Ser Pro Phe Asp Gly
                165                 170                 175

Pro Gly Gly Asn Leu Ala His Ala Phe Gln Pro Gly Pro Gly Ile Gly
            180                 185                 190

Gly Asp Ala His Phe Asp Glu Asp Glu Arg Trp Thr Asn Asn Phe Arg
        195                 200                 205

Glu Tyr Asn Leu His Arg Val Ala Ala His Glu Leu Gly His Ser Leu
    210                 215                 220

Gly Leu Ser His Ser Thr Asp Ile Gly Ala Leu Met Tyr Pro Ser Tyr
225                 230                 235                 240

Thr Phe Ser Gly Asp Val Gln Leu Ala Gln Asp Asp Ile Asp Gly Ile
                245                 250                 255

Gln Ala Ile Tyr Gly Arg Ser Gln Asn Pro Val Gln Pro Ile Gly Pro
            260                 265                 270

Gln Thr Pro Lys Ala Cys Asp Ser Lys Leu Thr Phe Asp Ala Ile Thr
        275                 280                 285

Thr Ile Arg Gly Glu Val Met Phe Phe Lys Asp Arg Phe Tyr Met Arg
    290                 295                 300

Thr Asn Pro Phe Tyr Pro Glu Val Glu Leu Asn Phe Ile Ser Val Phe
305                 310                 315                 320

Trp Pro Gln Leu Pro Asn Gly Leu Glu Ala Ala Tyr Glu Phe Ala Asp
                325                 330                 335
```

```
Arg Asp Glu Val Arg Phe Phe Lys Gly Asn Lys Tyr Trp Ala Val Gln
            340                 345                 350

Gly Gln Asn Val Leu His Gly Tyr Pro Lys Asp Ile Tyr Ser Ser Phe
        355                 360                 365

Gly Phe Pro Arg Thr Val Lys His Ile Asp Ala Ala Leu Ser Glu Glu
    370                 375                 380

Asn Thr Gly Lys Thr Tyr Phe Phe Val Ala Asn Lys Tyr Trp Arg Tyr
385                 390                 395                 400

Asp Glu Tyr Lys Arg Ser Met Asp Pro Gly Tyr Pro Lys Met Ile Ala
                405                 410                 415

His Asp Phe Pro Gly Ile Gly His Lys Val Asp Ala Val Phe Met Lys
            420                 425                 430

Asp Gly Phe Phe Tyr Phe Phe His Gly Thr Arg Gln Tyr Lys Phe Asp
        435                 440                 445

Pro Lys Thr Lys Arg Ile Leu Thr Leu Gln Lys Ala Asn Ser Trp Phe
    450                 455                 460

Asn Cys Arg Lys Asn
465


<210>  130
<211>  403
<212>  PRT
<213>  Homo sapiens

<400>  130

Met Gln Glu Phe Phe Gly Leu Lys Val Thr Gly Lys Pro Asp Ala Glu
1               5                   10                  15

Thr Leu Lys Val Met Lys Gln Pro Arg Cys Gly Val Pro Asp Val Ala
            20                  25                  30

Gln Phe Val Leu Thr Glu Gly Asn Pro Arg Trp Glu Gln Thr His Leu
        35                  40                  45

Thr Tyr Arg Ile Glu Asn Tyr Thr Pro Asp Leu Pro Arg Ala Asp Val
    50                  55                  60

Asp His Ala Ile Glu Lys Ala Phe Gln Leu Trp Ser Asn Val Thr Pro
65                  70                  75                  80

Leu Thr Phe Thr Lys Val Ser Glu Gly Gln Ala Asp Ile Met Ile Ser
                85                  90                  95
```

```
Phe Val Arg Gly Asp His Arg Asp Asn Ser Pro Phe Asp Gly Pro Gly
            100                 105                 110

Gly Asn Leu Ala His Ala Phe Gln Pro Gly Pro Gly Ile Gly Gly Asp
        115                 120                 125

Ala His Phe Asp Glu Asp Glu Arg Trp Thr Asn Asn Phe Arg Glu Tyr
    130                 135                 140

Asn Leu His Arg Val Ala Ala His Glu Leu Gly His Ser Leu Gly Leu
145                 150                 155                 160

Ser His Ser Thr Asp Ile Gly Ala Leu Met Tyr Pro Ser Tyr Thr Phe
                165                 170                 175

Ser Gly Asp Val Gln Leu Ala Gln Asp Asp Ile Asp Gly Ile Gln Ala
            180                 185                 190

Ile Tyr Gly Arg Ser Gln Asn Pro Val Gln Pro Ile Gly Pro Gln Thr
        195                 200                 205

Pro Lys Ala Cys Asp Ser Lys Leu Thr Phe Asp Ala Ile Thr Thr Ile
    210                 215                 220

Arg Gly Glu Val Met Phe Phe Lys Asp Arg Phe Tyr Met Arg Thr Asn
225                 230                 235                 240

Pro Phe Tyr Pro Glu Val Glu Leu Asn Phe Ile Ser Val Phe Trp Pro
                245                 250                 255

Gln Leu Pro Asn Gly Leu Glu Ala Ala Tyr Glu Phe Ala Asp Arg Asp
            260                 265                 270

Glu Val Arg Phe Phe Lys Gly Asn Lys Tyr Trp Ala Val Gln Gly Gln
        275                 280                 285

Asn Val Leu His Gly Tyr Pro Lys Asp Ile Tyr Ser Ser Phe Gly Phe
    290                 295                 300

Pro Arg Thr Val Lys His Ile Asp Ala Ala Leu Ser Glu Glu Asn Thr
305                 310                 315                 320

Gly Lys Thr Tyr Phe Phe Val Ala Asn Lys Tyr Trp Arg Tyr Asp Glu
                325                 330                 335

Tyr Lys Arg Ser Met Asp Pro Gly Tyr Pro Lys Met Ile Ala His Asp
            340                 345                 350

Phe Pro Gly Ile Gly His Lys Val Asp Ala Val Phe Met Lys Asp Gly
        355                 360                 365
```

Phe Phe Tyr Phe Phe His Gly Thr Arg Gln Tyr Lys Phe Asp Pro Lys
370 375 380

Thr Lys Arg Ile Leu Thr Leu Gln Lys Ala Asn Ser Trp Phe Asn Cys
385 390 395 400

Arg Lys Asn

<210> 131
<211> 467
<212> PRT
<213> Homo sapiens

<400> 131

Met Phe Ser Leu Lys Thr Leu Pro Phe Leu Leu Leu Leu His Val Gln
1 5 10 15

Ile Ser Lys Ala Phe Pro Val Ser Ser Lys Glu Lys Asn Thr Lys Thr
20 25 30

Val Gln Asp Tyr Leu Glu Lys Phe Tyr Gln Leu Pro Ser Asn Gln Tyr
35 40 45

Gln Ser Thr Arg Lys Asn Gly Thr Asn Val Ile Val Glu Lys Leu Lys
50 55 60

Glu Met Gln Arg Phe Phe Gly Leu Asn Val Thr Gly Lys Pro Asn Glu
65 70 75 80

Glu Thr Leu Asp Met Met Lys Lys Pro Arg Cys Gly Val Pro Asp Ser
85 90 95

Gly Gly Phe Met Leu Thr Pro Gly Asn Pro Lys Trp Glu Arg Thr Asn
100 105 110

Leu Thr Tyr Arg Ile Arg Asn Tyr Thr Pro Gln Leu Ser Glu Ala Glu
115 120 125

Val Glu Arg Ala Ile Lys Asp Ala Phe Glu Leu Trp Ser Val Ala Ser
130 135 140

Pro Leu Ile Phe Thr Arg Ile Ser Gln Gly Glu Ala Asp Ile Asn Ile
145 150 155 160

Ala Phe Tyr Gln Arg Asp His Gly Asp Asn Ser Pro Phe Asp Gly Pro
165 170 175

Asn Gly Ile Leu Ala His Ala Phe Gln Pro Gly Gln Gly Ile Gly Gly
180 185 190

Asp Ala His Phe Asp Ala Glu Glu Thr Trp Thr Asn Thr Ser Ala Asn

195 200 205

Tyr Asn Leu Phe Leu Val Ala Ala His Glu Phe Gly His Ser Leu Gly
210 215 220

Leu Ala His Ser Ser Asp Pro Gly Ala Leu Met Tyr Pro Asn Tyr Ala
225 230 235 240

Phe Arg Glu Thr Ser Asn Tyr Ser Leu Pro Gln Asp Asp Ile Asp Gly
245 250 255

Ile Gln Ala Ile Tyr Gly Leu Ser Ser Asn Pro Ile Gln Pro Thr Gly
260 265 270

Pro Ser Thr Pro Lys Pro Cys Asp Pro Ser Leu Thr Phe Asp Ala Ile
275 280 285

Thr Thr Leu Arg Gly Glu Ile Leu Phe Phe Lys Asp Arg Tyr Phe Trp
290 295 300

Arg Arg His Pro Gln Leu Gln Arg Val Glu Met Asn Phe Ile Ser Leu
305 310 315 320

Phe Trp Pro Ser Leu Pro Thr Gly Ile Gln Ala Ala Tyr Glu Asp Phe
325 330 335

Asp Arg Asp Leu Ile Phe Leu Phe Lys Gly Asn Gln Tyr Trp Ala Leu
340 345 350

Ser Gly Tyr Asp Ile Leu Gln Gly Tyr Pro Lys Asp Ile Ser Asn Tyr
355 360 365

Gly Phe Pro Ser Ser Val Gln Ala Ile Asp Ala Ala Val Phe Tyr Arg
370 375 380

Ser Lys Thr Tyr Phe Phe Val Asn Asp Gln Phe Trp Arg Tyr Asp Asn
385 390 395 400

Gln Arg Gln Phe Met Glu Pro Gly Tyr Pro Lys Ser Ile Ser Gly Ala
405 410 415

Phe Pro Gly Ile Glu Ser Lys Val Asp Ala Val Phe Gln Gln Glu His
420 425 430

Phe Phe His Val Phe Ser Gly Pro Arg Tyr Tyr Ala Phe Asp Leu Ile
435 440 445

Ala Gln Arg Val Thr Arg Val Ala Arg Gly Asn Lys Trp Leu Asn Cys
450 455 460

Arg Tyr Gly

465

<210> 132
<211> 476
<212> PRT
<213> Homo sapiens

<400> 132

Met Met His Leu Ala Phe Leu Val Leu Leu Cys Leu Pro Val Cys Ser
1 5 10 15

Ala Tyr Pro Leu Ser Gly Ala Ala Lys Glu Glu Asp Ser Asn Lys Asp
20 25 30

Leu Ala Gln Gln Tyr Leu Glu Lys Tyr Tyr Asn Leu Glu Lys Asp Val
35 40 45

Lys Gln Phe Arg Arg Lys Asp Ser Asn Leu Ile Val Lys Lys Ile Gln
50 55 60

Gly Met Gln Lys Phe Leu Gly Leu Glu Val Thr Gly Lys Leu Asp Thr
65 70 75 80

Asp Thr Leu Glu Val Met Arg Lys Pro Arg Cys Gly Val Pro Asp Val
85 90 95

Gly His Phe Ser Ser Phe Pro Gly Met Pro Lys Trp Arg Lys Thr His
100 105 110

Leu Thr Tyr Arg Ile Val Asn Tyr Thr Pro Asp Leu Pro Arg Asp Ala
115 120 125

Val Asp Ser Ala Ile Glu Lys Ala Leu Lys Val Trp Glu Glu Val Thr
130 135 140

Pro Leu Thr Phe Ser Arg Leu Tyr Glu Gly Glu Ala Asp Ile Met Ile
145 150 155 160

Ser Phe Ala Val Lys Glu His Gly Asp Phe Tyr Ser Phe Asp Gly Pro
165 170 175

Gly His Ser Leu Ala His Ala Tyr Pro Pro Gly Pro Gly Leu Tyr Gly
180 185 190

Asp Ile His Phe Asp Asp Asp Glu Lys Trp Thr Glu Asp Ala Ser Gly
195 200 205

Thr Asn Leu Phe Leu Val Ala Ala His Glu Leu Gly His Ser Leu Gly
210 215 220

Leu Phe His Ser Ala Asn Thr Glu Ala Leu Met Tyr Pro Leu Tyr Asn
225 230 235 240

```
Ser Phe Thr Glu Leu Ala Gln Phe Arg Leu Ser Gln Asp Asp Val Asn
                245                 250                 255

Gly Ile Gln Ser Leu Tyr Gly Pro Pro Pro Ala Ser Thr Glu Glu Pro
            260                 265                 270

Leu Val Pro Thr Lys Ser Val Pro Ser Gly Ser Glu Met Pro Ala Lys
        275                 280                 285

Cys Asp Pro Ala Leu Ser Phe Asp Ala Ile Ser Thr Leu Arg Gly Glu
    290                 295                 300

Tyr Leu Phe Phe Lys Asp Arg Tyr Phe Trp Arg Arg Ser His Trp Asn
305                 310                 315                 320

Pro Glu Pro Glu Phe His Leu Ile Ser Ala Phe Trp Pro Ser Leu Pro
                325                 330                 335

Ser Tyr Leu Asp Ala Ala Tyr Glu Val Asn Ser Arg Asp Thr Val Phe
            340                 345                 350

Ile Phe Lys Gly Asn Glu Phe Trp Ala Ile Arg Gly Asn Glu Val Gln
        355                 360                 365

Ala Gly Tyr Pro Arg Gly Ile His Thr Leu Gly Phe Pro Pro Thr Ile
    370                 375                 380

Arg Lys Ile Asp Ala Ala Val Ser Asp Lys Glu Lys Lys Lys Thr Tyr
385                 390                 395                 400

Phe Phe Ala Ala Asp Lys Tyr Trp Arg Phe Asp Glu Asn Ser Gln Ser
                405                 410                 415

Met Glu Gln Gly Phe Pro Arg Leu Ile Ala Asp Asp Phe Pro Gly Val
            420                 425                 430

Glu Pro Lys Val Asp Ala Val Leu Gln Ala Phe Gly Phe Phe Tyr Phe
        435                 440                 445

Phe Ser Gly Ser Ser Gln Phe Glu Phe Asp Pro Asn Ala Arg Met Val
    450                 455                 460

Thr His Ile Leu Lys Ser Asn Ser Trp Leu His Cys
465                 470                 475


<210>  133
<211>  470
<212>  PRT
<213>  Homo sapiens

<400>  133
```

```
Met Lys Phe Leu Leu Ile Leu Leu Leu Gln Ala Thr Ala Ser Gly Ala
1               5                  10                  15

Leu Pro Leu Asn Ser Ser Thr Ser Leu Glu Lys Asn Asn Val Leu Phe
            20                  25                  30

Gly Glu Arg Tyr Leu Glu Lys Phe Tyr Gly Leu Glu Ile Asn Lys Leu
        35                  40                  45

Pro Val Thr Lys Met Lys Tyr Ser Gly Asn Leu Met Lys Glu Lys Ile
    50                  55                  60

Gln Glu Met Gln His Phe Leu Gly Leu Lys Val Thr Gly Gln Leu Asp
65                  70                  75                  80

Thr Ser Thr Leu Glu Met Met His Ala Pro Arg Cys Gly Val Pro Asp
                85                  90                  95

Val His His Phe Arg Glu Met Pro Gly Gly Pro Val Trp Arg Lys His
            100                 105                 110

Tyr Ile Thr Tyr Arg Ile Asn Asn Tyr Thr Pro Asp Met Asn Arg Glu
        115                 120                 125

Asp Val Asp Tyr Ala Ile Arg Lys Ala Phe Gln Val Trp Ser Asn Val
    130                 135                 140

Thr Pro Leu Lys Phe Ser Lys Ile Asn Thr Gly Met Ala Asp Ile Leu
145                 150                 155                 160

Val Val Phe Ala Arg Gly Ala His Gly Asp Phe His Ala Phe Asp Gly
                165                 170                 175

Lys Gly Gly Ile Leu Ala His Ala Phe Gly Pro Gly Ser Gly Ile Gly
            180                 185                 190

Gly Asp Ala His Phe Asp Glu Asp Glu Phe Trp Thr Thr His Ser Gly
        195                 200                 205

Gly Thr Asn Leu Phe Leu Thr Ala Val His Glu Ile Gly His Ser Leu
    210                 215                 220

Gly Leu Gly His Ser Ser Asp Pro Lys Ala Val Met Phe Pro Thr Tyr
225                 230                 235                 240

Lys Tyr Val Asp Ile Asn Thr Phe Arg Leu Ser Ala Asp Asp Ile Arg
                245                 250                 255

Gly Ile Gln Ser Leu Tyr Gly Asp Pro Lys Glu Asn Gln Arg Leu Pro
            260                 265                 270
```

```
Asn Pro Asp Asn Ser Glu Pro Ala Leu Cys Asp Pro Asn Leu Ser Phe
        275                 280                 285

Asp Ala Val Thr Thr Val Gly Asn Lys Ile Phe Phe Phe Lys Asp Arg
    290                 295                 300

Phe Phe Trp Leu Lys Val Ser Glu Arg Pro Lys Thr Ser Val Asn Leu
305                 310                 315                 320

Ile Ser Ser Leu Trp Pro Thr Leu Pro Ser Gly Ile Glu Ala Ala Tyr
                325                 330                 335

Glu Ile Glu Ala Arg Asn Gln Val Phe Leu Phe Lys Asp Asp Lys Tyr
            340                 345                 350

Trp Leu Ile Ser Asn Leu Arg Pro Glu Pro Asn Tyr Pro Lys Ser Ile
        355                 360                 365

His Ser Phe Gly Phe Pro Asn Phe Val Lys Lys Ile Asp Ala Ala Val
    370                 375                 380

Phe Asn Pro Arg Phe Tyr Arg Thr Tyr Phe Phe Val Asp Asn Gln Tyr
385                 390                 395                 400

Trp Arg Tyr Asp Glu Arg Arg Gln Met Met Asp Pro Gly Tyr Pro Lys
                405                 410                 415

Leu Ile Thr Lys Asn Phe Gln Gly Ile Gly Pro Lys Ile Asp Ala Val
            420                 425                 430

Phe Tyr Ser Lys Asn Lys Tyr Tyr Tyr Phe Phe Gln Gly Ser Asn Gln
        435                 440                 445

Phe Glu Tyr Asp Phe Leu Leu Gln Arg Ile Thr Lys Thr Leu Lys Ser
    450                 455                 460

Asn Ser Trp Phe Gly Cys
465                 470


<210>  134
<211>  2871
<212>  PRT
<213>  Homo sapiens

<400>  134

Met Arg Arg Gly Arg Leu Leu Glu Ile Ala Leu Gly Phe Thr Val Leu
1               5                   10                  15

Leu Ala Ser Tyr Thr Ser His Gly Ala Asp Ala Asn Leu Glu Ala Gly
            20                  25                  30
```

```
Asn Val Lys Glu Thr Arg Ala Ser Arg Ala Lys Arg Arg Gly Gly Gly
        35                  40                  45

Gly His Asp Ala Leu Lys Gly Pro Asn Val Cys Gly Ser Arg Tyr Asn
    50                  55                  60

Ala Tyr Cys Cys Pro Gly Trp Lys Thr Leu Pro Gly Gly Asn Gln Cys
65                  70                  75                  80

Ile Val Pro Ile Cys Arg His Ser Cys Gly Asp Gly Phe Cys Ser Arg
                85                  90                  95

Pro Asn Met Cys Thr Cys Pro Ser Gly Gln Ile Ala Pro Ser Cys Gly
            100                 105                 110

Ser Arg Ser Ile Gln His Cys Asn Ile Arg Cys Met Asn Gly Gly Ser
        115                 120                 125

Cys Ser Asp Asp His Cys Leu Cys Gln Lys Gly Tyr Ile Gly Thr His
    130                 135                 140

Cys Gly Gln Pro Val Cys Glu Ser Gly Cys Leu Asn Gly Gly Arg Cys
145                 150                 155                 160

Val Ala Pro Asn Arg Cys Ala Cys Thr Tyr Gly Phe Thr Gly Pro Gln
                165                 170                 175

Cys Glu Arg Asp Tyr Arg Thr Gly Pro Cys Phe Thr Val Ile Ser Asn
            180                 185                 190

Gln Met Cys Gln Gly Gln Leu Ser Gly Ile Val Cys Thr Lys Thr Leu
        195                 200                 205

Cys Cys Ala Thr Val Gly Arg Ala Trp Gly His Pro Cys Glu Met Cys
    210                 215                 220

Pro Ala Gln Pro His Pro Cys Arg Arg Gly Phe Ile Pro Asn Ile Arg
225                 230                 235                 240

Thr Gly Ala Cys Gln Asp Val Asp Glu Cys Gln Ala Ile Pro Gly Leu
                245                 250                 255

Cys Gln Gly Gly Asn Cys Ile Asn Thr Val Gly Ser Phe Glu Cys Lys
            260                 265                 270

Cys Pro Ala Gly His Lys Leu Asn Glu Val Ser Gln Lys Cys Glu Asp
        275                 280                 285

Ile Asp Glu Cys Ser Thr Ile Pro Gly Ile Cys Glu Gly Gly Glu Cys
    290                 295                 300
```

```
Thr Asn Thr Val Ser Ser Tyr Phe Cys Lys Cys Pro Pro Gly Phe Tyr
305                 310                 315                 320

Thr Ser Pro Asp Gly Thr Arg Cys Ile Asp Val Arg Pro Gly Tyr Cys
                325                 330                 335

Tyr Thr Ala Leu Thr Asn Gly Arg Cys Ser Asn Gln Leu Pro Gln Ser
            340                 345                 350

Ile Thr Lys Met Gln Cys Cys Cys Asp Ala Gly Arg Cys Trp Ser Pro
        355                 360                 365

Gly Val Thr Val Ala Pro Glu Met Cys Pro Ile Arg Ala Thr Glu Asp
    370                 375                 380

Phe Asn Lys Leu Cys Ser Val Pro Met Val Ile Pro Gly Arg Pro Glu
385                 390                 395                 400

Tyr Pro Pro Pro Pro Leu Gly Pro Ile Pro Pro Val Leu Pro Val Pro
                405                 410                 415

Pro Gly Phe Pro Pro Gly Pro Gln Ile Pro Val Pro Arg Pro Pro Val
            420                 425                 430

Glu Tyr Leu Tyr Pro Ser Arg Glu Pro Pro Arg Val Leu Pro Val Asn
        435                 440                 445

Val Thr Asp Tyr Cys Gln Leu Val Arg Tyr Leu Cys Gln Asn Gly Arg
    450                 455                 460

Cys Ile Pro Thr Pro Gly Ser Tyr Arg Cys Glu Cys Asn Lys Gly Phe
465                 470                 475                 480

Gln Leu Asp Leu Arg Gly Glu Cys Ile Asp Val Asp Glu Cys Glu Lys
                485                 490                 495

Asn Pro Cys Ala Gly Gly Glu Cys Ile Asn Asn Gln Gly Ser Tyr Thr
            500                 505                 510

Cys Gln Cys Arg Ala Gly Tyr Gln Ser Thr Leu Thr Arg Thr Glu Cys
        515                 520                 525

Arg Asp Ile Asp Glu Cys Leu Gln Asn Gly Arg Ile Cys Asn Asn Gly
    530                 535                 540

Arg Cys Ile Asn Thr Asp Gly Ser Phe His Cys Val Cys Asn Ala Gly
545                 550                 555                 560

Phe His Val Thr Arg Asp Gly Lys Asn Cys Glu Asp Met Asp Glu Cys
                565                 570                 575
```

```
Ser Ile Arg Asn Met Cys Leu Asn Gly Met Cys Ile Asn Glu Asp Gly
            580                 585                 590

Ser Phe Lys Cys Ile Cys Lys Pro Gly Phe Gln Leu Ala Ser Asp Gly
        595                 600                 605

Arg Tyr Cys Lys Asp Ile Asn Glu Cys Glu Thr Pro Gly Ile Cys Met
    610                 615                 620

Asn Gly Arg Cys Val Asn Thr Asp Gly Ser Tyr Arg Cys Glu Cys Phe
625                 630                 635                 640

Pro Gly Leu Ala Val Gly Leu Asp Gly Arg Val Cys Val Asp Thr His
                645                 650                 655

Met Arg Ser Thr Cys Tyr Gly Gly Tyr Lys Arg Gly Gln Cys Ile Lys
            660                 665                 670

Pro Leu Phe Gly Ala Val Thr Lys Ser Glu Cys Cys Cys Ala Ser Thr
        675                 680                 685

Glu Tyr Ala Phe Gly Glu Pro Cys Gln Pro Cys Pro Ala Gln Asn Ser
    690                 695                 700

Ala Glu Tyr Gln Ala Leu Cys Ser Ser Gly Pro Gly Met Thr Ser Ala
705                 710                 715                 720

Gly Ser Asp Ile Asn Glu Cys Ala Leu Asp Pro Asp Ile Cys Pro Asn
                725                 730                 735

Gly Ile Cys Glu Asn Leu Arg Gly Thr Tyr Lys Cys Ile Cys Asn Ser
            740                 745                 750

Gly Tyr Glu Val Asp Ser Thr Gly Lys Asn Cys Val Asp Ile Asn Glu
        755                 760                 765

Cys Val Leu Asn Ser Leu Leu Cys Asp Asn Gly Gln Cys Arg Asn Thr
    770                 775                 780

Pro Gly Ser Phe Val Cys Thr Cys Pro Lys Gly Phe Ile Tyr Lys Pro
785                 790                 795                 800

Asp Leu Lys Thr Cys Glu Asp Ile Asp Glu Cys Glu Ser Ser Pro Cys
                805                 810                 815

Ile Asn Gly Val Cys Lys Asn Ser Pro Gly Ser Phe Ile Cys Glu Cys
            820                 825                 830

Ser Ser Glu Ser Thr Leu Asp Pro Thr Lys Thr Ile Cys Ile Glu Thr
        835                 840                 845
```

```
Ile Lys Gly Thr Cys Trp Gln Thr Val Ile Asp Gly Arg Cys Glu Ile
    850                 855                 860

Asn Ile Asn Gly Ala Thr Leu Lys Ser Gln Cys Cys Ser Ser Leu Gly
865                 870                 875                 880

Ala Ala Trp Gly Ser Pro Cys Thr Leu Cys Gln Val Asp Pro Ile Cys
                885                 890                 895

Gly Lys Gly Tyr Ser Arg Ile Lys Gly Thr Gln Cys Glu Asp Ile Asp
            900                 905                 910

Glu Cys Glu Val Phe Pro Gly Val Cys Lys Asn Gly Leu Cys Val Asn
        915                 920                 925

Thr Arg Gly Ser Phe Lys Cys Gln Cys Pro Ser Gly Met Thr Leu Asp
    930                 935                 940

Ala Thr Gly Arg Ile Cys Leu Asp Ile Arg Leu Glu Thr Cys Phe Leu
945                 950                 955                 960

Arg Tyr Glu Asp Glu Glu Cys Thr Leu Pro Ile Ala Gly Arg His Arg
                965                 970                 975

Met Asp Ala Cys Cys Cys Ser Val Gly Ala Ala Trp Gly Thr Glu Glu
            980                 985                 990

Cys Glu Glu Cys Pro Met Arg Asn  Thr Pro Glu Tyr Glu  Glu Leu Cys
        995                 1000                1005

Pro Arg  Gly Pro Gly Phe Ala  Thr Lys Glu Ile Thr  Asn Gly Lys
    1010                1015                1020

Pro Phe  Phe Lys Asp Ile Asn  Glu Cys Lys Met Ile  Pro Ser Leu
    1025                1030                1035

Cys Thr  His Gly Lys Cys Arg  Asn Thr Ile Gly Ser  Phe Lys Cys
    1040                1045                1050

Arg Cys  Asp Ser Gly Phe Ala  Leu Asp Ser Glu Glu  Arg Asn Cys
    1055                1060                1065

Thr Asp  Ile Asp Glu Cys Arg  Ile Ser Pro Asp Leu  Cys Gly Arg
    1070                1075                1080

Gly Gln  Cys Val Asn Thr Pro  Gly Asp Phe Glu Cys  Lys Cys Asp
    1085                1090                1095

Glu Gly  Tyr Glu Ser Gly Phe  Met Met Met Lys Asn  Cys Met Asp
    1100                1105                1110
```

```
Ile Asp  Glu Cys Gln Arg Asp  Pro Leu Leu Cys Arg  Gly Gly Val
    1115                 1120                 1125

Cys His  Asn Thr Glu Gly Ser  Tyr Arg Cys Glu Cys  Pro Pro Gly
    1130                 1135                 1140

His Gln  Leu Ser Pro Asn Ile  Ser Ala Cys Ile Asp  Ile Asn Glu
    1145                 1150                 1155

Cys Glu  Leu Ser Ala His Leu  Cys Pro Asn Gly Arg  Cys Val Asn
    1160                 1165                 1170

Leu Ile  Gly Lys Tyr Gln Cys  Ala Cys Asn Pro Gly  Tyr His Ser
    1175                 1180                 1185

Thr Pro  Asp Arg Leu Phe Cys  Val Asp Ile Asp Glu  Cys Ser Ile
    1190                 1195                 1200

Met Asn  Gly Gly Cys Glu Thr  Phe Cys Thr Asn Ser  Glu Gly Ser
    1205                 1210                 1215

Tyr Glu  Cys Ser Cys Gln Pro  Gly Phe Ala Leu Met  Pro Asp Gln
    1220                 1225                 1230

Arg Ser  Cys Thr Asp Ile Asp  Glu Cys Glu Asp Asn  Pro Asn Ile
    1235                 1240                 1245

Cys Asp  Gly Gly Gln Cys Thr  Asn Ile Pro Gly Glu  Tyr Arg Cys
    1250                 1255                 1260

Leu Cys  Tyr Asp Gly Phe Met  Ala Ser Glu Asp Met  Lys Thr Cys
    1265                 1270                 1275

Val Asp  Val Asn Glu Cys Asp  Leu Asn Pro Asn Ile  Cys Leu Ser
    1280                 1285                 1290

Gly Thr  Cys Glu Asn Thr Lys  Gly Ser Phe Ile Cys  His Cys Asp
    1295                 1300                 1305

Met Gly  Tyr Ser Gly Lys Lys  Gly Lys Thr Gly Cys  Thr Asp Ile
    1310                 1315                 1320

Asn Glu  Cys Glu Ile Gly Ala  His Asn Cys Gly Lys  His Ala Val
    1325                 1330                 1335

Cys Thr  Asn Thr Ala Gly Ser  Phe Lys Cys Ser Cys  Ser Pro Gly
    1340                 1345                 1350

Trp Ile  Gly Asp Gly Ile Lys  Cys Thr Asp Leu Asp  Glu Cys Ser
    1355                 1360                 1365
```

```
Asn Gly  Thr His Met Cys Ser  Gln His Ala Asp Cys  Lys Asn Thr
    1370                 1375                 1380

Met Gly  Ser Tyr Arg Cys Leu  Cys Lys Glu Gly Tyr  Thr Gly Asp
    1385                 1390                 1395

Gly Phe  Thr Cys Thr Asp Leu  Asp Glu Cys Ser Glu  Asn Leu Asn
    1400                 1405                 1410

Leu Cys  Gly Asn Gly Gln Cys  Leu Asn Ala Pro Gly  Gly Tyr Arg
    1415                 1420                 1425

Cys Glu  Cys Asp Met Gly Phe  Val Pro Ser Ala Asp  Gly Lys Ala
    1430                 1435                 1440

Cys Glu  Asp Ile Asp Glu Cys  Ser Leu Pro Asn Ile  Cys Val Phe
    1445                 1450                 1455

Gly Thr  Cys His Asn Leu Pro  Gly Leu Phe Arg Cys  Glu Cys Glu
    1460                 1465                 1470

Ile Gly  Tyr Glu Leu Asp Arg  Ser Gly Gly Asn Cys  Thr Asp Val
    1475                 1480                 1485

Asn Glu  Cys Leu Asp Pro Thr  Thr Cys Ile Ser Gly  Asn Cys Val
    1490                 1495                 1500

Asn Thr  Pro Gly Ser Tyr Ile  Cys Asp Cys Pro Pro  Asp Phe Glu
    1505                 1510                 1515

Leu Asn  Pro Thr Arg Val Gly  Cys Val Asp Thr Arg  Ser Gly Asn
    1520                 1525                 1530

Cys Tyr  Leu Asp Ile Arg Pro  Arg Gly Asp Asn Gly  Asp Thr Ala
    1535                 1540                 1545

Cys Ser  Asn Glu Ile Gly Val  Gly Val Ser Lys Ala  Ser Cys Cys
    1550                 1555                 1560

Cys Ser  Leu Gly Lys Ala Trp  Gly Thr Pro Cys Glu  Met Cys Pro
    1565                 1570                 1575

Ala Val  Asn Thr Ser Glu Tyr  Lys Ile Leu Cys Pro  Gly Gly Glu
    1580                 1585                 1590

Gly Phe  Arg Pro Asn Pro Ile  Thr Val Ile Leu Glu  Asp Ile Asp
    1595                 1600                 1605

Glu Cys  Gln Glu Leu Pro Gly  Leu Cys Gln Gly Gly  Lys Cys Ile
    1610                 1615                 1620
```

```
Asn Thr  Phe Gly Ser Phe Gln  Cys Arg Cys Pro Thr  Gly Tyr Tyr
    1625                1630                1635

Leu Asn  Glu Asp Thr Arg Val  Cys Asp Asp Val Asn  Glu Cys Glu
    1640                1645                1650

Thr Pro  Gly Ile Cys Gly Pro  Gly Thr Cys Tyr Asn  Thr Val Gly
    1655                1660                1665

Asn Tyr  Thr Cys Ile Cys Pro  Pro Asp Tyr Met Gln  Val Asn Gly
    1670                1675                1680

Gly Asn  Asn Cys Met Asp Met  Arg Arg Ser Leu Cys  Tyr Arg Asn
    1685                1690                1695

Tyr Tyr  Ala Asp Asn Gln Thr  Cys Asp Gly Glu Leu  Leu Phe Asn
    1700                1705                1710

Met Thr  Lys Lys Met Cys Cys  Cys Ser Tyr Asn Ile  Gly Arg Ala
    1715                1720                1725

Trp Asn  Lys Pro Cys Glu Gln  Cys Pro Ile Pro Ser  Thr Asp Glu
    1730                1735                1740

Phe Ala  Thr Leu Cys Gly Ser  Gln Arg Pro Gly Phe  Val Ile Asp
    1745                1750                1755

Ile Tyr  Thr Gly Leu Pro Val  Asp Ile Asp Glu Cys  Arg Glu Ile
    1760                1765                1770

Pro Gly  Val Cys Glu Asn Gly  Val Cys Ile Asn Met  Val Gly Ser
    1775                1780                1785

Phe Arg  Cys Glu Cys Pro Val  Gly Phe Phe Tyr Asn  Asp Lys Leu
    1790                1795                1800

Leu Val  Cys Glu Asp Ile Asp  Glu Cys Gln Asn Gly  Pro Val Cys
    1805                1810                1815

Gln Arg  Asn Ala Glu Cys Ile  Asn Thr Ala Gly Ser  Tyr Arg Cys
    1820                1825                1830

Asp Cys  Lys Pro Gly Tyr Arg  Phe Thr Ser Thr Gly  Gln Cys Asn
    1835                1840                1845

Asp Arg  Asn Glu Cys Gln Glu  Ile Pro Asn Ile Cys  Ser His Gly
    1850                1855                1860

Gln Cys  Ile Asp Thr Val Gly  Ser Phe Tyr Cys Leu  Cys His Thr
    1865                1870                1875
```

```
Gly Phe  Lys Thr Asn Asp Asp  Gln Thr Met Cys Leu  Asp Ile Asn
    1880                1885                1890

Glu Cys  Glu Arg Asp Ala Cys  Gly Asn Gly Thr Cys  Arg Asn Thr
    1895                1900                1905

Ile Gly  Ser Phe Asn Cys Arg  Cys Asn His Gly Phe  Ile Leu Ser
    1910                1915                1920

His Asn  Asn Asp Cys Ile Asp  Val Asp Glu Cys Ala  Ser Gly Asn
    1925                1930                1935

Gly Asn  Leu Cys Arg Asn Gly  Gln Cys Ile Asn Thr  Val Gly Ser
    1940                1945                1950

Phe Gln  Cys Gln Cys Asn Glu  Gly Tyr Glu Val Ala  Pro Asp Gly
    1955                1960                1965

Arg Thr  Cys Val Asp Ile Asn  Glu Cys Leu Leu Glu  Pro Arg Lys
    1970                1975                1980

Cys Ala  Pro Gly Thr Cys Gln  Asn Leu Asp Gly Ser  Tyr Arg Cys
    1985                1990                1995

Ile Cys  Pro Pro Gly Tyr Ser  Leu Gln Asn Glu Lys  Cys Glu Asp
    2000                2005                2010

Ile Asp  Glu Cys Val Glu Glu  Pro Glu Ile Cys Ala  Leu Gly Thr
    2015                2020                2025

Cys Ser  Asn Thr Glu Gly Ser  Phe Lys Cys Leu Cys  Pro Glu Gly
    2030                2035                2040

Phe Ser  Leu Ser Ser Ser Gly  Arg Arg Cys Gln Asp  Leu Arg Met
    2045                2050                2055

Ser Tyr  Cys Tyr Ala Lys Phe  Glu Gly Gly Lys Cys  Ser Ser Pro
    2060                2065                2070

Lys Ser  Arg Asn His Ser Lys  Gln Glu Cys Cys Cys  Ala Leu Lys
    2075                2080                2085

Gly Glu  Gly Trp Gly Asp Pro  Cys Glu Leu Cys Pro  Thr Glu Pro
    2090                2095                2100

Asp Glu  Ala Phe Arg Gln Ile  Cys Pro Tyr Gly Ser  Gly Ile Ile
    2105                2110                2115

Val Gly  Pro Asp Asp Ser Ala  Val Asp Met Asp Glu  Cys Lys Glu
    2120                2125                2130
```

```
Pro Asp  Val Cys Lys His Gly  Gln Cys Ile Asn Thr  Asp Gly Ser
    2135                 2140                 2145

Tyr Arg  Cys Glu Cys Pro Phe  Gly Tyr Ile Leu Ala  Gly Asn Glu
    2150                 2155                 2160

Cys Val  Asp Thr Asp Glu Cys  Ser Val Gly Asn Pro  Cys Gly Asn
    2165                 2170                 2175

Gly Thr  Cys Lys Asn Val Ile  Gly Gly Phe Glu Cys  Thr Cys Glu
    2180                 2185                 2190

Glu Gly  Phe Glu Pro Gly Pro  Met Met Thr Cys Glu  Asp Ile Asn
    2195                 2200                 2205

Glu Cys  Ala Gln Asn Pro Leu  Leu Cys Ala Phe Arg  Cys Val Asn
    2210                 2215                 2220

Thr Tyr  Gly Ser Tyr Glu Cys  Lys Cys Pro Val Gly  Tyr Val Leu
    2225                 2230                 2235

Arg Glu  Asp Arg Arg Met Cys  Lys Asp Glu Asp Glu  Cys Glu Glu
    2240                 2245                 2250

Gly Lys  His Asp Cys Thr Glu  Lys Gln Met Glu Cys  Lys Asn Leu
    2255                 2260                 2265

Ile Gly  Thr Tyr Met Cys Ile  Cys Gly Pro Gly Tyr  Gln Arg Arg
    2270                 2275                 2280

Pro Asp  Gly Glu Gly Cys Val  Asp Glu Asn Glu Cys  Gln Thr Lys
    2285                 2290                 2295

Pro Gly  Ile Cys Glu Asn Gly  Arg Cys Leu Asn Thr  Arg Gly Ser
    2300                 2305                 2310

Tyr Thr  Cys Glu Cys Asn Asp  Gly Phe Thr Ala Ser  Pro Asn Gln
    2315                 2320                 2325

Asp Glu  Cys Leu Asp Asn Arg  Glu Gly Tyr Cys Phe  Thr Glu Val
    2330                 2335                 2340

Leu Gln  Asn Met Cys Gln Ile  Gly Ser Ser Asn Arg  Asn Pro Val
    2345                 2350                 2355

Thr Lys  Ser Glu Cys Cys Cys  Asp Gly Gly Arg Gly  Trp Gly Pro
    2360                 2365                 2370

His Cys  Glu Ile Cys Pro Phe  Gln Gly Thr Val Ala  Phe Lys Lys
    2375                 2380                 2385
```

```
Leu Cys  Pro His Gly Arg Gly  Phe Met Thr Asn Gly  Ala Asp Ile
    2390                 2395                 2400

Asp Glu  Cys Lys Val Ile His  Asp Val Cys Arg Asn  Gly Glu Cys
    2405                 2410                 2415

Val Asn  Asp Arg Gly Ser Tyr  His Cys Ile Cys Lys  Thr Gly Tyr
    2420                 2425                 2430

Thr Pro  Asp Ile Thr Gly Thr  Ser Cys Val Asp Leu  Asn Glu Cys
    2435                 2440                 2445

Asn Gln  Ala Pro Lys Pro Cys  Asn Phe Ile Cys Lys  Asn Thr Glu
    2450                 2455                 2460

Gly Ser  Tyr Gln Cys Ser Cys  Pro Lys Gly Tyr Ile  Leu Gln Glu
    2465                 2470                 2475

Asp Gly  Arg Ser Cys Lys Asp  Leu Asp Glu Cys Ala  Thr Lys Gln
    2480                 2485                 2490

His Asn  Cys Gln Phe Leu Cys  Val Asn Thr Ile Gly  Gly Phe Thr
    2495                 2500                 2505

Cys Lys  Cys Pro Pro Gly Phe  Thr Gln His His Thr  Ser Cys Ile
    2510                 2515                 2520

Asp Asn  Asn Glu Cys Thr Ser  Asp Ile Asn Leu Cys  Gly Ser Lys
    2525                 2530                 2535

Gly Ile  Cys Gln Asn Thr Pro  Gly Ser Phe Thr Cys  Glu Cys Gln
    2540                 2545                 2550

Arg Gly  Phe Ser Leu Asp Gln  Thr Gly Ser Ser Cys  Glu Asp Val
    2555                 2560                 2565

Asp Glu  Cys Glu Gly Asn His  Arg Cys Gln His Gly  Cys Gln Asn
    2570                 2575                 2580

Ile Ile  Gly Gly Tyr Arg Cys  Ser Cys Pro Gln Gly  Tyr Leu Gln
    2585                 2590                 2595

His Tyr  Gln Trp Asn Gln Cys  Val Asp Glu Asn Glu  Cys Leu Ser
    2600                 2605                 2610

Ala His  Ile Cys Gly Gly Ala  Ser Cys His Asn Thr  Leu Gly Ser
    2615                 2620                 2625

Tyr Lys  Cys Met Cys Pro Ala  Gly Phe Gln Tyr Glu  Gln Phe Ser
    2630                 2635                 2640
```

```
Gly Gly  Cys Gln Asp Ile Asn  Glu Cys Gly Ser Ala  Gln Ala Pro
    2645                 2650                 2655

Cys Ser  Tyr Gly Cys Ser Asn  Thr Glu Gly Gly Tyr  Leu Cys Gly
    2660                 2665                 2670

Cys Pro  Pro Gly Tyr Phe Arg  Ile Gly Gln Gly His  Cys Val Ser
    2675                 2680                 2685

Gly Met  Gly Met Gly Arg Gly  Asn Pro Glu Pro Pro  Val Ser Gly
    2690                 2695                 2700

Glu Met  Asp Asp Asn Ser Leu  Ser Pro Glu Ala Cys  Tyr Glu Cys
    2705                 2710                 2715

Lys Ile  Asn Gly Tyr Pro Lys  Arg Gly Arg Lys Arg  Arg Ser Thr
    2720                 2725                 2730

Asn Glu  Thr Asp Ala Ser Asn  Ile Glu Asp Gln Ser  Glu Thr Glu
    2735                 2740                 2745

Ala Asn  Val Ser Leu Ala Ser  Trp Asp Val Glu Lys  Thr Ala Ile
    2750                 2755                 2760

Phe Ala  Phe Asn Ile Ser His  Val Ser Asn Lys Val  Arg Ile Leu
    2765                 2770                 2775

Glu Leu  Leu Pro Ala Leu Thr  Thr Leu Thr Asn His  Asn Arg Tyr
    2780                 2785                 2790

Leu Ile  Glu Ser Gly Asn Glu  Asp Gly Phe Phe Lys  Ile Asn Gln
    2795                 2800                 2805

Lys Glu  Gly Ile Ser Tyr Leu  His Phe Thr Lys Lys  Lys Pro Val
    2810                 2815                 2820

Ala Gly  Thr Tyr Ser Leu Gln  Ile Ser Ser Thr Pro  Leu Tyr Lys
    2825                 2830                 2835

Lys Lys  Glu Leu Asn Gln Leu  Glu Asp Lys Tyr Asp  Lys Asp Tyr
    2840                 2845                 2850

Leu Ser  Gly Glu Leu Gly Asp  Asn Leu Lys Met Lys  Ile Gln Val
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Leu Leu  His
    2870
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<211> 2912
<212> PRT
<213> Homo sapiens

<400> 135

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Gly Cys Val Val Leu Trp Ala Gln Gly Thr Ala Gly Gln Pro Gln Pro
            20                  25                  30

Pro Pro Pro Lys Pro Pro Arg Pro Gln Pro Pro Pro Gln Gln Val Arg
        35                  40                  45

Ser Ala Thr Ala Gly Ser Glu Gly Gly Phe Leu Ala Pro Glu Tyr Arg
    50                  55                  60

Glu Glu Gly Ala Ala Val Ala Ser Arg Val Arg Arg Gly Gln Gln
65                  70                  75                  80

Asp Val Leu Arg Gly Pro Asn Val Cys Gly Ser Arg Phe His Ser Tyr
                85                  90                  95

Cys Cys Pro Gly Trp Lys Thr Leu Pro Gly Gly Asn Gln Cys Ile Val
            100                 105                 110

Pro Ile Cys Arg Asn Ser Cys Gly Asp Gly Phe Cys Ser Arg Pro Asn
        115                 120                 125

Met Cys Thr Cys Ser Ser Gly Gln Ile Ser Ser Thr Cys Gly Ser Lys
    130                 135                 140

Ser Ile Gln Gln Cys Ser Val Arg Cys Met Asn Gly Gly Thr Cys Ala
145                 150                 155                 160

Asp Asp His Cys Gln Cys Gln Lys Gly Tyr Ile Gly Thr Tyr Cys Gly
                165                 170                 175

Gln Pro Val Cys Glu Asn Gly Cys Gln Asn Gly Gly Arg Cys Ile Gly
            180                 185                 190

Pro Asn Arg Cys Ala Cys Val Tyr Gly Phe Thr Gly Pro Gln Cys Glu
        195                 200                 205

Arg Asp Tyr Arg Thr Gly Pro Cys Phe Thr Gln Val Asn Asn Gln Met
    210                 215                 220

Cys Gln Gly Gln Leu Thr Gly Ile Val Cys Thr Lys Thr Leu Cys Cys
225                 230                 235                 240

Ala Thr Ile Gly Arg Ala Trp Gly His Pro Cys Glu Met Cys Pro Ala
                245                 250                 255

Gln Pro Gln Pro Cys Arg Arg Gly Phe Ile Pro Asn Ile Arg Thr Gly
```

260 265 270

Ala Cys Gln Asp Val Asp Glu Cys Gln Ala Ile Pro Gly Ile Cys Gln
275 280 285

Gly Gly Asn Cys Ile Asn Thr Val Gly Ser Phe Glu Cys Arg Cys Pro
290 295 300

Ala Gly His Lys Gln Ser Glu Thr Thr Gln Lys Cys Glu Asp Ile Asp
305 310 315 320

Glu Cys Ser Ile Ile Pro Gly Ile Cys Glu Thr Gly Glu Cys Ser Asn
325 330 335

Thr Val Gly Ser Tyr Phe Cys Val Cys Pro Arg Gly Tyr Val Thr Ser
340 345 350

Thr Asp Gly Ser Arg Cys Ile Asp Gln Arg Thr Gly Met Cys Phe Ser
355 360 365

Gly Leu Val Asn Gly Arg Cys Ala Gln Glu Leu Pro Gly Arg Met Thr
370 375 380

Lys Met Gln Cys Cys Cys Glu Pro Gly Arg Cys Trp Gly Ile Gly Thr
385 390 395 400

Ile Pro Glu Ala Cys Pro Val Arg Gly Ser Glu Glu Tyr Arg Arg Leu
405 410 415

Cys Met Asp Gly Leu Pro Met Gly Gly Ile Pro Gly Ser Ala Gly Ser
420 425 430

Arg Pro Gly Gly Thr Gly Gly Asn Gly Phe Ala Pro Ser Gly Asn Gly
435 440 445

Asn Gly Tyr Gly Pro Gly Gly Thr Gly Phe Ile Pro Ile Pro Gly Gly
450 455 460

Asn Gly Phe Ser Pro Gly Val Gly Gly Ala Gly Val Gly Ala Gly Gly
465 470 475 480

Gln Gly Pro Ile Ile Thr Gly Leu Thr Ile Leu Asn Gln Thr Ile Asp
485 490 495

Ile Cys Lys His His Ala Asn Leu Cys Leu Asn Gly Arg Cys Ile Pro
500 505 510

Thr Val Ser Ser Tyr Arg Cys Glu Cys Asn Met Gly Tyr Lys Gln Asp
515 520 525

Ala Asn Gly Asp Cys Ile Asp Val Asp Glu Cys Thr Ser Asn Pro Cys

530 535 540

Thr Asn Gly Asp Cys Val Asn Thr Pro Gly Ser Tyr Tyr Cys Lys Cys
545 550 555 560

His Ala Gly Phe Gln Arg Thr Pro Thr Lys Gln Ala Cys Ile Asp Ile
565 570 575

Asp Glu Cys Ile Gln Asn Gly Val Leu Cys Lys Asn Gly Arg Cys Val
580 585 590

Asn Thr Asp Gly Ser Phe Gln Cys Ile Cys Asn Ala Gly Phe Glu Leu
595 600 605

Thr Thr Asp Gly Lys Asn Cys Val Asp His Asp Glu Cys Thr Thr Thr
610 615 620

Asn Met Cys Leu Asn Gly Met Cys Ile Asn Glu Asp Gly Ser Phe Lys
625 630 635 640

Cys Ile Cys Lys Pro Gly Phe Val Leu Ala Pro Asn Gly Arg Tyr Cys
645 650 655

Thr Asp Val Asp Glu Cys Gln Thr Pro Gly Ile Cys Met Asn Gly His
660 665 670

Cys Ile Asn Ser Glu Gly Ser Phe Arg Cys Asp Cys Pro Pro Gly Leu
675 680 685

Ala Val Gly Met Asp Gly Arg Val Cys Val Asp Thr His Met Arg Ser
690 695 700

Thr Cys Tyr Gly Gly Ile Lys Lys Gly Val Cys Val Arg Pro Phe Pro
705 710 715 720

Gly Ala Val Thr Lys Ser Glu Cys Cys Cys Ala Asn Pro Asp Tyr Gly
725 730 735

Phe Gly Glu Pro Cys Gln Pro Cys Pro Ala Lys Asn Ser Ala Glu Phe
740 745 750

His Gly Leu Cys Ser Ser Gly Val Gly Ile Thr Val Asp Gly Arg Asp
755 760 765

Ile Asn Glu Cys Ala Leu Asp Pro Asp Ile Cys Ala Asn Gly Ile Cys
770 775 780

Glu Asn Leu Arg Gly Ser Tyr Arg Cys Asn Cys Asn Ser Gly Tyr Glu
785 790 795 800

Pro Asp Ala Ser Gly Arg Asn Cys Ile Asp Ile Asp Glu Cys Leu Val

805 810 815

Asn Arg Leu Leu Cys Asp Asn Gly Leu Cys Arg Asn Thr Pro Gly Ser
820 825 830

Tyr Ser Cys Thr Cys Pro Pro Gly Tyr Val Phe Arg Thr Glu Thr Glu
835 840 845

Thr Cys Glu Asp Ile Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly
850 855 860

Ala Cys Arg Asn Asn Leu Gly Ser Phe Asn Cys Glu Cys Ser Pro Gly
865 870 875 880

Ser Lys Leu Ser Ser Thr Gly Leu Ile Cys Ile Asp Ser Leu Lys Gly
885 890 895

Thr Cys Trp Leu Asn Ile Gln Asp Ser Arg Cys Glu Val Asn Ile Asn
900 905 910

Gly Ala Thr Leu Lys Ser Glu Cys Cys Ala Thr Leu Gly Ala Ala Trp
915 920 925

Gly Ser Pro Cys Glu Arg Cys Glu Leu Asp Thr Ala Cys Pro Arg Gly
930 935 940

Leu Ala Arg Ile Lys Gly Val Thr Cys Glu Asp Val Asn Glu Cys Glu
945 950 955 960

Val Phe Pro Gly Val Cys Pro Asn Gly Arg Cys Val Asn Ser Lys Gly
965 970 975

Ser Phe His Cys Glu Cys Pro Glu Gly Leu Thr Leu Asp Gly Thr Gly
980 985 990

Arg Val Cys Leu Asp Ile Arg Met Glu Gln Cys Tyr Leu Lys Trp Asp
995 1000 1005

Glu Asp Glu Cys Ile His Pro Val Pro Gly Lys Phe Arg Met Asp
1010 1015 1020

Ala Cys Cys Cys Ala Val Gly Ala Ala Trp Gly Thr Glu Cys Glu
1025 1030 1035

Glu Cys Pro Lys Pro Gly Thr Lys Glu Tyr Glu Thr Leu Cys Pro
1040 1045 1050

Arg Gly Ala Gly Phe Ala Asn Arg Gly Asp Val Leu Thr Gly Arg
1055 1060 1065

Pro Phe Tyr Lys Asp Ile Asn Glu Cys Lys Ala Phe Pro Gly Met

1070 1075 1080

Cys Thr Tyr Gly Lys Cys Arg Asn Thr Ile Gly Ser Phe Lys Cys
1085 1090 1095

Arg Cys Asn Ser Gly Phe Ala Leu Asp Met Glu Glu Arg Asn Cys
1100 1105 1110

Thr Asp Ile Asp Glu Cys Arg Ile Ser Pro Asp Leu Cys Gly Ser
1115 1120 1125

Gly Ile Cys Val Asn Thr Pro Gly Ser Phe Glu Cys Glu Cys Phe
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Glu Gly Tyr Glu Ser Gly Phe Met Met Met Lys Asn Cys Met Asp
1145 1150 1155

Ile Asp Glu Cys Glu Arg Asn Pro Leu Leu Cys Arg Gly Gly Thr
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Cys Val Asn Thr Glu Gly Ser Phe Gln Cys Asp Cys Pro Leu Gly
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His Glu Leu Ser Pro Ser Arg Glu Asp Cys Val Asp Ile Asn Glu
1190 1195 1200

Cys Ser Leu Ser Asp Asn Leu Cys Arg Asn Gly Lys Cys Val Asn
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Met Ile Gly Thr Tyr Gln Cys Ser Cys Asn Pro Gly Tyr Gln Ala
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Thr Pro Asp Arg Gln Gly Cys Thr Asp Ile Asp Glu Cys Met Ile
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Met Asn Gly Gly Cys Asp Thr Gln Cys Thr Asn Ser Glu Gly Ser
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Tyr Glu Cys Ser Cys Ser Glu Gly Tyr Ala Leu Met Pro Asp Gly
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Arg Ser Cys Ala Asp Ile Asp Glu Cys Glu Asn Asn Pro Asp Ile
1280 1285 1290

Cys Asp Gly Gly Gln Cys Thr Asn Ile Pro Gly Glu Tyr Arg Cys
1295 1300 1305

Leu Cys Tyr Asp Gly Phe Met Ala Ser Met Asp Met Lys Thr Cys
1310 1315 1320

Ile Asp Val Asn Glu Cys Asp Leu Asn Ser Asn Ile Cys Met Phe

1325 1330 1335

Gly Glu Cys Glu Asn Thr Lys Gly Ser Phe Ile Cys His Cys Gln
1340 1345 1350

Leu Gly Tyr Ser Val Lys Lys Gly Thr Thr Gly Cys Thr Asp Val
1355 1360 1365

Asp Glu Cys Glu Ile Gly Ala His Asn Cys Asp Met His Ala Ser
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Cys Leu Asn Ile Pro Gly Ser Phe Lys Cys Ser Cys Arg Glu Gly
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Trp Ile Gly Asn Gly Ile Lys Cys Ile Asp Leu Asp Glu Cys Ser
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Asn Gly Thr His Gln Cys Ser Ile Asn Ala Gln Cys Val Asn Thr
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Pro Gly Ser Tyr Arg Cys Ala Cys Ser Glu Gly Phe Thr Gly Asp
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Gly Phe Thr Cys Ser Asp Val Asp Glu Cys Ala Glu Asn Ile Asn
1445 1450 1455

Leu Cys Glu Asn Gly Gln Cys Leu Asn Val Pro Gly Ala Tyr Arg
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Cys Glu Cys Glu Met Gly Phe Thr Pro Ala Ser Asp Ser Arg Ser
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Cys Gln Asp Ile Asp Glu Cys Ser Phe Gln Asn Ile Cys Val Phe
1490 1495 1500

Gly Thr Cys Asn Asn Leu Pro Gly Met Phe His Cys Ile Cys Asp
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Asp Gly Tyr Glu Leu Asp Arg Thr Gly Gly Asn Cys Thr Asp Ile
1520 1525 1530

Asp Glu Cys Ala Asp Pro Ile Asn Cys Val Asn Gly Leu Cys Val
1535 1540 1545

Asn Thr Pro Gly Arg Tyr Glu Cys Asn Cys Pro Pro Asp Phe Gln
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Leu Asn Pro Thr Gly Val Gly Cys Val Asp Asn Arg Val Gly Asn
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Cys Tyr Leu Lys Phe Gly Pro Arg Gly Asp Gly Ser Leu Ser Cys

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Asn Thr Glu Ile Gly Val Gly Val Ser Arg Ser Ser Cys Cys Cys
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Ser Leu Gly Lys Ala Trp Gly Asn Pro Cys Glu Thr Cys Pro Pro
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Val Asn Ser Thr Glu Tyr Tyr Thr Leu Cys Pro Gly Gly Glu Gly
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Phe Arg Pro Asn Pro Ile Thr Ile Ile Leu Glu Asp Ile Asp Glu
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Cys Gln Glu Leu Pro Gly Leu Cys Gln Gly Gly Asn Cys Ile Asn
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Ser Glu Asp Thr Arg Ile Cys Glu Asp Ile Asp Glu Cys Phe Ala
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His Pro Gly Val Cys Gly Pro Gly Thr Cys Tyr Asn Thr Leu Gly
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Asn Tyr Thr Cys Ile Cys Pro Pro Glu Tyr Met Gln Val Asn Gly
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Gly His Asn Cys Met Asp Met Arg Lys Ser Phe Cys Tyr Arg Ser
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Tyr Asn Gly Thr Thr Cys Glu Asn Glu Leu Pro Phe Asn Val Thr
1745 1750 1755

Lys Arg Met Cys Cys Cys Thr Tyr Asn Val Gly Lys Ala Trp Asn
1760 1765 1770

Lys Pro Cys Glu Pro Cys Pro Thr Pro Gly Thr Ala Asp Phe Lys
1775 1780 1785

Thr Ile Cys Gly Asn Ile Pro Gly Phe Thr Phe Asp Ile His Thr
1790 1795 1800

Gly Lys Ala Val Asp Ile Asp Glu Cys Lys Glu Ile Pro Gly Ile
1805 1810 1815

Cys Ala Asn Gly Val Cys Ile Asn Gln Ile Gly Ser Phe Arg Cys
1820 1825 1830

Glu Cys Pro Thr Gly Phe Ser Tyr Asn Asp Leu Leu Leu Val Cys

1835 1840 1845

Glu Asp Ile Asp Glu Cys Ser Asn Gly Asp Asn Leu Cys Gln Arg
1850 1855 1860

Asn Ala Asp Cys Ile Asn Ser Pro Gly Ser Tyr Arg Cys Glu Cys
1865 1870 1875

Ala Ala Gly Phe Lys Leu Ser Pro Asn Gly Ala Cys Val Asp Arg
1880 1885 1890

Asn Glu Cys Leu Glu Ile Pro Asn Val Cys Ser His Gly Leu Cys
1895 1900 1905

Val Asp Leu Gln Gly Ser Tyr Gln Cys Ile Cys His Asn Gly Phe
1910 1915 1920

Lys Ala Ser Gln Asp Gln Thr Met Cys Met Asp Val Asp Glu Cys
1925 1930 1935

Glu Arg His Pro Cys Gly Asn Gly Thr Cys Lys Asn Thr Val Gly
1940 1945 1950

Ser Tyr Asn Cys Leu Cys Tyr Pro Gly Phe Glu Leu Thr His Asn
1955 1960 1965

Asn Asp Cys Leu Asp Ile Asp Glu Cys Ser Ser Phe Phe Gly Gln
1970 1975 1980

Val Cys Arg Asn Gly Arg Cys Phe Asn Glu Ile Gly Ser Phe Lys
1985 1990 1995

Cys Leu Cys Asn Glu Gly Tyr Glu Leu Thr Pro Asp Gly Lys Asn
2000 2005 2010

Cys Ile Asp Thr Asn Glu Cys Val Ala Leu Pro Gly Ser Cys Ser
2015 2020 2025

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Pro Pro Gly Tyr Glu Val Lys Ser Glu Asn Cys Ile Asp Ile Asn
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Glu Cys Asp Glu Asp Pro Asn Ile Cys Leu Phe Gly Ser Cys Thr
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Asn Thr Pro Gly Gly Phe Gln Cys Leu Cys Pro Pro Gly Phe Val
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Leu Ser Asp Asn Gly Arg Arg Cys Phe Asp Thr Arg Gln Ser Phe

2090 2095 2100

Cys Phe Thr Asn Phe Glu Asn Gly Lys Cys Ser Val Pro Lys Ala
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Phe Asn Thr Thr Lys Ala Lys Cys Cys Cys Ser Lys Met Pro Gly
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Glu Gly Trp Gly Asp Pro Cys Glu Leu Cys Pro Lys Asp Asp Glu
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Val Ala Phe Gln Asp Leu Cys Pro Tyr Gly His Gly Thr Val Pro
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Ser Leu His Asp Thr Arg Glu Asp Val Asn Glu Cys Leu Glu Ser
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Pro Gly Ile Cys Ser Asn Gly Gln Cys Ile Asn Thr Asp Gly Ser
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Val Arg Cys Val Asp Thr Asp Glu Cys Ser Ile Gly Asn Pro Cys
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Gly Asn Gly Thr Cys Thr Asn Val Ile Gly Ser Phe Glu Cys Asn
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Cys Asn Glu Gly Phe Glu Pro Gly Pro Met Met Asn Cys Glu Asp
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Ile Asn Glu Cys Ala Gln Asn Pro Leu Leu Cys Ala Phe Arg Cys
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Met Asn Thr Phe Gly Ser Tyr Glu Cys Thr Cys Pro Ile Gly Tyr
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Ala Leu Arg Glu Asp Gln Lys Met Cys Lys Asp Leu Asp Glu Cys
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Ala Glu Gly Leu His Asp Cys Glu Ser Arg Gly Met Met Cys Lys
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Thr Lys Pro Gly Ile Cys Glu Asn Gly Arg Cys Val Asn Ile Ile

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Lys Lys Ile Cys Pro His Gly Pro Gly Tyr Thr Thr Asp Gly Arg
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Asp Ile Asp Glu Cys Lys Val Met Pro Asn Leu Cys Thr Asn Gly
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Gln Cys Ile Asn Thr Met Gly Ser Phe Arg Cys Phe Cys Lys Val
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Gly Tyr Thr Thr Asp Ile Ser Gly Thr Ser Cys Ile Asp Leu Asp
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Glu Cys Ser Gln Ser Pro Lys Pro Cys Asn Tyr Ile Cys Lys Asn
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Lys Gln His Asn Cys Gln Phe Leu Cys Val Asn Thr Leu Gly Gly
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Phe Thr Cys Lys Cys Pro Pro Gly Phe Thr Gln His His Thr Ala
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Ile Gln His Tyr Gln Trp Asn Gln Cys Val Asp Glu Asn Glu Cys
2645 2650 2655

Ser Asn Pro Asn Ala Cys Gly Ser Ala Ser Cys Tyr Asn Thr Leu
2660 2665 2670

Gly Ser Tyr Lys Cys Ala Cys Pro Ser Gly Phe Ser Phe Asp Gln
2675 2680 2685

Phe Ser Ser Ala Cys His Asp Val Asn Glu Cys Ser Ser Ser Lys
2690 2695 2700

Asn Pro Cys Asn Tyr Gly Cys Ser Asn Thr Glu Gly Gly Tyr Leu
2705 2710 2715

Cys Gly Cys Pro Pro Gly Tyr Tyr Arg Val Gly Gln Gly His Cys
2720 2725 2730

Val Ser Gly Met Gly Phe Asn Lys Gly Gln Tyr Leu Ser Leu Asp
2735 2740 2745

Thr Glu Val Asp Glu Glu Asn Ala Leu Ser Pro Glu Ala Cys Tyr
2750 2755 2760

Glu Cys Lys Ile Asn Gly Tyr Ser Lys Lys Asp Ser Arg Gln Lys
2765 2770 2775

Arg Ser Ile His Glu Pro Asp Pro Thr Ala Val Glu Gln Ile Ser
2780 2785 2790

Leu Glu Ser Val Asp Met Asp Ser Pro Val Asn Met Lys Phe Asn
2795 2800 2805

Leu Ser His Leu Gly Ser Lys Glu His Ile Leu Glu Leu Arg Pro
2810 2815 2820

Ala Ile Gln Pro Leu Asn Asn His Ile Arg Tyr Val Ile Ser Gln
2825 2830 2835

Gly Asn Asp Asp Ser Val Phe Arg Ile His Gln Arg Asn Gly Leu
2840 2845 2850

Ser Tyr Leu His Thr Ala Lys Lys Lys Leu Met Pro Gly Thr Tyr

2855 2860 2865

Thr Leu Glu Ile Thr Ser Ile Pro Leu Tyr Lys Lys Lys Glu Leu
2870 2875 2880

Lys Lys Leu Glu Glu Ser Asn Glu Asp Asp Tyr Leu Leu Gly Glu
2885 2890 2895

Leu Gly Glu Ala Leu Arg Met Arg Leu Gln Ile Gln Leu Tyr
2900 2905 2910

<210> 136
<211> 574
<212> PRT
<213> Homo sapiens

<400> 136

Met Ala Leu Ala Arg Gly Ser Arg Gln Leu Gly Ala Leu Val Trp Gly
1 5 10 15

Ala Cys Leu Cys Val Leu Val His Gly Gln Gln Ala Gln Pro Gly Gln
20 25 30

Gly Ser Asp Pro Ala Arg Trp Arg Gln Leu Ile Gln Trp Glu Asn Asn
35 40 45

Gly Gln Val Tyr Ser Leu Leu Asn Ser Gly Ser Glu Tyr Val Pro Ala
50 55 60

Gly Pro Gln Arg Ser Glu Ser Ser Ser Arg Val Leu Leu Ala Gly Ala
65 70 75 80

Pro Gln Ala Gln Gln Arg Arg Ser His Gly Ser Pro Arg Arg Arg Gln
85 90 95

Ala Pro Ser Leu Pro Leu Pro Gly Arg Val Gly Ser Asp Thr Val Arg
100 105 110

Gly Gln Ala Arg His Pro Phe Gly Phe Gly Gln Val Pro Asp Asn Trp
115 120 125

Arg Glu Val Ala Val Gly Asp Ser Thr Gly Met Ala Arg Ala Arg Thr
130 135 140

Ser Val Ser Gln Gln Arg His Gly Gly Ser Ala Ser Ser Val Ser Ala
145 150 155 160

Ser Ala Phe Ala Ser Thr Tyr Arg Gln Gln Pro Ser Tyr Pro Gln Gln
165 170 175

Phe Pro Tyr Pro Gln Ala Pro Phe Val Ser Gln Tyr Glu Asn Tyr Asp
180 185 190

```
Pro Ala Ser Arg Thr Tyr Asp Gln Gly Phe Val Tyr Tyr Arg Pro Ala
        195                 200                 205

Gly Gly Gly Val Gly Ala Gly Ala Ala Ala Val Ala Ser Ala Gly Val
    210                 215                 220

Ile Tyr Pro Tyr Gln Pro Arg Ala Arg Tyr Glu Glu Tyr Gly Gly Gly
225                 230                 235                 240

Glu Glu Leu Pro Glu Tyr Pro Pro Gln Gly Phe Tyr Pro Ala Pro Glu
                245                 250                 255

Arg Pro Tyr Val Pro Pro Pro Pro Pro Pro Pro Asp Gly Leu Asp Arg
            260                 265                 270

Arg Tyr Ser His Ser Leu Tyr Ser Glu Gly Thr Pro Gly Phe Glu Gln
        275                 280                 285

Ala Tyr Pro Asp Pro Gly Pro Glu Ala Ala Gln Ala His Gly Gly Asp
    290                 295                 300

Pro Arg Leu Gly Trp Tyr Pro Pro Tyr Ala Asn Pro Pro Pro Glu Ala
305                 310                 315                 320

Tyr Gly Pro Pro Arg Ala Leu Glu Pro Pro Tyr Leu Pro Val Arg Ser
                325                 330                 335

Ser Asp Thr Pro Pro Pro Gly Gly Glu Arg Asn Gly Ala Gln Gln Gly
            340                 345                 350

Arg Leu Ser Val Gly Ser Val Tyr Arg Pro Asn Gln Asn Gly Arg Gly
        355                 360                 365

Leu Pro Asp Leu Val Pro Asp Pro Asn Tyr Val Gln Ala Ser Thr Tyr
    370                 375                 380

Val Gln Arg Ala His Leu Tyr Ser Leu Arg Cys Ala Ala Glu Glu Lys
385                 390                 395                 400

Cys Leu Ala Ser Thr Ala Tyr Ala Pro Glu Ala Thr Asp Tyr Asp Val
                405                 410                 415

Arg Val Leu Leu Arg Phe Pro Gln Arg Val Lys Asn Gln Gly Thr Ala
            420                 425                 430

Asp Phe Leu Pro Asn Arg Pro Arg His Thr Trp Glu Trp His Ser Cys
        435                 440                 445

His Gln His Tyr His Ser Met Asp Glu Phe Ser His Tyr Asp Leu Leu
    450                 455                 460
```

```
Asp Ala Ala Thr Gly Lys Lys Val Ala Glu Gly His Lys Ala Ser Phe
465                 470                 475                 480

Cys Leu Glu Asp Ser Thr Cys Asp Phe Gly Asn Leu Lys Arg Tyr Ala
                485                 490                 495

Cys Thr Ser His Thr Gln Gly Leu Ser Pro Gly Cys Tyr Asp Thr Tyr
            500                 505                 510

Asn Ala Asp Ile Asp Cys Gln Trp Ile Asp Ile Thr Asp Val Gln Pro
        515                 520                 525

Gly Asn Tyr Ile Leu Lys Val His Val Asn Pro Lys Tyr Ile Val Leu
    530                 535                 540

Glu Ser Asp Phe Thr Asn Asn Val Val Arg Cys Asn Ile His Tyr Thr
545                 550                 555                 560

Gly Arg Tyr Val Ser Ala Thr Asn Cys Lys Ile Val Gln Ser
                565                 570


<210>  137
<211>  774
<212>  PRT
<213>  Homo sapiens

<400>  137

Met Glu Arg Pro Leu Cys Ser His Leu Cys Ser Cys Leu Ala Met Leu
1               5                   10                  15

Ala Leu Leu Ser Pro Leu Ser Leu Ala Gln Tyr Asp Ser Trp Pro His
            20                  25                  30

Tyr Pro Glu Tyr Phe Gln Gln Pro Ala Pro Glu Tyr His Gln Pro Gln
        35                  40                  45

Ala Pro Ala Asn Val Ala Lys Ile Gln Leu Arg Leu Ala Gly Gln Lys
    50                  55                  60

Arg Lys His Ser Glu Gly Arg Val Glu Val Tyr Tyr Asp Gly Gln Trp
65                  70                  75                  80

Gly Thr Val Cys Asp Asp Asp Phe Ser Ile His Ala Ala His Val Val
                85                  90                  95

Cys Arg Glu Leu Gly Tyr Val Glu Ala Lys Ser Trp Thr Ala Ser Ser
            100                 105                 110

Ser Tyr Gly Lys Gly Glu Gly Pro Ile Trp Leu Asp Asn Leu His Cys
        115                 120                 125
```

```
Thr Gly Asn Glu Ala Thr Leu Ala Ala Cys Thr Ser Asn Gly Trp Gly
    130                 135                 140

Val Thr Asp Cys Lys His Thr Glu Asp Val Gly Val Val Cys Ser Asp
145                 150                 155                 160

Lys Arg Ile Pro Gly Phe Lys Phe Asp Asn Ser Leu Ile Asn Gln Ile
                165                 170                 175

Glu Asn Leu Asn Ile Gln Val Glu Asp Ile Arg Ile Arg Ala Ile Leu
            180                 185                 190

Ser Thr Tyr Arg Lys Arg Thr Pro Val Met Glu Gly Tyr Val Glu Val
        195                 200                 205

Lys Glu Gly Lys Thr Trp Lys Gln Ile Cys Asp Lys His Trp Thr Ala
    210                 215                 220

Lys Asn Ser Arg Val Val Cys Gly Met Phe Gly Phe Pro Gly Glu Arg
225                 230                 235                 240

Thr Tyr Asn Thr Lys Val Tyr Lys Met Phe Ala Ser Arg Arg Lys Gln
                245                 250                 255

Arg Tyr Trp Pro Phe Ser Met Asp Cys Thr Gly Thr Glu Ala His Ile
            260                 265                 270

Ser Ser Cys Lys Leu Gly Pro Gln Val Ser Leu Asp Pro Met Lys Asn
        275                 280                 285

Val Thr Cys Glu Asn Gly Leu Pro Ala Val Val Ser Cys Val Pro Gly
    290                 295                 300

Gln Val Phe Ser Pro Asp Gly Pro Ser Arg Phe Arg Lys Ala Tyr Lys
305                 310                 315                 320

Pro Glu Gln Pro Leu Val Arg Leu Arg Gly Gly Ala Tyr Ile Gly Glu
                325                 330                 335

Gly Arg Val Glu Val Leu Lys Asn Gly Glu Trp Gly Thr Val Cys Asp
            340                 345                 350

Asp Lys Trp Asp Leu Val Ser Ala Ser Val Val Cys Arg Glu Leu Gly
        355                 360                 365

Phe Gly Ser Ala Lys Glu Ala Val Thr Gly Ser Arg Leu Gly Gln Gly
    370                 375                 380

Ile Gly Pro Ile His Leu Asn Glu Ile Gln Cys Thr Gly Asn Glu Lys
385                 390                 395                 400
```

```
Ser Ile Ile Asp Cys Lys Phe Asn Ala Glu Ser Gln Gly Cys Asn His
                405                 410                 415

Glu Glu Asp Ala Gly Val Arg Cys Asn Thr Pro Ala Met Gly Leu Gln
            420                 425                 430

Lys Lys Leu Arg Leu Asn Gly Gly Arg Asn Pro Tyr Glu Gly Arg Val
        435                 440                 445

Glu Val Leu Val Glu Arg Asn Gly Ser Leu Val Trp Gly Met Val Cys
    450                 455                 460

Gly Gln Asn Trp Gly Ile Val Glu Ala Met Val Val Cys Arg Gln Leu
465                 470                 475                 480

Gly Leu Gly Phe Ala Ser Asn Ala Phe Gln Glu Thr Trp Tyr Trp His
                485                 490                 495

Gly Asp Val Asn Ser Asn Lys Val Val Met Ser Gly Val Lys Cys Ser
            500                 505                 510

Gly Thr Glu Leu Ser Leu Ala His Cys Arg His Asp Gly Glu Asp Val
        515                 520                 525

Ala Cys Pro Gln Gly Gly Val Gln Tyr Gly Ala Gly Val Ala Cys Ser
    530                 535                 540

Glu Thr Ala Pro Asp Leu Val Leu Asn Ala Glu Met Val Gln Gln Thr
545                 550                 555                 560

Thr Tyr Leu Glu Asp Arg Pro Met Phe Met Leu Gln Cys Ala Met Glu
                565                 570                 575

Glu Asn Cys Leu Ser Ala Ser Ala Ala Gln Thr Asp Pro Thr Thr Gly
            580                 585                 590

Tyr Arg Arg Leu Leu Arg Phe Ser Ser Gln Ile His Asn Asn Gly Gln
        595                 600                 605

Ser Asp Phe Arg Pro Lys Asn Gly Arg His Ala Trp Ile Trp His Asp
    610                 615                 620

Cys His Arg His Tyr His Ser Met Glu Val Phe Thr His Tyr Asp Leu
625                 630                 635                 640

Leu Asn Leu Asn Gly Thr Lys Val Ala Glu Gly His Lys Ala Ser Phe
                645                 650                 655

Cys Leu Glu Asp Thr Glu Cys Glu Gly Asp Ile Gln Lys Asn Tyr Glu
            660                 665                 670
```

```
Cys Ala Asn Phe Gly Asp Gln Gly Ile Thr Met Gly Cys Trp Asp Met
        675                 680                 685

Tyr Arg His Asp Ile Asp Cys Gln Trp Val Asp Ile Thr Asp Val Pro
    690                 695                 700

Pro Gly Asp Tyr Leu Phe Gln Val Val Ile Asn Pro Asn Phe Glu Val
705                 710                 715                 720

Ala Glu Ser Asp Tyr Ser Asn Asn Ile Met Lys Cys Arg Ser Arg Tyr
                725                 730                 735

Asp Gly His Arg Ile Trp Met Tyr Asn Cys His Ile Gly Gly Ser Phe
            740                 745                 750

Ser Glu Glu Thr Glu Lys Lys Phe Glu His Phe Ser Gly Leu Leu Asn
        755                 760                 765

Asn Gln Leu Ser Pro Gln
    770


<210>  138
<211>  753
<212>  PRT
<213>  Homo sapiens

<400>  138

Met Arg Pro Val Ser Val Trp Gln Trp Ser Pro Trp Gly Leu Leu Leu
1               5                   10                  15

Cys Leu Leu Cys Ser Ser Cys Leu Gly Ser Pro Ser Pro Ser Thr Gly
            20                  25                  30

Pro Glu Lys Lys Ala Gly Ser Gln Gly Leu Arg Phe Arg Leu Ala Gly
        35                  40                  45

Phe Pro Arg Lys Pro Tyr Glu Gly Arg Val Glu Ile Gln Arg Ala Gly
    50                  55                  60

Glu Trp Gly Thr Ile Cys Asp Asp Asp Phe Thr Leu Gln Ala Ala His
65                  70                  75                  80

Ile Leu Cys Arg Glu Leu Gly Phe Thr Glu Ala Thr Gly Trp Thr His
                85                  90                  95

Ser Ala Lys Tyr Gly Pro Gly Thr Gly Arg Ile Trp Leu Asp Asn Leu
            100                 105                 110

Ser Cys Ser Gly Thr Glu Gln Ser Val Thr Glu Cys Ala Ser Arg Gly
        115                 120                 125
```

```
Trp Gly Asn Ser Asp Cys Thr His Asp Glu Asp Ala Gly Val Ile Cys
    130                 135                 140

Lys Asp Gln Arg Leu Pro Gly Phe Ser Asp Ser Asn Val Ile Glu Val
145                 150                 155                 160

Glu His His Leu Gln Val Glu Glu Val Arg Ile Arg Pro Ala Val Gly
                165                 170                 175

Trp Gly Arg Arg Pro Leu Pro Val Thr Glu Gly Leu Val Glu Val Arg
            180                 185                 190

Leu Pro Asp Gly Trp Ser Gln Val Cys Asp Lys Gly Trp Ser Ala His
        195                 200                 205

Asn Ser His Val Val Cys Gly Met Leu Gly Phe Pro Ser Glu Lys Arg
    210                 215                 220

Val Asn Ala Ala Phe Tyr Arg Leu Leu Ala Gln Arg Gln Gln His Ser
225                 230                 235                 240

Phe Gly Leu His Gly Val Ala Cys Val Gly Thr Glu Ala His Leu Ser
                245                 250                 255

Leu Cys Ser Leu Glu Phe Tyr Arg Ala Asn Asp Thr Ala Arg Cys Pro
            260                 265                 270

Gly Gly Gly Pro Ala Val Val Ser Cys Val Pro Gly Pro Val Tyr Ala
        275                 280                 285

Ala Ser Ser Gly Gln Lys Lys Gln Gln Gln Ser Lys Pro Gln Gly Glu
    290                 295                 300

Ala Arg Val Arg Leu Lys Gly Gly Ala His Pro Gly Glu Gly Arg Val
305                 310                 315                 320

Glu Val Leu Lys Ala Ser Thr Trp Gly Thr Val Cys Asp Arg Lys Trp
                325                 330                 335

Asp Leu His Ala Ala Ser Val Val Cys Arg Glu Leu Gly Phe Gly Ser
            340                 345                 350

Ala Arg Glu Ala Leu Ser Gly Ala Arg Met Gly Gln Gly Met Gly Ala
        355                 360                 365

Ile His Leu Ser Glu Val Arg Cys Ser Gly Gln Glu Leu Ser Leu Trp
    370                 375                 380

Lys Cys Pro His Lys Asn Ile Thr Ala Glu Asp Cys Ser His Ser Gln
385                 390                 395                 400
```

```
Asp Ala Gly Val Arg Cys Asn Leu Pro Tyr Thr Gly Ala Glu Thr Arg
                405                 410                 415

Ile Arg Leu Ser Gly Gly Arg Ser Gln His Glu Gly Arg Val Glu Val
            420                 425                 430

Gln Ile Gly Gly Pro Gly Pro Leu Arg Trp Gly Leu Ile Cys Gly Asp
        435                 440                 445

Asp Trp Gly Thr Leu Glu Ala Met Val Ala Cys Arg Gln Leu Gly Leu
    450                 455                 460

Gly Tyr Ala Asn His Gly Leu Gln Glu Thr Trp Tyr Trp Asp Ser Gly
465                 470                 475                 480

Asn Ile Thr Glu Val Val Met Ser Gly Val Arg Cys Thr Gly Thr Glu
                485                 490                 495

Leu Ser Leu Asp Gln Cys Ala His His Gly Thr His Ile Thr Cys Lys
            500                 505                 510

Arg Thr Gly Thr Arg Phe Thr Ala Gly Val Ile Cys Ser Glu Thr Ala
        515                 520                 525

Ser Asp Leu Leu Leu His Ser Ala Leu Val Gln Glu Thr Ala Tyr Ile
    530                 535                 540

Glu Asp Arg Pro Leu His Met Leu Tyr Cys Ala Ala Glu Glu Asn Cys
545                 550                 555                 560

Leu Ala Ser Ser Ala Arg Ser Ala Asn Trp Pro Tyr Gly His Arg Arg
                565                 570                 575

Leu Leu Arg Phe Ser Ser Gln Ile His Asn Leu Gly Arg Ala Asp Phe
            580                 585                 590

Arg Pro Lys Ala Gly Arg His Ser Trp Val Trp His Glu Cys His Gly
        595                 600                 605

His Tyr His Ser Met Asp Ile Phe Thr His Tyr Asp Ile Leu Thr Pro
    610                 615                 620

Asn Gly Thr Lys Val Ala Glu Gly His Lys Ala Ser Phe Cys Leu Glu
625                 630                 635                 640

Asp Thr Glu Cys Gln Glu Asp Val Ser Lys Arg Tyr Glu Cys Ala Asn
                645                 650                 655

Phe Gly Glu Gln Gly Ile Thr Val Gly Cys Trp Asp Leu Tyr Arg His
            660                 665                 670
```

Asp Ile Asp Cys Gln Trp Ile Asp Ile Thr Asp Val Lys Pro Gly Asn
675 680 685

Tyr Ile Leu Gln Val Val Ile Asn Pro Asn Phe Glu Val Ala Glu Ser
690 695 700

Asp Phe Thr Asn Asn Ala Met Lys Cys Asn Cys Lys Tyr Asp Gly His
705 710 715 720

Arg Ile Trp Val His Asn Cys His Ile Gly Asp Ala Phe Ser Glu Glu
725 730 735

Ala Asn Arg Arg Phe Glu Arg Tyr Pro Gly Gln Thr Ser Asn Gln Ile
740 745 750

Ile

<210> 139
<211> 608
<212> PRT
<213> Homo sapiens

<400> 139

Met Arg Pro Val Ser Val Trp Gln Trp Ser Pro Trp Gly Leu Leu Leu
1 5 10 15

Cys Leu Leu Cys Ser Ser Cys Leu Gly Ser Pro Ser Pro Ser Thr Gly
20 25 30

Pro Glu Lys Lys Ala Gly Ser Gln Gly Leu Arg Phe Arg Leu Ala Gly
35 40 45

Phe Pro Arg Lys Pro Tyr Glu Gly Arg Val Glu Ile Gln Arg Ala Gly
50 55 60

Glu Trp Gly Thr Ile Cys Asp Asp Asp Phe Thr Leu Gln Ala Ala His
65 70 75 80

Ile Leu Cys Arg Glu Leu Gly Phe Thr Glu Ala Thr Gly Trp Thr His
85 90 95

Ser Ala Lys Tyr Gly Pro Gly Thr Gly Arg Ile Trp Leu Asp Asn Leu
100 105 110

Ser Cys Ser Gly Thr Glu Gln Ser Val Thr Glu Cys Ala Ser Arg Gly
115 120 125

Trp Gly Asn Ser Asp Cys Thr His Asp Glu Asp Ala Gly Val Ile Cys
130 135 140

Lys Asp Gln Arg Leu Pro Gly Phe Ser Asp Ser Asn Val Ile Glu Ala

```
145                 150                 155                 160

Arg Val Arg Leu Lys Gly Gly Ala His Pro Gly Glu Gly Arg Val Glu
                165                 170                 175

Val Leu Lys Ala Ser Thr Trp Gly Thr Val Cys Asp Arg Lys Trp Asp
            180                 185                 190

Leu His Ala Ala Ser Val Val Cys Arg Glu Leu Gly Phe Gly Ser Ala
        195                 200                 205

Arg Glu Ala Leu Ser Gly Ala Arg Met Gly Gln Gly Met Gly Ala Ile
    210                 215                 220

His Leu Ser Glu Val Arg Cys Ser Gly Gln Glu Leu Ser Leu Trp Lys
225                 230                 235                 240

Cys Pro His Lys Asn Ile Thr Ala Glu Asp Cys Ser His Ser Gln Asp
                245                 250                 255

Ala Gly Val Arg Cys Asn Leu Pro Tyr Thr Gly Ala Glu Thr Arg Ile
            260                 265                 270

Arg Leu Ser Gly Gly Arg Ser Gln His Glu Gly Arg Val Glu Val Gln
        275                 280                 285

Ile Gly Gly Pro Gly Pro Leu Arg Trp Gly Leu Ile Cys Gly Asp Asp
    290                 295                 300

Trp Gly Thr Leu Glu Ala Met Val Ala Cys Arg Gln Leu Gly Leu Gly
305                 310                 315                 320

Tyr Ala Asn His Gly Leu Gln Glu Thr Trp Tyr Trp Asp Ser Gly Asn
                325                 330                 335

Ile Thr Glu Val Val Met Ser Gly Val Arg Cys Thr Gly Thr Glu Leu
            340                 345                 350

Ser Leu Asp Gln Cys Ala His His Gly Thr His Ile Thr Cys Lys Arg
        355                 360                 365

Thr Gly Thr Arg Phe Thr Ala Gly Val Ile Cys Ser Glu Thr Ala Ser
    370                 375                 380

Asp Leu Leu Leu His Ser Ala Leu Val Gln Glu Thr Ala Tyr Ile Glu
385                 390                 395                 400

Asp Arg Pro Leu His Met Leu Tyr Cys Ala Ala Glu Glu Asn Cys Leu
                405                 410                 415

Ala Ser Ser Ala Arg Ser Ala Asn Trp Pro Tyr Gly His Arg Arg Leu
```

420 425 430

Leu Arg Phe Ser Ser Gln Ile His Asn Leu Gly Arg Ala Asp Phe Arg
435 440 445

Pro Lys Ala Gly Arg His Ser Trp Val Trp His Glu Cys His Gly His
450 455 460

Tyr His Ser Met Asp Ile Phe Thr His Tyr Asp Ile Leu Thr Pro Asn
465 470 475 480

Gly Thr Lys Val Ala Glu Gly His Lys Ala Ser Phe Cys Leu Glu Asp
485 490 495

Thr Glu Cys Gln Glu Asp Val Ser Lys Arg Tyr Glu Cys Ala Asn Phe
500 505 510

Gly Glu Gln Gly Ile Thr Val Gly Cys Trp Asp Leu Tyr Arg His Asp
515 520 525

Ile Asp Cys Gln Trp Ile Asp Ile Thr Asp Val Lys Pro Gly Asn Tyr
530 535 540

Ile Leu Gln Val Val Ile Asn Pro Asn Phe Glu Val Ala Glu Ser Asp
545 550 555 560

Phe Thr Asn Asn Ala Met Lys Cys Asn Cys Lys Tyr Asp Gly His Arg
565 570 575

Ile Trp Val His Asn Cys His Ile Gly Asp Ala Phe Ser Glu Glu Ala
580 585 590

Asn Arg Arg Phe Glu Arg Tyr Pro Gly Gln Thr Ser Asn Gln Ile Ile
595 600 605

<210> 140
<211> 392
<212> PRT
<213> Homo sapiens

<400> 140

Met Gly Gln Gly Met Gly Ala Ile His Leu Ser Glu Val Arg Cys Ser
1 5 10 15

Gly Gln Glu Leu Ser Leu Trp Lys Cys Pro His Lys Asn Ile Thr Ala
20 25 30

Glu Asp Cys Ser His Ser Gln Asp Ala Gly Val Arg Cys Asn Leu Pro
35 40 45

Tyr Thr Gly Ala Glu Thr Arg Ile Arg Leu Ser Gly Gly Arg Ser Gln
50 55 60

```
His Glu Gly Arg Val Glu Val Gln Ile Gly Gly Pro Gly Pro Leu Arg
65                  70                  75                  80

Trp Gly Leu Ile Cys Gly Asp Asp Trp Gly Thr Leu Glu Ala Met Val
                85                  90                  95

Ala Cys Arg Gln Leu Gly Leu Gly Tyr Ala Asn His Gly Leu Gln Glu
            100                 105                 110

Thr Trp Tyr Trp Asp Ser Gly Asn Ile Thr Glu Val Val Met Ser Gly
        115                 120                 125

Val Arg Cys Thr Gly Thr Glu Leu Ser Leu Asp Gln Cys Ala His His
    130                 135                 140

Gly Thr His Ile Thr Cys Lys Arg Thr Gly Thr Arg Phe Thr Ala Gly
145                 150                 155                 160

Val Ile Cys Ser Glu Thr Ala Ser Asp Leu Leu Leu His Ser Ala Leu
                165                 170                 175

Val Gln Glu Thr Ala Tyr Ile Glu Asp Arg Pro Leu His Met Leu Tyr
            180                 185                 190

Cys Ala Ala Glu Glu Asn Cys Leu Ala Ser Ser Ala Arg Ser Ala Asn
        195                 200                 205

Trp Pro Tyr Gly His Arg Arg Leu Leu Arg Phe Ser Ser Gln Ile His
    210                 215                 220

Asn Leu Gly Arg Ala Asp Phe Arg Pro Lys Ala Gly Arg His Ser Trp
225                 230                 235                 240

Val Trp His Glu Cys His Gly His Tyr His Ser Met Asp Ile Phe Thr
                245                 250                 255

His Tyr Asp Ile Leu Thr Pro Asn Gly Thr Lys Val Ala Glu Gly His
            260                 265                 270

Lys Ala Ser Phe Cys Leu Glu Asp Thr Glu Cys Gln Glu Asp Val Ser
        275                 280                 285

Lys Arg Tyr Glu Cys Ala Asn Phe Gly Glu Gln Gly Ile Thr Val Gly
    290                 295                 300

Cys Trp Asp Leu Tyr Arg His Asp Ile Asp Cys Gln Trp Ile Asp Ile
305                 310                 315                 320

Thr Asp Val Lys Pro Gly Asn Tyr Ile Leu Gln Val Val Ile Asn Pro
                325                 330                 335
```

```
Asn Phe Glu Val Ala Glu Ser Asp Phe Thr Asn Asn Ala Met Lys Cys
            340                 345                 350


Asn Cys Lys Tyr Asp Gly His Arg Ile Trp Val His Asn Cys His Ile
        355                 360                 365


Gly Asp Ala Phe Ser Glu Glu Ala Asn Arg Arg Phe Glu Arg Tyr Pro
    370                 375                 380


Gly Gln Thr Ser Asn Gln Ile Ile
385                 390


<210>  141
<211>  756
<212>  PRT
<213>  Homo sapiens

<400>  141

Met Ala Trp Ser Pro Pro Ala Thr Leu Phe Leu Phe Leu Leu Leu Leu
1               5                   10                  15


Gly Gln Pro Pro Pro Ser Arg Pro Gln Ser Leu Gly Thr Thr Lys Leu
            20                  25                  30


Arg Leu Val Gly Pro Glu Ser Lys Pro Glu Glu Gly Arg Leu Glu Val
        35                  40                  45


Leu His Gln Gly Gln Trp Gly Thr Val Cys Asp Asp Asn Phe Ala Ile
    50                  55                  60


Gln Glu Ala Thr Val Ala Cys Arg Gln Leu Gly Phe Glu Ala Ala Leu
65                  70                  75                  80


Thr Trp Ala His Ser Ala Lys Tyr Gly Gln Gly Glu Gly Pro Ile Trp
                85                  90                  95


Leu Asp Asn Val Arg Cys Val Gly Thr Glu Ser Ser Leu Asp Gln Cys
            100                 105                 110


Gly Ser Asn Gly Trp Gly Val Ser Asp Cys Ser His Ser Glu Asp Val
        115                 120                 125


Gly Val Ile Cys His Pro Arg Arg His Arg Gly Tyr Leu Ser Glu Thr
    130                 135                 140


Val Ser Asn Ala Leu Gly Pro Gln Gly Arg Arg Leu Glu Glu Val Arg
145                 150                 155                 160


Leu Lys Pro Ile Leu Ala Ser Ala Lys Gln His Ser Pro Val Thr Glu
                165                 170                 175
```

```
Gly Ala Val Glu Val Lys Tyr Glu Gly His Trp Arg Gln Val Cys Asp
            180                 185                 190

Gln Gly Trp Thr Met Asn Asn Ser Arg Val Val Cys Gly Met Leu Gly
        195                 200                 205

Phe Pro Ser Glu Val Pro Val Asp Ser His Tyr Tyr Arg Lys Val Trp
    210                 215                 220

Asp Leu Lys Met Arg Asp Pro Lys Ser Arg Leu Lys Ser Leu Thr Asn
225                 230                 235                 240

Lys Asn Ser Phe Trp Ile His Gln Val Thr Cys Leu Gly Thr Glu Pro
                245                 250                 255

His Met Ala Asn Cys Gln Val Gln Val Ala Pro Ala Arg Gly Lys Leu
            260                 265                 270

Arg Pro Ala Cys Pro Gly Gly Met His Ala Val Val Ser Cys Val Ala
        275                 280                 285

Gly Pro His Phe Arg Pro Pro Lys Thr Lys Pro Gln Arg Lys Gly Ser
    290                 295                 300

Trp Ala Glu Glu Pro Arg Val Arg Leu Arg Ser Gly Ala Gln Val Gly
305                 310                 315                 320

Glu Gly Arg Val Glu Val Leu Met Asn Arg Gln Trp Gly Thr Val Cys
                325                 330                 335

Asp His Arg Trp Asn Leu Ile Ser Ala Ser Val Val Cys Arg Gln Leu
            340                 345                 350

Gly Phe Gly Ser Ala Arg Glu Ala Leu Phe Gly Ala Arg Leu Gly Gln
        355                 360                 365

Gly Leu Gly Pro Ile His Leu Ser Glu Val Arg Cys Arg Gly Tyr Glu
    370                 375                 380

Arg Thr Leu Ser Asp Cys Pro Ala Leu Glu Gly Ser Gln Asn Gly Cys
385                 390                 395                 400

Gln His Glu Asn Asp Ala Ala Val Arg Cys Asn Val Pro Asn Met Gly
                405                 410                 415

Phe Gln Asn Gln Val Arg Leu Ala Gly Gly Arg Ile Pro Glu Glu Gly
            420                 425                 430

Leu Leu Glu Val Gln Val Glu Val Asn Gly Val Pro Arg Trp Gly Ser
        435                 440                 445
```

```
Val Cys Ser Glu Asn Trp Gly Leu Thr Glu Ala Met Val Ala Cys Arg
    450                 455                 460

Gln Leu Gly Leu Gly Phe Ala Ile His Ala Tyr Lys Glu Thr Trp Phe
465                 470                 475                 480

Trp Ser Gly Thr Pro Arg Ala Gln Glu Val Val Met Ser Gly Val Arg
                485                 490                 495

Cys Ser Gly Thr Glu Leu Ala Leu Gln Gln Cys Gln Arg His Gly Pro
            500                 505                 510

Val His Cys Ser His Gly Gly Gly Arg Phe Leu Ala Gly Val Ser Cys
        515                 520                 525

Met Asp Ser Ala Pro Asp Leu Val Met Asn Ala Gln Leu Val Gln Glu
    530                 535                 540

Thr Ala Tyr Leu Glu Asp Arg Pro Leu Ser Gln Leu Tyr Cys Ala His
545                 550                 555                 560

Glu Glu Asn Cys Leu Ser Lys Ser Ala Asp His Met Asp Trp Pro Tyr
                565                 570                 575

Gly Tyr Arg Arg Leu Leu Arg Phe Ser Thr Gln Ile Tyr Asn Leu Gly
            580                 585                 590

Arg Thr Asp Phe Arg Pro Lys Thr Gly Arg Asp Ser Trp Val Trp His
        595                 600                 605

Gln Cys His Arg His Tyr His Ser Ile Glu Val Phe Thr His Tyr Asp
    610                 615                 620

Leu Leu Thr Leu Asn Gly Ser Lys Val Ala Glu Gly His Lys Ala Ser
625                 630                 635                 640

Phe Cys Leu Glu Asp Thr Asn Cys Pro Thr Gly Leu Gln Arg Arg Tyr
                645                 650                 655

Ala Cys Ala Asn Phe Gly Glu Gln Gly Val Thr Val Gly Cys Trp Asp
            660                 665                 670

Thr Tyr Arg His Asp Ile Asp Cys Gln Trp Val Asp Ile Thr Asp Val
        675                 680                 685

Gly Pro Gly Asn Tyr Ile Phe Gln Val Ile Val Asn Pro His Tyr Glu
    690                 695                 700

Val Ala Glu Ser Asp Phe Ser Asn Asn Met Leu Gln Cys Arg Cys Lys
705                 710                 715                 720
```

```
Tyr Asp Gly His Arg Val Trp Leu His Asn Cys His Thr Gly Asn Ser
                725                 730                 735


Tyr Pro Ala Asn Ala Glu Leu Ser Leu Glu Gln Glu Gln Arg Leu Arg
            740                 745                 750


Asn Asn Leu Ile
        755


<210>  142
<211>  183
<212>  PRT
<213>  Homo sapiens

<400>  142

Met Arg Ala Ala Tyr Leu Phe Leu Leu Phe Leu Pro Ala Gly Leu Leu
1               5                   10                  15


Ala Gln Gly Gln Tyr Asp Leu Asp Pro Leu Pro Pro Phe Pro Asp His
            20                  25                  30


Val Gln Tyr Thr His Tyr Ser Asp Gln Ile Asp Asn Pro Asp Tyr Tyr
        35                  40                  45


Asp Tyr Gln Glu Val Thr Pro Arg Pro Ser Glu Glu Gln Phe Gln Phe
    50                  55                  60


Gln Ser Gln Gln Gln Val Gln Gln Glu Val Ile Pro Ala Pro Thr Pro
65                  70                  75                  80


Glu Pro Gly Asn Ala Glu Leu Glu Pro Thr Glu Pro Gly Pro Leu Asp
                85                  90                  95


Cys Arg Glu Glu Gln Tyr Pro Cys Thr Arg Leu Tyr Ser Ile His Arg
            100                 105                 110


Pro Cys Lys Gln Cys Leu Asn Glu Val Cys Phe Tyr Ser Leu Arg Arg
        115                 120                 125


Val Tyr Val Ile Asn Lys Glu Ile Cys Val Arg Thr Val Cys Ala His
    130                 135                 140


Glu Glu Leu Leu Arg Ala Asp Leu Cys Arg Asp Lys Phe Ser Lys Cys
145                 150                 155                 160


Gly Val Met Ala Ser Ser Gly Leu Cys Gln Ser Val Ala Ala Ser Cys
                165                 170                 175


Ala Arg Ser Cys Gly Ser Cys
            180
```

<210> 143
<211> 182
<212> PRT
<213> Homo sapiens

<400> 143

Met Arg Ala Ala Tyr Leu Phe Leu Leu Phe Leu Pro Gly Leu Leu Ala
1 5 10 15

Gln Gly Gln Tyr Asp Leu Asp Pro Leu Pro Pro Phe Pro Asp His Val
20 25 30

Gln Tyr Thr His Tyr Ser Asp Gln Ile Asp Asn Pro Asp Tyr Tyr Asp
35 40 45

Tyr Gln Glu Val Thr Pro Arg Pro Ser Glu Glu Gln Phe Gln Phe Gln
50 55 60

Ser Gln Gln Gln Val Gln Gln Glu Val Ile Pro Ala Pro Thr Pro Glu
65 70 75 80

Pro Gly Asn Ala Glu Leu Glu Pro Thr Glu Pro Gly Pro Leu Asp Cys
85 90 95

Arg Glu Glu Gln Tyr Pro Cys Thr Arg Leu Tyr Ser Ile His Arg Pro
100 105 110

Cys Lys Gln Cys Leu Asn Glu Val Cys Phe Tyr Ser Leu Arg Arg Val
115 120 125

Tyr Val Ile Asn Lys Glu Ile Cys Val Arg Thr Val Cys Ala His Glu
130 135 140

Glu Leu Leu Arg Ala Asp Leu Cys Arg Asp Lys Phe Ser Lys Cys Gly
145 150 155 160

Val Met Ala Ser Ser Gly Leu Cys Gln Ser Val Ala Ala Ser Cys Ala
165 170 175

Arg Ser Cys Gly Ser Cys
180

<210> 144
<211> 173
<212> PRT
<213> Homo sapiens

<400> 144

Met Ser Leu Leu Gly Pro Lys Val Leu Leu Phe Leu Ala Ala Phe Ile
1 5 10 15

Ile Thr Ser Asp Trp Ile Pro Leu Gly Val Asn Ser Gln Arg Gly Asp
20 25 30

```
Asp Val Thr Gln Ala Thr Pro Glu Thr Phe Thr Glu Asp Pro Asn Leu
        35                  40                  45

Val Asn Asp Pro Ala Thr Asp Glu Thr Val Leu Ala Val Leu Ala Asp
    50                  55                  60

Ile Ala Pro Ser Thr Asp Asp Leu Ala Ser Leu Ser Glu Lys Asn Thr
65                  70                  75                  80

Thr Ala Glu Cys Trp Asp Glu Lys Phe Thr Cys Thr Arg Leu Tyr Ser
                85                  90                  95

Val His Arg Pro Val Lys Gln Cys Ile His Gln Leu Cys Phe Thr Ser
            100                 105                 110

Leu Arg Arg Met Tyr Ile Val Asn Lys Glu Ile Cys Ser Arg Leu Val
        115                 120                 125

Cys Lys Glu His Glu Ala Met Lys Asp Glu Leu Cys Arg Gln Met Ala
    130                 135                 140

Gly Leu Pro Pro Arg Arg Leu Arg Arg Ser Asn Tyr Phe Arg Leu Pro
145                 150                 155                 160

Pro Cys Glu Asn Val Asp Leu Gln Arg Pro Asn Gly Leu
                165                 170

<210>  145
<211>  824
<212>  PRT
<213>  Homo sapiens

<400>  145

Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu
1               5                   10                  15

Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu
            20                  25                  30

Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser
        35                  40                  45

Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr
    50                  55                  60

His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys
65                  70                  75                  80

Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val
                85                  90                  95
```

```
Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln
            100                 105                 110

Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu
        115                 120                 125

Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly
    130                 135                 140

Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys
145                 150                 155                 160

Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser
                165                 170                 175

Arg Leu Gln Ser Pro Lys Val Cys Gly Tyr Leu Lys Val Asp Asn Glu
            180                 185                 190

Glu Leu Leu Pro Lys Gly Leu Val Asp Arg Glu Pro Pro Glu Glu Leu
        195                 200                 205

Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro Met Lys Asn Thr
    210                 215                 220

Cys Lys Leu Leu Val Val Ala Asp His Arg Phe Tyr Arg Tyr Met Gly
225                 230                 235                 240

Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile Glu Leu Ile Asp
                245                 250                 255

Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp Asn Ala Gly Phe
            260                 265                 270

Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile Leu Lys Ser Pro
        275                 280                 285

Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met Ala Lys Ser Tyr
    290                 295                 300

Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met Leu Leu Glu Gln
305                 310                 315                 320

Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val Cys Leu Ala His
                325                 330                 335

Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu Gly Leu Ala Tyr
            340                 345                 350

Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val Cys Pro Lys Ala
        355                 360                 365
```

```
Tyr Tyr Ser Pro Val Gly Lys Lys Asn Ile Tyr Leu Asn Ser Gly Leu
    370                 375                 380

Thr Ser Thr Lys Asn Tyr Gly Lys Thr Ile Leu Thr Lys Glu Ala Asp
385                 390                 395                 400

Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly Ala Glu His Asp
                405                 410                 415

Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp Gln Gly Gly Lys
            420                 425                 430

Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His Glu Asn Asn Lys
        435                 440                 445

Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys Thr Ile Glu Ser
    450                 455                 460

Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys Val Cys Gly Asn
465                 470                 475                 480

Ser Arg Val Asp Glu Gly Glu Glu Cys Asp Pro Gly Ile Met Tyr Leu
                485                 490                 495

Asn Asn Asp Thr Cys Cys Asn Ser Asp Cys Thr Leu Lys Glu Gly Val
            500                 505                 510

Gln Cys Ser Asp Arg Asn Ser Pro Cys Cys Lys Asn Cys Gln Phe Glu
        515                 520                 525

Thr Ala Gln Lys Lys Cys Gln Glu Ala Ile Asn Ala Thr Cys Lys Gly
    530                 535                 540

Val Ser Tyr Cys Thr Gly Asn Ser Ser Glu Cys Pro Pro Pro Gly Asn
545                 550                 555                 560

Ala Glu Asp Asp Thr Val Cys Leu Asp Leu Gly Lys Cys Lys Asp Gly
                565                 570                 575

Lys Cys Ile Pro Phe Cys Glu Arg Glu Gln Gln Leu Glu Ser Cys Ala
            580                 585                 590

Cys Asn Glu Thr Asp Asn Ser Cys Lys Val Cys Cys Arg Asp Leu Ser
        595                 600                 605

Gly Arg Cys Val Pro Tyr Val Asp Ala Glu Gln Lys Asn Leu Phe Leu
    610                 615                 620

Arg Lys Gly Lys Pro Cys Thr Val Gly Phe Cys Asp Met Asn Gly Lys
625                 630                 635                 640
```

```
Cys Glu Lys Arg Val Gln Asp Val Ile Glu Arg Phe Trp Asp Phe Ile
                645                 650                 655

Asp Gln Leu Ser Ile Asn Thr Phe Gly Lys Phe Leu Ala Asp Asn Ile
            660                 665                 670

Val Gly Ser Val Leu Val Phe Ser Leu Ile Phe Trp Ile Pro Phe Ser
        675                 680                 685

Ile Leu Val His Cys Val Asp Lys Lys Leu Asp Lys Gln Tyr Glu Ser
    690                 695                 700

Leu Ser Leu Phe His Pro Ser Asn Val Glu Met Leu Ser Ser Met Asp
705                 710                 715                 720

Ser Ala Ser Val Arg Ile Ile Lys Pro Phe Pro Ala Pro Gln Thr Pro
                725                 730                 735

Gly Arg Leu Gln Pro Ala Pro Val Ile Pro Ser Ala Pro Ala Ala Pro
            740                 745                 750

Lys Leu Asp His Gln Arg Met Asp Thr Ile Gln Glu Asp Pro Ser Thr
        755                 760                 765

Asp Ser His Met Asp Glu Asp Gly Phe Glu Lys Asp Pro Phe Pro Asn
    770                 775                 780

Ser Ser Thr Ala Ala Lys Ser Phe Glu Asp Leu Thr Asp His Pro Val
785                 790                 795                 800

Thr Arg Ser Glu Lys Ala Ala Ser Phe Lys Leu Gln Arg Gln Asn Arg
                805                 810                 815

Val Asp Ser Lys Glu Thr Glu Cys
            820


<210>  146
<211>  824
<212>  PRT
<213>  Homo sapiens

<400>  146

Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu
1               5                   10                  15

Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu
            20                  25                  30

Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser
        35                  40                  45
```

```
Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr
    50                  55                  60

His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys
65                  70                  75                  80

Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val
                85                  90                  95

Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln
            100                 105                 110

Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu
        115                 120                 125

Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly
    130                 135                 140

Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys
145                 150                 155                 160

Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser
                165                 170                 175

Arg Leu Gln Ser Pro Lys Val Cys Gly Tyr Leu Lys Val Asp Asn Glu
            180                 185                 190

Glu Leu Leu Pro Lys Gly Leu Val Asp Arg Glu Pro Pro Glu Glu Leu
        195                 200                 205

Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro Met Lys Asn Thr
    210                 215                 220

Cys Lys Leu Leu Val Val Ala Asp His Arg Phe Tyr Arg Tyr Met Gly
225                 230                 235                 240

Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile Glu Leu Ile Asp
                245                 250                 255

Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp Asn Ala Gly Phe
            260                 265                 270

Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile Leu Lys Ser Pro
        275                 280                 285

Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met Ala Lys Ser Tyr
    290                 295                 300

Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met Leu Leu Glu Gln
305                 310                 315                 320
```

```
Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val Cys Leu Ala His
                325                 330                 335

Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu Gly Leu Ala Tyr
            340                 345                 350

Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val Cys Pro Lys Ala
        355                 360                 365

Tyr Tyr Ser Pro Val Gly Lys Lys Asn Ile Tyr Leu Asn Ser Gly Leu
    370                 375                 380

Thr Ser Thr Lys Asn Tyr Gly Lys Thr Ile Leu Thr Lys Glu Ala Asp
385                 390                 395                 400

Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly Ala Glu His Asp
                405                 410                 415

Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp Gln Gly Gly Lys
            420                 425                 430

Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His Glu Asn Asn Lys
        435                 440                 445

Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys Thr Ile Glu Ser
    450                 455                 460

Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys Val Cys Gly Asn
465                 470                 475                 480

Ser Arg Val Asp Glu Gly Glu Glu Cys Asp Pro Gly Ile Met Tyr Leu
                485                 490                 495

Asn Asn Asp Thr Cys Cys Asn Ser Asp Cys Thr Leu Lys Glu Gly Val
            500                 505                 510

Gln Cys Ser Asp Arg Asn Ser Pro Cys Cys Lys Asn Cys Gln Phe Glu
        515                 520                 525

Thr Ala Gln Lys Lys Cys Gln Glu Ala Ile Asn Ala Thr Cys Lys Gly
    530                 535                 540

Val Ser Tyr Cys Thr Gly Asn Ser Ser Glu Cys Pro Pro Pro Gly Asn
545                 550                 555                 560

Ala Glu Asp Asp Thr Val Cys Leu Asp Leu Gly Lys Cys Lys Asp Gly
                565                 570                 575

Lys Cys Ile Pro Phe Cys Glu Arg Glu Gln Gln Leu Glu Ser Cys Ala
            580                 585                 590
```

```
Cys Asn Glu Thr Asp Asn Ser Cys Lys Val Cys Cys Arg Asp Leu Ser
        595                 600                 605

Gly Arg Cys Val Pro Tyr Val Asp Ala Glu Gln Lys Asn Leu Phe Leu
    610                 615                 620

Arg Lys Gly Lys Pro Cys Thr Val Gly Phe Cys Asp Met Asn Gly Lys
625                 630                 635                 640

Cys Glu Lys Arg Val Gln Asp Val Ile Glu Arg Phe Trp Asp Phe Ile
                645                 650                 655

Asp Gln Leu Ser Ile Asn Thr Phe Gly Lys Phe Leu Ala Asp Asn Ile
            660                 665                 670

Val Gly Ser Val Leu Val Phe Ser Leu Ile Phe Trp Ile Pro Phe Ser
        675                 680                 685

Ile Leu Val His Cys Val Asp Lys Lys Leu Asp Lys Gln Tyr Glu Ser
    690                 695                 700

Leu Ser Leu Phe His Pro Ser Asn Val Glu Met Leu Ser Ser Met Asp
705                 710                 715                 720

Ser Ala Ser Val Arg Ile Ile Lys Pro Phe Pro Ala Pro Gln Thr Pro
                725                 730                 735

Gly Arg Leu Gln Pro Ala Pro Val Ile Pro Ser Ala Pro Ala Ala Pro
            740                 745                 750

Lys Leu Asp His Gln Arg Met Asp Thr Ile Gln Glu Asp Pro Ser Thr
        755                 760                 765

Asp Ser His Met Asp Glu Asp Gly Phe Glu Lys Asp Pro Phe Pro Asn
    770                 775                 780

Ser Ser Thr Ala Ala Lys Ser Phe Glu Asp Leu Thr Asp His Pro Val
785                 790                 795                 800

Thr Arg Ser Glu Lys Ala Ala Ser Phe Lys Leu Gln Arg Gln Asn Arg
                805                 810                 815

Val Asp Ser Lys Glu Thr Glu Cys
            820


<210>  147
<211>  713
<212>  PRT
<213>  Homo sapiens

<400>  147

Met Ala Thr Gly Gln Asp Arg Val Val Ala Leu Val Asp Met Asp Cys
```

1 5 10 15

Phe Phe Val Gln Val Glu Gln Arg Gln Asn Pro His Leu Arg Asn Lys
20 25 30

Pro Cys Ala Val Val Gln Tyr Lys Ser Trp Lys Gly Gly Gly Ile Ile
35 40 45

Ala Val Ser Tyr Glu Ala Arg Ala Phe Gly Val Thr Arg Ser Met Trp
50 55 60

Ala Asp Asp Ala Lys Lys Leu Cys Pro Asp Leu Leu Leu Ala Gln Val
65 70 75 80

Arg Glu Ser Arg Gly Lys Ala Asn Leu Thr Lys Tyr Arg Glu Ala Ser
85 90 95

Val Glu Val Met Glu Ile Met Ser Arg Phe Ala Val Ile Glu Arg Ala
100 105 110

Ser Ile Asp Glu Ala Tyr Val Asp Leu Thr Ser Ala Val Gln Glu Arg
115 120 125

Leu Gln Lys Leu Gln Gly Gln Pro Ile Ser Ala Asp Leu Leu Pro Ser
130 135 140

Thr Tyr Ile Glu Gly Leu Pro Gln Gly Pro Thr Thr Ala Glu Glu Thr
145 150 155 160

Val Gln Lys Glu Gly Met Arg Lys Gln Gly Leu Phe Gln Trp Leu Asp
165 170 175

Ser Leu Gln Ile Asp Asn Leu Thr Ser Pro Asp Leu Gln Leu Thr Val
180 185 190

Gly Ala Val Ile Val Glu Glu Met Arg Ala Ala Ile Glu Arg Glu Thr
195 200 205

Gly Phe Gln Cys Ser Ala Gly Ile Ser His Asn Lys Val Leu Ala Lys
210 215 220

Leu Ala Cys Gly Leu Asn Lys Pro Asn Arg Gln Thr Leu Val Ser His
225 230 235 240

Gly Ser Val Pro Gln Leu Phe Ser Gln Met Pro Ile Arg Lys Ile Arg
245 250 255

Ser Leu Gly Gly Lys Leu Gly Ala Ser Val Ile Glu Ile Leu Gly Ile
260 265 270

Glu Tyr Met Gly Glu Leu Thr Gln Phe Thr Glu Ser Gln Leu Gln Ser

```
        275                 280                 285

His Phe Gly Glu Lys Asn Gly Ser Trp Leu Tyr Ala Met Cys Arg Gly
    290                 295                 300

Ile Glu His Asp Pro Val Lys Pro Arg Gln Leu Pro Lys Thr Ile Gly
305                 310                 315                 320

Cys Ser Lys Asn Phe Pro Gly Lys Thr Ala Leu Ala Thr Arg Glu Gln
                325                 330                 335

Val Gln Trp Trp Leu Leu Gln Leu Ala Gln Glu Leu Glu Glu Arg Leu
            340                 345                 350

Thr Lys Asp Arg Asn Asp Asn Asp Arg Val Ala Thr Gln Leu Val Val
        355                 360                 365

Ser Ile Arg Val Gln Gly Asp Lys Arg Leu Ser Ser Leu Arg Arg Cys
    370                 375                 380

Cys Ala Leu Thr Arg Tyr Asp Ala His Lys Met Ser His Asp Ala Phe
385                 390                 395                 400

Thr Val Ile Lys Asn Cys Asn Thr Ser Gly Ile Gln Thr Glu Trp Ser
                405                 410                 415

Pro Pro Leu Thr Met Leu Phe Leu Cys Ala Thr Lys Phe Ser Ala Ser
            420                 425                 430

Ala Pro Ser Ser Ser Thr Asp Ile Thr Ser Phe Leu Ser Ser Asp Pro
        435                 440                 445

Ser Ser Leu Pro Lys Val Pro Val Thr Ser Ser Glu Ala Lys Thr Gln
    450                 455                 460

Gly Ser Gly Pro Ala Val Thr Ala Thr Lys Lys Ala Thr Thr Ser Leu
465                 470                 475                 480

Glu Ser Phe Phe Gln Lys Ala Ala Glu Arg Gln Lys Val Lys Glu Ala
                485                 490                 495

Ser Leu Ser Ser Leu Thr Ala Pro Thr Gln Ala Pro Met Ser Asn Ser
            500                 505                 510

Pro Ser Lys Pro Ser Leu Pro Phe Gln Thr Ser Gln Ser Thr Gly Thr
        515                 520                 525

Glu Pro Phe Phe Lys Gln Lys Ser Leu Leu Leu Lys Gln Lys Gln Leu
    530                 535                 540

Asn Asn Ser Ser Val Ser Ser Pro Gln Gln Asn Pro Trp Ser Asn Cys
```

545 550 555 560

Lys Ala Leu Pro Asn Ser Leu Pro Thr Glu Tyr Pro Gly Cys Val Pro
565 570 575

Val Cys Glu Gly Val Ser Lys Leu Glu Glu Ser Ser Lys Ala Thr Pro
580 585 590

Ala Glu Met Asp Leu Ala His Asn Ser Gln Ser Met His Ala Ser Ser
595 600 605

Ala Ser Lys Ser Val Leu Glu Val Thr Gln Lys Ala Thr Pro Asn Pro
610 615 620

Ser Leu Leu Ala Ala Glu Asp Gln Val Pro Cys Glu Lys Cys Gly Ser
625 630 635 640

Leu Val Pro Val Trp Asp Met Pro Glu His Met Asp Tyr His Phe Ala
645 650 655

Leu Glu Leu Gln Lys Ser Phe Leu Gln Pro His Ser Ser Asn Pro Gln
660 665 670

Val Val Ser Ala Val Ser His Gln Gly Lys Arg Asn Pro Lys Ser Pro
675 680 685

Leu Ala Cys Thr Asn Lys Arg Pro Arg Pro Glu Gly Met Gln Thr Leu
690 695 700

Glu Ser Phe Phe Lys Pro Leu Thr His
705 710

<210> 148
<211> 589
<212> PRT
<213> Homo sapiens

<400> 148

Met Lys Leu Val His Leu Glu Ser Leu Glu Val Cys Gly Gln Met Met
1 5 10 15

Leu Arg Ser Tyr Val Gln Ile Phe Tyr Trp His Lys Phe Val Ser Pro
20 25 30

Val Gly Lys Leu Thr Ser Pro Lys Gly Met Arg Lys Gln Gly Leu Phe
35 40 45

Gln Trp Leu Asp Ser Leu Gln Ile Asp Asn Leu Thr Ser Pro Asp Leu
50 55 60

Gln Leu Thr Val Gly Ala Val Ile Val Glu Glu Met Arg Ala Ala Ile
65 70 75 80

```
Glu Arg Glu Thr Gly Phe Gln Cys Ser Ala Gly Ile Ser His Asn Lys
                85                  90                  95

Val Leu Ala Lys Leu Ala Cys Gly Leu Asn Lys Pro Asn Arg Gln Thr
            100                 105                 110

Leu Val Ser His Gly Ser Val Pro Gln Leu Phe Ser Gln Met Pro Ile
        115                 120                 125

Arg Lys Ile Arg Ser Leu Gly Gly Lys Leu Gly Ala Ser Val Ile Glu
    130                 135                 140

Ile Leu Gly Ile Glu Tyr Met Gly Glu Leu Thr Gln Phe Thr Glu Ser
145                 150                 155                 160

Gln Leu Gln Ser His Phe Gly Glu Lys Asn Gly Ser Trp Leu Tyr Ala
                165                 170                 175

Met Cys Arg Gly Ile Glu His Asp Pro Val Lys Pro Arg Gln Leu Pro
            180                 185                 190

Lys Thr Ile Gly Cys Ser Lys Asn Phe Pro Gly Lys Thr Ala Leu Ala
        195                 200                 205

Thr Arg Glu Gln Val Gln Trp Trp Leu Leu Gln Leu Ala Gln Glu Leu
    210                 215                 220

Glu Glu Arg Leu Thr Lys Asp Arg Asn Asp Asn Asp Arg Val Ala Thr
225                 230                 235                 240

Gln Leu Val Val Ser Ile Arg Val Gln Gly Asp Lys Arg Leu Ser Ser
                245                 250                 255

Leu Arg Arg Cys Cys Ala Leu Thr Arg Tyr Asp Ala His Lys Met Ser
            260                 265                 270

His Asp Ala Phe Thr Val Ile Lys Asn Cys Asn Thr Ser Gly Ile Gln
        275                 280                 285

Thr Glu Trp Ser Pro Pro Leu Thr Met Leu Phe Leu Cys Ala Thr Lys
    290                 295                 300

Phe Ser Ala Ser Ala Pro Ser Ser Ser Thr Asp Ile Thr Ser Phe Leu
305                 310                 315                 320

Ser Ser Asp Pro Ser Ser Leu Pro Lys Val Pro Val Thr Ser Ser Glu
                325                 330                 335

Ala Lys Thr Gln Gly Ser Gly Pro Ala Val Thr Ala Thr Lys Lys Ala
            340                 345                 350
```

```
Thr Thr Ser Leu Glu Ser Phe Phe Gln Lys Ala Ala Glu Arg Gln Lys
        355                 360                 365

Val Lys Glu Ala Ser Leu Ser Ser Leu Thr Ala Pro Thr Gln Ala Pro
    370                 375                 380

Met Ser Asn Ser Pro Ser Lys Pro Ser Leu Pro Phe Gln Thr Ser Gln
385                 390                 395                 400

Ser Thr Gly Thr Glu Pro Phe Phe Lys Gln Lys Ser Leu Leu Leu Lys
                405                 410                 415

Gln Lys Gln Leu Asn Asn Ser Ser Val Ser Ser Pro Gln Gln Asn Pro
            420                 425                 430

Trp Ser Asn Cys Lys Ala Leu Pro Asn Ser Leu Pro Thr Glu Tyr Pro
        435                 440                 445

Gly Cys Val Pro Val Cys Glu Gly Val Ser Lys Leu Glu Glu Ser Ser
    450                 455                 460

Lys Ala Thr Pro Ala Glu Met Asp Leu Ala His Asn Ser Gln Ser Met
465                 470                 475                 480

His Ala Ser Ser Ala Ser Lys Ser Val Leu Glu Val Thr Gln Lys Ala
                485                 490                 495

Thr Pro Asn Pro Ser Leu Leu Ala Ala Glu Asp Gln Val Pro Cys Glu
            500                 505                 510

Lys Cys Gly Ser Leu Val Pro Val Trp Asp Met Pro Glu His Met Asp
        515                 520                 525

Tyr His Phe Ala Leu Glu Leu Gln Lys Ser Phe Leu Gln Pro His Ser
    530                 535                 540

Ser Asn Pro Gln Val Val Ser Ala Val Ser His Gln Gly Lys Arg Asn
545                 550                 555                 560

Pro Lys Ser Pro Leu Ala Cys Thr Asn Lys Arg Pro Arg Pro Glu Gly
                565                 570                 575

Met Gln Thr Leu Glu Ser Phe Phe Lys Pro Leu Thr His
            580                 585

<210>  149
<211>  414
<212>  PRT
<213>  Homo sapiens

<400>  149
```

```
Met Ala Thr Gly Gln Asp Arg Val Val Ala Leu Val Asp Met Asp Cys
1               5                  10                  15

Phe Phe Val Gln Val Glu Gln Arg Gln Asn Pro His Leu Arg Asn Lys
            20                  25                  30

Pro Cys Ala Val Val Gln Tyr Lys Ser Trp Lys Gly Gly Gly Ile Ile
        35                  40                  45

Ala Val Ser Tyr Glu Ala Arg Ala Phe Gly Val Thr Arg Ser Met Trp
    50                  55                  60

Ala Asp Asp Ala Lys Lys Leu Cys Pro Asp Leu Leu Leu Ala Gln Val
65                  70                  75                  80

Arg Glu Ser Arg Gly Lys Ala Asn Leu Thr Lys Tyr Arg Glu Ala Ser
                85                  90                  95

Val Glu Val Met Glu Ile Met Ser Arg Phe Ala Val Ile Glu Arg Ala
            100                 105                 110

Ser Ile Asp Glu Ala Tyr Val Asp Leu Thr Ser Ala Val Gln Glu Arg
        115                 120                 125

Leu Gln Lys Leu Gln Gly Gln Pro Ile Ser Ala Asp Leu Leu Pro Ser
    130                 135                 140

Thr Tyr Ile Glu Gly Leu Pro Gln Gly Pro Thr Thr Ala Glu Glu Thr
145                 150                 155                 160

Val Gln Lys Glu Gly Met Arg Lys Gln Gly Leu Phe Gln Trp Leu Asp
                165                 170                 175

Ser Leu Gln Ile Asp Asn Leu Thr Ser Pro Asp Leu Gln Leu Thr Val
            180                 185                 190

Gly Ala Val Ile Val Glu Glu Met Arg Ala Ala Ile Glu Arg Glu Thr
        195                 200                 205

Gly Phe Gln Cys Ser Ala Gly Ile Ser His Asn Lys Val Leu Ala Lys
    210                 215                 220

Leu Ala Cys Gly Leu Asn Lys Pro Asn Arg Gln Thr Leu Val Ser His
225                 230                 235                 240

Gly Ser Val Pro Gln Leu Phe Ser Gln Met Pro Ile Arg Lys Ile Arg
                245                 250                 255

Ser Leu Gly Gly Lys Leu Gly Ala Ser Val Ile Glu Ile Leu Gly Ile
            260                 265                 270
```

```
Glu Tyr Met Gly Glu Leu Thr Gln Phe Thr Glu Ser Gln Leu Gln Ser
        275                 280                 285

His Phe Gly Glu Lys Asn Gly Ser Trp Leu Tyr Ala Met Cys Arg Gly
    290                 295                 300

Ile Glu His Asp Pro Val Lys Pro Arg Gln Leu Pro Lys Thr Ile Gly
305                 310                 315                 320

Cys Ser Lys Asn Phe Pro Gly Lys Thr Ala Leu Ala Thr Arg Glu Gln
                325                 330                 335

Val Gln Trp Trp Leu Leu Gln Leu Ala Gln Glu Leu Glu Glu Arg Leu
            340                 345                 350

Thr Lys Asp Arg Asn Asp Asn Asp Arg Val Ala Thr Gln Leu Val Val
        355                 360                 365

Ser Ile Arg Val Gln Gly Asp Lys Arg Leu Ser Ser Leu Arg Arg Cys
    370                 375                 380

Cys Ala Leu Thr Arg Tyr Asp Ala His Lys Met Ser His Asp Ala Phe
385                 390                 395                 400

Thr Val Ile Lys Asn Cys Asn Thr Ser Gly Ile Gln Thr Glu
                405                 410


<210>  150
<211>  429
<212>  PRT
<213>  Homo sapiens

<400>  150

Met Arg Ser Leu Gly Ala Asn Met Ala Ala Ala Leu Arg Ala Ala Gly
1               5                   10                  15

Val Leu Leu Arg Asp Pro Leu Ala Ser Ser Ser Trp Arg Val Cys Gln
            20                  25                  30

Pro Trp Arg Trp Lys Ser Gly Ala Ala Ala Ala Ala Val Thr Thr Glu
        35                  40                  45

Thr Ala Gln His Ala Gln Gly Ala Lys Pro Gln Val Gln Pro Gln Lys
    50                  55                  60

Arg Tyr Glu Ser Asn Ile Arg Lys Pro Lys Thr Gly Ile Leu Met Leu
65                  70                  75                  80

Asn Met Gly Gly Pro Glu Thr Leu Gly Asp Val His Asp Phe Leu Leu
                85                  90                  95
```

```
Arg Leu Phe Leu Asp Arg Asp Leu Met Thr Leu Pro Ile Gln Asn Lys
            100                 105                 110

Leu Ala Pro Phe Ile Ala Lys Arg Arg Thr Pro Lys Ile Gln Glu Gln
        115                 120                 125

Tyr Arg Arg Ile Gly Gly Gly Ser Pro Ile Lys Ile Trp Thr Ser Lys
    130                 135                 140

Gln Gly Glu Gly Met Val Lys Leu Leu Asp Glu Leu Ser Pro Asn Thr
145                 150                 155                 160

Ala Pro His Lys Tyr Tyr Ile Gly Phe Arg Tyr Val His Pro Leu Thr
                165                 170                 175

Glu Glu Ala Ile Glu Glu Met Glu Arg Asp Gly Leu Glu Arg Ala Ile
            180                 185                 190

Ala Phe Thr Gln Tyr Pro Gln Tyr Ser Cys Ser Thr Thr Gly Ser Ser
        195                 200                 205

Leu Asn Ala Ile Tyr Arg Tyr Tyr Asn Gln Val Gly Arg Lys Pro Thr
    210                 215                 220

Met Lys Trp Ser Thr Ile Asp Arg Trp Pro Thr His His Leu Leu Ile
225                 230                 235                 240

Gln Cys Phe Ala Asp His Ile Leu Lys Glu Leu Asp His Phe Pro Leu
                245                 250                 255

Glu Lys Arg Ser Glu Val Val Ile Leu Phe Ser Ala His Ser Leu Pro
            260                 265                 270

Met Ser Val Val Asn Arg Gly Asp Pro Tyr Pro Gln Glu Val Ser Ala
        275                 280                 285

Thr Val Gln Lys Val Met Glu Arg Leu Glu Tyr Cys Asn Pro Tyr Arg
    290                 295                 300

Leu Val Trp Gln Ser Lys Val Gly Pro Met Pro Trp Leu Gly Pro Gln
305                 310                 315                 320

Thr Asp Glu Ser Ile Lys Gly Leu Cys Glu Arg Gly Arg Lys Asn Ile
                325                 330                 335

Leu Leu Val Pro Ile Ala Phe Thr Ser Asp His Ile Glu Thr Leu Tyr
            340                 345                 350

Glu Leu Asp Ile Glu Tyr Ser Gln Val Leu Ala Lys Glu Cys Gly Val
        355                 360                 365
```

```
Glu Asn Ile Arg Arg Ala Glu Ser Leu Asn Gly Asn Pro Leu Phe Ser
    370                 375                 380

Lys Ala Leu Ala Asp Leu Val His Ser His Ile Gln Ser Asn Glu Leu
385                 390                 395                 400

Cys Ser Lys Gln Leu Thr Leu Ser Cys Pro Leu Cys Val Asn Pro Val
                405                 410                 415

Cys Arg Glu Thr Lys Ser Phe Phe Thr Ser Gln Gln Leu
            420                 425


<210>  151
<211>  423
<212>  PRT
<213>  Homo sapiens

<400>  151

Met Arg Ser Leu Gly Ala Asn Met Ala Ala Ala Leu Arg Ala Ala Gly
1               5                   10                  15

Val Leu Leu Arg Asp Pro Leu Ala Ser Ser Ser Trp Arg Val Cys Gln
            20                  25                  30

Pro Trp Arg Trp Lys Ser Gly Ala Ala Ala Ala Ala Val Thr Thr Glu
        35                  40                  45

Thr Ala Gln His Ala Gln Gly Ala Lys Pro Gln Val Gln Pro Gln Lys
    50                  55                  60

Arg Lys Pro Lys Thr Gly Ile Leu Met Leu Asn Met Gly Gly Pro Glu
65                  70                  75                  80

Thr Leu Gly Asp Val His Asp Phe Leu Leu Arg Leu Phe Leu Asp Arg
                85                  90                  95

Asp Leu Met Thr Leu Pro Ile Gln Asn Lys Leu Ala Pro Phe Ile Ala
            100                 105                 110

Lys Arg Arg Thr Pro Lys Ile Gln Glu Gln Tyr Arg Arg Ile Gly Gly
        115                 120                 125

Gly Ser Pro Ile Lys Ile Trp Thr Ser Lys Gln Gly Glu Gly Met Val
    130                 135                 140

Lys Leu Leu Asp Glu Leu Ser Pro Asn Thr Ala Pro His Lys Tyr Tyr
145                 150                 155                 160

Ile Gly Phe Arg Tyr Val His Pro Leu Thr Glu Glu Ala Ile Glu Glu
                165                 170                 175

Met Glu Arg Asp Gly Leu Glu Arg Ala Ile Ala Phe Thr Gln Tyr Pro
```

180 185 190

Gln Tyr Ser Cys Ser Thr Thr Gly Ser Ser Leu Asn Ala Ile Tyr Arg
195 200 205

Tyr Tyr Asn Gln Val Gly Arg Lys Pro Thr Met Lys Trp Ser Thr Ile
210 215 220

Asp Arg Trp Pro Thr His His Leu Leu Ile Gln Cys Phe Ala Asp His
225 230 235 240

Ile Leu Lys Glu Leu Asp His Phe Pro Leu Glu Lys Arg Ser Glu Val
245 250 255

Val Ile Leu Phe Ser Ala His Ser Leu Pro Met Ser Val Val Asn Arg
260 265 270

Gly Asp Pro Tyr Pro Gln Glu Val Ser Ala Thr Val Gln Lys Val Met
275 280 285

Glu Arg Leu Glu Tyr Cys Asn Pro Tyr Arg Leu Val Trp Gln Ser Lys
290 295 300

Val Gly Pro Met Pro Trp Leu Gly Pro Gln Thr Asp Glu Ser Ile Lys
305 310 315 320

Gly Leu Cys Glu Arg Gly Arg Lys Asn Ile Leu Leu Val Pro Ile Ala
325 330 335

Phe Thr Ser Asp His Ile Glu Thr Leu Tyr Glu Leu Asp Ile Glu Tyr
340 345 350

Ser Gln Val Leu Ala Lys Glu Cys Gly Val Glu Asn Ile Arg Arg Ala
355 360 365

Glu Ser Leu Asn Gly Asn Pro Leu Phe Ser Lys Ala Leu Ala Asp Leu
370 375 380

Val His Ser His Ile Gln Ser Asn Glu Leu Cys Ser Lys Gln Leu Thr
385 390 395 400

Leu Ser Cys Pro Leu Cys Val Asn Pro Val Cys Arg Glu Thr Lys Ser
405 410 415

Phe Phe Thr Ser Gln Gln Leu
420

<210> 152
<211> 4061
<212> PRT
<213> Homo sapiens

<400> 152

```
Met Ser Thr Leu Leu Glu Asn Ile Phe Ala Ile Ile Asn Leu Phe Lys
1               5                  10                  15

Gln Tyr Ser Lys Lys Asp Lys Asn Thr Asp Thr Leu Ser Lys Lys Glu
            20                  25                  30

Leu Lys Glu Leu Leu Glu Lys Glu Phe Arg Gln Ile Leu Lys Asn Pro
        35                  40                  45

Asp Asp Pro Asp Met Val Asp Val Phe Met Asp His Leu Asp Ile Asp
    50                  55                  60

His Asn Lys Lys Ile Asp Phe Thr Glu Phe Leu Leu Met Val Phe Lys
65                  70                  75                  80

Leu Ala Gln Ala Tyr Tyr Glu Ser Thr Arg Lys Glu Asn Leu Pro Ile
                85                  90                  95

Ser Gly His Lys His Arg Lys His Ser His His Asp Lys His Glu Asp
            100                 105                 110

Asn Lys Gln Glu Glu Asn Lys Glu Asn Arg Lys Arg Pro Ser Ser Leu
        115                 120                 125

Glu Arg Arg Asn Asn Arg Lys Gly Asn Lys Gly Arg Ser Lys Ser Pro
    130                 135                 140

Arg Glu Thr Gly Gly Lys Arg His Glu Ser Ser Ser Glu Lys Lys Glu
145                 150                 155                 160

Arg Lys Gly Tyr Ser Pro Thr His Arg Glu Glu Glu Tyr Gly Lys Asn
                165                 170                 175

His His Asn Ser Ser Lys Lys Glu Lys Asn Lys Thr Glu Asn Thr Arg
            180                 185                 190

Leu Gly Asp Asn Arg Lys Arg Leu Ser Glu Arg Leu Glu Glu Lys Glu
        195                 200                 205

Asp Asn Glu Glu Gly Val Tyr Asp Tyr Glu Asn Thr Gly Arg Met Thr
    210                 215                 220

Gln Lys Trp Ile Gln Ser Gly His Ile Ala Thr Tyr Tyr Thr Ile Gln
225                 230                 235                 240

Asp Glu Ala Tyr Asp Thr Thr Asp Ser Leu Leu Glu Glu Asn Lys Ile
                245                 250                 255

Tyr Glu Arg Ser Arg Ser Ser Asp Gly Lys Ser Ser Ser Gln Val Asn
            260                 265                 270
```

```
Arg Ser Arg His Glu Asn Thr Ser Gln Val Pro Leu Gln Glu Ser Arg
        275                 280                 285

Thr Arg Lys Arg Arg Gly Ser Arg Val Ser Gln Asp Arg Asp Ser Glu
    290                 295                 300

Gly His Ser Glu Asp Ser Glu Arg His Ser Gly Ser Ala Ser Arg Asn
305                 310                 315                 320

His His Gly Ser Ala Trp Glu Gln Ser Arg Asp Gly Ser Arg His Pro
                325                 330                 335

Arg Ser His Asp Glu Asp Arg Ala Ser His Gly His Ser Ala Asp Ser
            340                 345                 350

Ser Arg Gln Ser Gly Thr Arg His Ala Glu Thr Ser Ser Arg Gly Gln
        355                 360                 365

Thr Ala Ser Ser His Glu Gln Ala Arg Ser Ser Pro Gly Glu Arg His
    370                 375                 380

Gly Ser Gly His Gln Gln Ser Ala Asp Ser Ser Arg His Ser Ala Thr
385                 390                 395                 400

Gly Arg Gly Gln Ala Ser Ser Ala Val Ser Asp Arg Gly His Arg Gly
                405                 410                 415

Ser Ser Gly Ser Gln Ala Ser Asp Ser Glu Gly His Ser Glu Asn Ser
            420                 425                 430

Asp Thr Gln Ser Val Ser Gly His Gly Lys Ala Gly Leu Arg Gln Gln
        435                 440                 445

Ser His Gln Glu Ser Thr Arg Gly Arg Ser Gly Glu Arg Ser Gly Arg
    450                 455                 460

Ser Gly Ser Ser Leu Tyr Gln Val Ser Thr His Glu Gln Pro Asp Ser
465                 470                 475                 480

Ala His Gly Arg Thr Gly Thr Ser Thr Gly Gly Arg Gln Gly Ser His
                485                 490                 495

His Glu Gln Ala Arg Asp Ser Ser Arg His Ser Ala Ser Gln Glu Gly
            500                 505                 510

Gln Asp Thr Ile Arg Gly His Pro Gly Ser Ser Arg Gly Gly Arg Gln
        515                 520                 525

Gly Ser His His Glu Gln Ser Val Asn Arg Ser Gly His Ser Gly Ser
    530                 535                 540
```

```
His His Ser His Thr Thr Ser Gln Gly Arg Ser Asp Ala Ser His Gly
545                 550                 555                 560

Gln Ser Gly Ser Arg Ser Ala Ser Arg Gln Thr Arg Asn Glu Glu Gln
                565                 570                 575

Ser Gly Asp Gly Thr Arg His Ser Gly Ser Arg His His Glu Ala Ser
            580                 585                 590

Ser Gln Ala Asp Ser Ser Arg His Ser Gln Val Gly Gln Gly Gln Ser
        595                 600                 605

Ser Gly Pro Arg Thr Ser Arg Asn Gln Gly Ser Ser Val Ser Gln Asp
    610                 615                 620

Ser Asp Ser Gln Gly His Ser Glu Asp Ser Glu Arg Trp Ser Gly Ser
625                 630                 635                 640

Ala Ser Arg Asn His His Gly Ser Ala Gln Glu Gln Ser Arg Asp Gly
                645                 650                 655

Ser Arg His Pro Arg Ser His His Glu Asp Arg Ala Gly His Gly His
            660                 665                 670

Ser Ala Asp Ser Ser Arg Lys Ser Gly Thr Arg His Thr Gln Asn Ser
        675                 680                 685

Ser Ser Gly Gln Ala Ala Ser Ser His Glu Gln Ala Arg Ser Ser Ala
    690                 695                 700

Gly Glu Arg His Gly Ser Arg His Gln Leu Gln Ser Ala Asp Ser Ser
705                 710                 715                 720

Arg His Ser Gly Thr Gly His Gly Gln Ala Ser Ser Ala Val Arg Asp
                725                 730                 735

Ser Gly His Arg Gly Ser Ser Gly Ser Gln Ala Thr Asp Ser Glu Gly
            740                 745                 750

His Ser Glu Asp Ser Asp Thr Gln Ser Val Ser Gly His Gly Gln Ala
        755                 760                 765

Gly His His Gln Gln Ser His Gln Glu Ser Ala Arg Asp Arg Ser Gly
    770                 775                 780

Glu Arg Ser Arg Arg Ser Gly Ser Phe Leu Tyr Gln Val Ser Thr His
785                 790                 795                 800

Lys Gln Ser Glu Ser Ser His Gly Trp Thr Gly Pro Ser Thr Gly Val
                805                 810                 815
```

```
Arg Gln Gly Ser His His Glu Gln Ala Arg Asp Asn Ser Arg His Ser
            820                 825                 830

Ala Ser Gln Asp Gly Gln Asp Thr Ile Arg Gly His Pro Gly Ser Ser
        835                 840                 845

Arg Arg Gly Arg Gln Gly Ser His His Glu Gln Ser Val Asp Arg Ser
    850                 855                 860

Gly His Ser Gly Ser His His Ser His Thr Thr Ser Gln Gly Arg Ser
865                 870                 875                 880

Asp Ala Ser Arg Gly Gln Ser Gly Ser Arg Ser Ala Ser Arg Thr Thr
                885                 890                 895

Arg Asn Glu Glu Gln Ser Arg Asp Gly Ser Arg His Ser Gly Ser Arg
            900                 905                 910

His His Glu Ala Ser Ser His Ala Asp Ile Ser Arg His Ser Gln Ala
        915                 920                 925

Gly Gln Gly Gln Ser Glu Gly Ser Arg Thr Ser Arg Arg Gln Gly Ser
    930                 935                 940

Ser Val Ser Gln Asp Ser Asp Ser Glu Gly His Ser Glu Asp Ser Glu
945                 950                 955                 960

Arg Trp Ser Gly Ser Ala Ser Arg Asn His Arg Gly Ser Ala Gln Glu
                965                 970                 975

Gln Ser Arg His Gly Ser Arg His Pro Arg Ser His His Glu Asp Arg
            980                 985                 990

Ala Gly His Gly His Ser Ala Asp  Ser Ser Arg Gln Ser  Gly Thr Pro
        995                 1000                1005

His Ala  Glu Thr Ser Ser Gly  Gly Gln Ala Ala Ser  Ser His Glu
    1010                1015                1020

Gln Ala  Arg Ser Ser Pro Gly  Glu Arg His Gly Ser  Arg His Gln
    1025                1030                1035

Gln Ser  Ala Asp Ser Ser Arg  His Ser Gly Ile Pro  Arg Arg Gln
    1040                1045                1050

Ala Ser  Ser Ala Val Arg Asp  Ser Gly His Trp Gly  Ser Ser Gly
    1055                1060                1065

Ser Gln  Ala Ser Asp Ser Glu  Gly His Ser Glu Glu  Ser Asp Thr
    1070                1075                1080
```

```
Gln Ser  Val Ser Gly His Gly  Gln Asp Gly Pro His  Gln Gln Ser
    1085                1090                1095

His Gln  Glu Ser Ala Arg Asp  Trp Ser Gly Gly Arg  Ser Gly Arg
    1100                1105                1110

Ser Gly  Ser Phe Ile Tyr Gln  Val Ser Thr His Glu  Gln Ser Glu
    1115                1120                1125

Ser Ala  His Gly Arg Thr Arg  Thr Ser Thr Gly Arg  Arg Gln Gly
    1130                1135                1140

Ser His  His Glu Gln Ala Arg  Asp Ser Ser Arg His  Ser Ala Ser
    1145                1150                1155

Gln Glu  Gly Gln Asp Thr Ile  Arg Ala His Pro Gly  Ser Arg Arg
    1160                1165                1170

Gly Gly  Arg Gln Gly Ser His  His Glu Gln Ser Val  Asp Arg Ser
    1175                1180                1185

Gly His  Ser Gly Ser His His  Ser His Thr Thr Ser  Gln Gly Arg
    1190                1195                1200

Ser Asp  Ala Ser His Gly Gln  Ser Gly Ser Arg Ser  Ala Ser Arg
    1205                1210                1215

Gln Thr  Arg Lys Asp Lys Gln  Ser Gly Asp Gly Ser  Arg His Ser
    1220                1225                1230

Gly Ser  Arg His His Glu Ala  Ala Ser Trp Ala Asp  Ser Ser Arg
    1235                1240                1245

His Ser  Gln Val Gly Gln Glu  Gln Ser Ser Gly Ser  Arg Thr Ser
    1250                1255                1260

Arg His  Gln Gly Ser Ser Val  Ser Gln Asp Ser Asp  Ser Glu Arg
    1265                1270                1275

His Ser  Asp Asp Ser Glu Arg  Leu Ser Gly Ser Ala  Ser Arg Asn
    1280                1285                1290

His His  Gly Ser Ser Arg Glu  Gln Ser Arg Asp Gly  Ser Arg His
    1295                1300                1305

Pro Gly  Phe His Gln Glu Asp  Arg Ala Ser His Gly  His Ser Ala
    1310                1315                1320

Asp Ser  Ser Arg Gln Ser Gly  Thr His His Thr Glu  Ser Ser Ser
    1325                1330                1335
```

```
His Gly  Gln Ala Val Ser Ser  His Glu Gln Ala Arg  Ser Ser Pro
    1340                1345                1350

Gly Glu  Arg His Gly Ser Arg  His Gln Gln Ser Ala  Asp Ser Ser
    1355                1360                1365

Arg His  Ser Gly Ile Gly His  Arg Gln Ala Ser Ser  Ala Val Arg
    1370                1375                1380

Asp Ser  Gly His Arg Gly Ser  Ser Gly Ser Gln Val  Thr Asn Ser
    1385                1390                1395

Glu Gly  His Ser Glu Asp Ser  Asp Thr Gln Ser Val  Ser Ala His
    1400                1405                1410

Gly Gln  Ala Gly Pro His Gln  Gln Ser His Lys Glu  Ser Ala Arg
    1415                1420                1425

Gly Gln  Ser Gly Glu Ser Ser  Gly Arg Ser Arg Ser  Phe Leu Tyr
    1430                1435                1440

Gln Val  Ser Ser His Glu Gln  Ser Glu Ser Thr His  Gly Gln Thr
    1445                1450                1455

Ala Pro  Ser Thr Gly Gly Arg  Gln Gly Ser Arg His  Glu Gln Ala
    1460                1465                1470

Arg Asn  Ser Ser Arg His Ser  Ala Ser Gln Asp Gly  Gln Asp Thr
    1475                1480                1485

Ile Arg  Gly His Pro Gly Ser  Ser Arg Gly Gly Arg  Gln Gly Ser
    1490                1495                1500

Tyr His  Glu Gln Ser Val Asp  Arg Ser Gly His Ser  Gly Tyr His
    1505                1510                1515

His Ser  His Thr Thr Pro Gln  Gly Arg Ser Asp Ala  Ser His Gly
    1520                1525                1530

Gln Ser  Gly Pro Arg Ser Ala  Ser Arg Gln Thr Arg  Asn Glu Glu
    1535                1540                1545

Gln Ser  Gly Asp Gly Ser Arg  His Ser Gly Ser Arg  His His Glu
    1550                1555                1560

Pro Ser  Thr Arg Ala Gly Ser  Ser Arg His Ser Gln  Val Gly Gln
    1565                1570                1575

Gly Glu  Ser Ala Gly Ser Lys  Thr Ser Arg Arg Gln  Gly Ser Ser
    1580                1585                1590
```

```
Val Ser  Gln Asp Arg Asp Ser  Glu Gly His Ser Glu  Asp Ser Glu
    1595                 1600                 1605

Arg Arg  Ser Glu Ser Ala Ser  Arg Asn His Tyr Gly  Ser Ala Arg
    1610                 1615                 1620

Glu Gln  Ser Arg His Gly Ser  Arg Asn Pro Arg Ser  His Gln Glu
    1625                 1630                 1635

Asp Arg  Ala Ser His Gly His  Ser Ala Glu Ser Ser  Arg Gln Ser
    1640                 1645                 1650

Gly Thr  Arg His Ala Glu Thr  Ser Ser Gly Gly Gln  Ala Ala Ser
    1655                 1660                 1665

Ser Gln  Glu Gln Ala Arg Ser  Ser Pro Gly Glu Arg  His Gly Ser
    1670                 1675                 1680

Arg His  Gln Gln Ser Ala Asp  Ser Ser Thr Asp Ser  Gly Thr Gly
    1685                 1690                 1695

Arg Arg  Gln Asp Ser Ser Val  Val Gly Asp Ser Gly  Asn Arg Gly
    1700                 1705                 1710

Ser Ser  Gly Ser Gln Ala Ser  Asp Ser Glu Gly His  Ser Glu Glu
    1715                 1720                 1725

Ser Asp  Thr Gln Ser Val Ser  Ala His Gly Gln Ala  Gly Pro His
    1730                 1735                 1740

Gln Gln  Ser His Gln Glu Ser  Thr Arg Gly Gln Ser  Gly Glu Arg
    1745                 1750                 1755

Ser Gly  Arg Ser Gly Ser Phe  Leu Tyr Gln Val Ser  Thr His Glu
    1760                 1765                 1770

Gln Ser  Glu Ser Ala His Gly  Arg Thr Gly Pro Ser  Thr Gly Gly
    1775                 1780                 1785

Arg Gln  Arg Ser Arg His Glu  Gln Ala Arg Asp Ser  Ser Arg His
    1790                 1795                 1800

Ser Ala  Ser Gln Glu Gly Gln  Asp Thr Ile Arg Gly  His Pro Gly
    1805                 1810                 1815

Ser Ser  Arg Gly Gly Arg Gln  Gly Ser His Tyr Glu  Gln Ser Val
    1820                 1825                 1830

Asp Ser  Ser Gly His Ser Gly  Ser His His Ser His  Thr Thr Ser
    1835                 1840                 1845
```

```
Gln Glu  Arg Ser Asp Val Ser  Arg Gly Gln Ser Gly  Ser Arg Ser
    1850                 1855                 1860

Val Ser  Arg Gln Thr Arg Asn  Glu Lys Gln Ser Gly  Asp Gly Ser
    1865                 1870                 1875

Arg His  Ser Gly Ser Arg His  His Glu Ala Ser Ser  Arg Ala Asp
    1880                 1885                 1890

Ser Ser  Arg His Ser Gln Val  Gly Gln Gly Gln Ser  Ser Gly Pro
    1895                 1900                 1905

Arg Thr  Ser Arg Asn Gln Gly  Ser Ser Val Ser Gln  Asp Ser Asp
    1910                 1915                 1920

Ser Gln  Gly His Ser Glu Asp  Ser Glu Arg Trp Ser  Gly Ser Ala
    1925                 1930                 1935

Ser Arg  Asn His Leu Gly Ser  Ala Trp Glu Gln Ser  Arg Asp Gly
    1940                 1945                 1950

Ser Arg  His Pro Gly Ser His  His Glu Asp Arg Ala  Gly His Gly
    1955                 1960                 1965

His Ser  Ala Asp Ser Ser Arg  Gln Ser Gly Thr Arg  His Thr Glu
    1970                 1975                 1980

Ser Ser  Ser Arg Gly Gln Ala  Ala Ser Ser His Glu  Gln Ala Arg
    1985                 1990                 1995

Ser Ser  Ala Gly Glu Arg His  Gly Ser His His Gln  Leu Gln Ser
    2000                 2005                 2010

Ala Asp  Ser Ser Arg His Ser  Gly Ile Gly His Gly  Gln Ala Ser
    2015                 2020                 2025

Ser Ala  Val Arg Asp Ser Gly  His Arg Gly Tyr Ser  Gly Ser Gln
    2030                 2035                 2040

Ala Ser  Asp Ser Glu Gly His  Ser Glu Asp Ser Asp  Thr Gln Ser
    2045                 2050                 2055

Val Ser  Ala Gln Gly Lys Ala  Gly Pro His Gln Gln  Ser His Lys
    2060                 2065                 2070

Glu Ser  Ala Arg Gly Gln Ser  Gly Glu Ser Ser Gly  Arg Ser Gly
    2075                 2080                 2085

Ser Phe  Leu Tyr Gln Val Ser  Thr His Glu Gln Ser  Glu Ser Thr
    2090                 2095                 2100
```

```
His Gly  Gln Ser Ala Pro Ser  Thr Gly Gly Arg Gln  Gly Ser His
    2105                 2110                 2115

Tyr Asp  Gln Ala Gln Asp Ser  Ser Arg His Ser Ala  Ser Gln Glu
    2120                 2125                 2130

Gly Gln  Asp Thr Ile Arg Gly  His Pro Gly Pro Ser  Arg Gly Gly
    2135                 2140                 2145

Arg Gln  Gly Ser His Gln Glu  Gln Ser Val Asp Arg  Ser Gly His
    2150                 2155                 2160

Ser Gly  Ser His His Ser His  Thr Thr Ser Gln Gly  Arg Ser Asp
    2165                 2170                 2175

Ala Ser  Arg Gly Gln Ser Gly  Ser Arg Ser Ala Ser  Arg Lys Thr
    2180                 2185                 2190

Tyr Asp  Lys Glu Gln Ser Gly  Asp Gly Ser Arg His  Ser Gly Ser
    2195                 2200                 2205

His His  His Glu Ala Ser Ser  Trp Ala Asp Ser Ser  Arg His Ser
    2210                 2215                 2220

Leu Val  Gly Gln Gly Gln Ser  Ser Gly Pro Arg Thr  Ser Arg Pro
    2225                 2230                 2235

Arg Gly  Ser Ser Val Ser Gln  Asp Ser Asp Ser Glu  Gly His Ser
    2240                 2245                 2250

Glu Asp  Ser Glu Arg Arg Ser  Gly Ser Ala Ser Arg  Asn His His
    2255                 2260                 2265

Gly Ser  Ala Gln Glu Gln Ser  Arg Asp Gly Ser Arg  His Pro Arg
    2270                 2275                 2280

Ser His  His Glu Asp Arg Ala  Gly His Gly His Ser  Ala Glu Ser
    2285                 2290                 2295

Ser Arg  Gln Ser Gly Thr His  His Ala Glu Asn Ser  Ser Gly Gly
    2300                 2305                 2310

Gln Ala  Ala Ser Ser His Glu  Gln Ala Arg Ser Ser  Ala Gly Glu
    2315                 2320                 2325

Arg His  Gly Ser His His Gln  Gln Ser Ala Asp Ser  Ser Arg His
    2330                 2335                 2340

Ser Gly  Ile Gly His Gly Gln  Ala Ser Ser Ala Val  Arg Asp Ser
    2345                 2350                 2355
```

```
Gly His  Arg Gly Ser Ser Gly  Ser Gln Ala Ser Asp  Ser Glu Gly
    2360                 2365                 2370

His Ser  Glu Asp Ser Asp Thr  Gln Ser Val Ser Ala  His Gly Gln
    2375                 2380                 2385

Ala Gly  Pro His Gln Gln Ser  His Gln Glu Ser Thr  Arg Gly Arg
    2390                 2395                 2400

Ser Ala  Gly Arg Ser Gly Arg  Ser Gly Ser Phe Leu  Tyr Gln Val
    2405                 2410                 2415

Ser Thr  His Glu Gln Ser Glu  Ser Ala His Gly Arg  Thr Gly Thr
    2420                 2425                 2430

Ser Thr  Gly Gly Arg Gln Gly  Ser His His Lys Gln  Ala Arg Asp
    2435                 2440                 2445

Ser Ser  Arg His Ser Thr Ser  Gln Glu Gly Gln Asp  Thr Ile His
    2450                 2455                 2460

Gly His  Pro Gly Ser Ser Ser  Gly Gly Arg Gln Gly  Ser His Tyr
    2465                 2470                 2475

Glu Gln  Leu Val Asp Arg Ser  Gly His Ser Gly Ser  His His Ser
    2480                 2485                 2490

His Thr  Thr Ser Gln Gly Arg  Ser Asp Ala Ser His  Gly His Ser
    2495                 2500                 2505

Gly Ser  Arg Ser Ala Ser Arg  Gln Thr Arg Asn Asp  Glu Gln Ser
    2510                 2515                 2520

Gly Asp  Gly Ser Arg His Ser  Gly Ser Arg His His  Glu Ala Ser
    2525                 2530                 2535

Ser Arg  Ala Asp Ser Ser Gly  His Ser Gln Val Gly  Gln Gly Gln
    2540                 2545                 2550

Ser Glu  Gly Pro Arg Thr Ser  Arg Asn Trp Gly Ser  Ser Phe Ser
    2555                 2560                 2565

Gln Asp  Ser Asp Ser Gln Gly  His Ser Glu Asp Ser  Glu Arg Trp
    2570                 2575                 2580

Ser Gly  Ser Ala Ser Arg Asn  His His Gly Ser Ala  Gln Glu Gln
    2585                 2590                 2595

Leu Arg  Asp Gly Ser Arg His  Pro Arg Ser His Gln  Glu Asp Arg
    2600                 2605                 2610
```

```
Ala Gly  His Gly His Ser Ala  Asp Ser Ser Arg Gln  Ser Gly Thr
    2615                 2620                 2625

Arg His  Thr Gln Thr Ser Ser  Gly Gly Gln Ala Ala  Ser Ser His
    2630                 2635                 2640

Glu Gln  Ala Arg Ser Ser Ala  Gly Glu Arg His Gly  Ser His His
    2645                 2650                 2655

Gln Gln  Ser Ala Asp Ser Ser  Arg His Ser Gly Ile  Gly His Gly
    2660                 2665                 2670

Gln Ala  Ser Ser Ala Val Arg  Asp Ser Gly His Arg  Gly Tyr Ser
    2675                 2680                 2685

Gly Ser  Gln Ala Ser Asp Asn  Glu Gly His Ser Glu  Asp Ser Asp
    2690                 2695                 2700

Thr Gln  Ser Val Ser Ala His  Gly Gln Ala Gly Ser  His Gln Gln
    2705                 2710                 2715

Ser His  Gln Glu Ser Ala Arg  Gly Arg Ser Gly Glu  Thr Ser Gly
    2720                 2725                 2730

His Ser  Gly Ser Phe Leu Tyr  Gln Val Ser Thr His  Glu Gln Ser
    2735                 2740                 2745

Glu Ser  Ser His Gly Trp Thr  Gly Pro Ser Thr Arg  Gly Arg Gln
    2750                 2755                 2760

Gly Ser  Arg His Glu Gln Ala  Gln Asp Ser Ser Arg  His Ser Ala
    2765                 2770                 2775

Ser Gln  Asp Gly Gln Asp Thr  Ile Arg Gly His Pro  Gly Ser Ser
    2780                 2785                 2790

Arg Gly  Gly Arg Gln Gly Tyr  His His Glu His Ser  Val Asp Ser
    2795                 2800                 2805

Ser Gly  His Ser Gly Ser His  His Ser His Thr Thr  Ser Gln Gly
    2810                 2815                 2820

Arg Ser  Asp Ala Ser Arg Gly  Gln Ser Gly Ser Arg  Ser Ala Ser
    2825                 2830                 2835

Arg Thr  Thr Arg Asn Glu Glu  Gln Ser Gly Asp Gly  Ser Arg His
    2840                 2845                 2850

Ser Gly  Ser Arg His His Glu  Ala Ser Thr His Ala  Asp Ile Ser
    2855                 2860                 2865
```

```
Arg His  Ser Gln Ala Val Gln  Gly Gln Ser Glu Gly  Ser Arg Arg
    2870                 2875                 2880

Ser Arg  Arg Gln Gly Ser Ser  Val Ser Gln Asp Ser  Asp Ser Glu
    2885                 2890                 2895

Gly His  Ser Glu Asp Ser Glu  Arg Trp Ser Gly Ser  Ala Ser Arg
    2900                 2905                 2910

Asn His  His Gly Ser Ala Gln  Glu Gln Leu Arg Asp  Gly Ser Arg
    2915                 2920                 2925

His Pro  Arg Ser His Gln Glu  Asp Arg Ala Gly His  Gly His Ser
    2930                 2935                 2940

Ala Asp  Ser Ser Arg Gln Ser  Gly Thr Arg His Thr  Gln Thr Ser
    2945                 2950                 2955

Ser Gly  Gly Gln Ala Ala Ser  Ser His Glu Gln Ala  Arg Ser Ser
    2960                 2965                 2970

Ala Gly  Glu Arg His Gly Ser  His His Gln Gln Ser  Ala Asp Ser
    2975                 2980                 2985

Ser Arg  His Ser Gly Ile Gly  His Gly Gln Ala Ser  Ser Ala Val
    2990                 2995                 3000

Arg Asp  Ser Gly His Arg Gly  Tyr Ser Gly Ser Gln  Ala Ser Asp
    3005                 3010                 3015

Asn Glu  Gly His Ser Glu Asp  Ser Asp Thr Gln Ser  Val Ser Ala
    3020                 3025                 3030

His Gly  Gln Ala Gly Ser His  Gln Gln Ser His Gln  Glu Ser Ala
    3035                 3040                 3045

Arg Gly  Arg Ser Gly Glu Thr  Ser Gly His Ser Gly  Ser Phe Leu
    3050                 3055                 3060

Tyr Gln  Val Ser Thr His Glu  Gln Ser Glu Ser Ser  His Gly Trp
    3065                 3070                 3075

Thr Gly  Pro Ser Thr Arg Gly  Arg Gln Gly Ser Arg  His Glu Gln
    3080                 3085                 3090

Ala Gln  Asp Ser Ser Arg His  Ser Ala Ser Gln Tyr  Gly Gln Asp
    3095                 3100                 3105

Thr Ile  Arg Gly His Pro Gly  Ser Ser Arg Gly Gly  Arg Gln Gly
    3110                 3115                 3120
```

```
Tyr His  His Glu His Ser Val  Asp Ser Ser Gly His  Ser Gly Ser
    3125                3130                3135

His His  Ser His Thr Thr Ser  Gln Gly Arg Ser Asp  Ala Ser Arg
    3140                3145                3150

Gly Gln  Ser Gly Ser Arg Ser  Ala Ser Arg Thr Thr  Arg Asn Glu
    3155                3160                3165

Glu Gln  Ser Gly Asp Ser Ser  Arg His Ser Val Ser  Arg His His
    3170                3175                3180

Glu Ala  Ser Thr His Ala Asp  Ile Ser Arg His Ser  Gln Ala Val
    3185                3190                3195

Gln Gly  Gln Ser Glu Gly Ser  Arg Arg Ser Arg Arg  Gln Gly Ser
    3200                3205                3210

Ser Val  Ser Gln Asp Ser Asp  Ser Glu Gly His Ser  Glu Asp Ser
    3215                3220                3225

Glu Arg  Trp Ser Gly Ser Ala  Ser Arg Asn His Arg  Gly Ser Val
    3230                3235                3240

Gln Glu  Gln Ser Arg His Gly  Ser Arg His Pro Arg  Ser His His
    3245                3250                3255

Glu Asp  Arg Ala Gly His Gly  His Ser Ala Asp Arg  Ser Arg Gln
    3260                3265                3270

Ser Gly  Thr Arg His Ala Glu  Thr Ser Ser Gly Gly  Gln Ala Ala
    3275                3280                3285

Ser Ser  His Glu Gln Ala Arg  Ser Ser Pro Gly Glu  Arg His Gly
    3290                3295                3300

Ser Arg  His Gln Gln Ser Ala  Asp Ser Ser Arg His  Ser Gly Ile
    3305                3310                3315

Pro Arg  Gly Gln Ala Ser Ser  Ala Val Arg Asp Ser  Arg His Trp
    3320                3325                3330

Gly Ser  Ser Gly Ser Gln Ala  Ser Asp Ser Glu Gly  His Ser Glu
    3335                3340                3345

Glu Ser  Asp Thr Gln Ser Val  Ser Gly His Gly Gln  Ala Gly Pro
    3350                3355                3360

His Gln  Gln Ser His Gln Glu  Ser Ala Arg Asp Arg  Ser Gly Gly
    3365                3370                3375
```

```
Arg Ser  Gly Arg Ser Gly Ser  Phe Leu Tyr Gln Val  Ser Thr His
    3380                 3385                 3390

Glu Gln  Ser Glu Ser Ala His  Gly Arg Thr Arg Thr  Ser Thr Gly
    3395                 3400                 3405

Arg Arg  Gln Gly Ser His His  Glu Gln Ala Arg Asp  Ser Ser Arg
    3410                 3415                 3420

His Ser  Ala Ser Gln Glu Gly  Gln Asp Thr Ile Arg  Gly His Pro
    3425                 3430                 3435

Gly Ser  Ser Arg Arg Gly Arg  Gln Gly Ser His Tyr  Glu Gln Ser
    3440                 3445                 3450

Val Asp  Arg Ser Gly His Ser  Gly Ser His His Ser  His Thr Thr
    3455                 3460                 3465

Ser Gln  Gly Arg Ser Asp Ala  Ser Arg Gly Gln Ser  Gly Ser Arg
    3470                 3475                 3480

Ser Ala  Ser Arg Gln Thr Arg  Asn Asp Glu Gln Ser  Gly Asp Gly
    3485                 3490                 3495

Ser Arg  His Ser Trp Ser His  His His Glu Ala Ser  Thr Gln Ala
    3500                 3505                 3510

Asp Ser  Ser Arg His Ser Gln  Ser Gly Gln Gly Gln  Ser Ala Gly
    3515                 3520                 3525

Pro Arg  Thr Ser Arg Asn Gln  Gly Ser Ser Val Ser  Gln Asp Ser
    3530                 3535                 3540

Asp Ser  Gln Gly His Ser Glu  Asp Ser Glu Arg Trp  Ser Gly Ser
    3545                 3550                 3555

Ala Ser  Arg Asn His Arg Gly  Ser Ala Gln Glu Gln  Ser Arg Asp
    3560                 3565                 3570

Gly Ser  Arg His Pro Thr Ser  His His Glu Asp Arg  Ala Gly His
    3575                 3580                 3585

Gly His  Ser Ala Glu Ser Ser  Arg Gln Ser Gly Thr  His His Ala
    3590                 3595                 3600

Glu Asn  Ser Ser Gly Gly Gln  Ala Ala Ser Ser His  Glu Gln Ala
    3605                 3610                 3615

Arg Ser  Ser Ala Gly Glu Arg  His Gly Ser His His  Gln Gln Ser
    3620                 3625                 3630
```

```
Ala Asp  Ser Ser Arg His Ser  Gly Ile Gly His Gly  Gln Ala Ser
    3635                 3640                 3645

Ser Ala  Val Arg Asp Ser Gly  His Arg Gly Ser Ser  Gly Ser Gln
    3650                 3655                 3660

Ala Ser  Asp Ser Glu Gly His  Ser Glu Asp Ser Asp  Thr Gln Ser
    3665                 3670                 3675

Val Ser  Ala His Gly Gln Ala  Gly Pro His Gln Gln  Ser His Gln
    3680                 3685                 3690

Glu Ser  Thr Arg Gly Arg Ser  Ala Gly Arg Ser Gly  Arg Ser Gly
    3695                 3700                 3705

Ser Phe  Leu Tyr Gln Val Ser  Thr His Glu Gln Ser  Glu Ser Ala
    3710                 3715                 3720

His Gly  Arg Ala Gly Pro Ser  Thr Gly Gly Arg Gln  Gly Ser Arg
    3725                 3730                 3735

His Glu  Gln Ala Arg Asp Ser  Ser Arg His Ser Ala  Ser Gln Glu
    3740                 3745                 3750

Gly Gln  Asp Thr Ile Arg Gly  His Pro Gly Ser Arg  Arg Gly Gly
    3755                 3760                 3765

Arg Gln  Gly Ser Tyr His Glu  Gln Ser Val Asp Arg  Ser Gly His
    3770                 3775                 3780

Ser Gly  Ser His His Ser His  Thr Thr Ser Gln Gly  Arg Ser Asp
    3785                 3790                 3795

Ala Ser  His Gly Gln Ser Gly  Ser Arg Ser Ala Ser  Arg Glu Thr
    3800                 3805                 3810

Arg Asn  Glu Glu Gln Ser Gly  Asp Gly Ser Arg His  Ser Gly Ser
    3815                 3820                 3825

Arg His  His Glu Ala Ser Thr  Gln Ala Asp Ser Ser  Arg His Ser
    3830                 3835                 3840

Gln Ser  Gly Gln Gly Glu Ser  Ala Gly Ser Arg Arg  Ser Arg Arg
    3845                 3850                 3855

Gln Gly  Ser Ser Val Ser Gln  Asp Ser Asp Ser Glu  Ala Tyr Pro
    3860                 3865                 3870

Glu Asp  Ser Glu Arg Arg Ser  Glu Ser Ala Ser Arg  Asn His His
    3875                 3880                 3885
```

```
Gly Ser  Ser Arg Glu Gln Ser  Arg Asp Gly Ser Arg  His Pro Gly
    3890                 3895                 3900

Ser Ser  His Arg Asp Thr Ala  Ser His Val Gln Ser  Ser Pro Val
    3905                 3910                 3915

Gln Ser  Asp Ser Ser Thr Ala  Lys Glu His Gly His  Phe Ser Ser
    3920                 3925                 3930

Leu Ser  Gln Asp Ser Ala Tyr  His Ser Gly Ile Gln  Ser Arg Gly
    3935                 3940                 3945

Ser Pro  His Ser Ser Ser Ser  Tyr His Tyr Gln Ser  Glu Gly Thr
    3950                 3955                 3960

Glu Arg  Gln Lys Gly Gln Ser  Gly Leu Val Trp Arg  His Gly Ser
    3965                 3970                 3975

Tyr Gly  Ser Ala Asp Tyr Asp  Tyr Gly Glu Ser Gly  Phe Arg His
    3980                 3985                 3990

Ser Gln  His Gly Ser Val Ser  Tyr Asn Ser Asn Pro  Val Val Phe
    3995                 4000                 4005

Lys Glu  Arg Ser Asp Ile Cys  Lys Ala Ser Ala Phe  Gly Lys Asp
    4010                 4015                 4020

His Pro  Arg Tyr Tyr Ala Thr  Tyr Ile Asn Lys Asp  Pro Gly Leu
    4025                 4030                 4035

Cys Gly  His Ser Ser Asp Ile  Ser Lys Gln Leu Gly  Phe Ser Gln
    4040                 4045                 4050

Ser Gln  Arg Tyr Tyr Tyr Tyr  Glu
    4055                 4060


<210>  153
<211>  578
<212>  PRT
<213>  Homo sapiens

<400>  153

Met Arg Gln Gln Asp Ala Pro Lys Pro Thr Pro Ala Ala Cys Arg Cys
1               5                  10                  15

Ser Gly Leu Ala Arg Arg Val Leu Thr Ile Ala Phe Ala Leu Leu Ile
            20                  25                  30

Leu Gly Leu Met Thr Trp Ala Tyr Ala Ala Gly Val Pro Leu Ala Ser
        35                  40                  45
```

```
Asp Arg Tyr Gly Leu Leu Ala Phe Gly Leu Tyr Gly Ala Phe Leu Ser
    50                  55                  60

Ala His Leu Val Ala Gln Ser Leu Phe Ala Tyr Leu Glu His Arg Arg
65                  70                  75                  80

Val Ala Ala Ala Ala Arg Gly Pro Leu Asp Ala Ala Thr Ala Arg Ser
                85                  90                  95

Val Ala Leu Thr Ile Ser Ala Tyr Gln Glu Asp Pro Ala Tyr Leu Arg
            100                 105                 110

Gln Cys Leu Ala Ser Ala Arg Ala Leu Leu Tyr Pro Arg Ala Arg Leu
        115                 120                 125

Arg Val Leu Met Val Val Asp Gly Asn Arg Ala Glu Asp Leu Tyr Met
    130                 135                 140

Val Asp Met Phe Arg Glu Val Phe Ala Asp Glu Asp Pro Ala Thr Tyr
145                 150                 155                 160

Val Trp Asp Gly Asn Tyr His Gln Pro Trp Glu Pro Ala Ala Ala Gly
                165                 170                 175

Ala Val Gly Ala Gly Ala Tyr Arg Glu Val Glu Ala Glu Asp Pro Gly
            180                 185                 190

Arg Leu Ala Val Glu Ala Leu Val Arg Thr Arg Arg Cys Val Cys Val
        195                 200                 205

Ala Gln Arg Trp Gly Gly Lys Arg Glu Val Met Tyr Thr Ala Phe Lys
    210                 215                 220

Ala Leu Gly Asp Ser Val Asp Tyr Val Gln Val Cys Asp Ser Asp Thr
225                 230                 235                 240

Arg Leu Asp Pro Met Ala Leu Leu Glu Leu Val Arg Val Leu Asp Glu
                245                 250                 255

Asp Pro Arg Val Gly Ala Val Gly Gly Asp Val Arg Ile Leu Asn Pro
            260                 265                 270

Leu Asp Ser Trp Val Ser Phe Leu Ser Ser Leu Arg Tyr Trp Val Ala
        275                 280                 285

Phe Asn Val Glu Arg Ala Cys Gln Ser Tyr Phe His Cys Val Ser Cys
    290                 295                 300

Ile Ser Gly Pro Leu Gly Leu Tyr Arg Asn Asn Leu Leu Gln Gln Phe
305                 310                 315                 320
```

```
Leu Glu Ala Trp Tyr Asn Gln Lys Phe Leu Gly Thr His Cys Thr Phe
                325                 330                 335

Gly Asp Asp Arg His Leu Thr Asn Arg Met Leu Ser Met Gly Tyr Ala
            340                 345                 350

Thr Lys Tyr Thr Ser Arg Ser Arg Cys Tyr Ser Glu Thr Pro Ser Ser
        355                 360                 365

Phe Leu Arg Trp Leu Ser Gln Gln Thr Arg Trp Ser Lys Ser Tyr Phe
    370                 375                 380

Arg Glu Trp Leu Tyr Asn Ala Leu Trp Trp His Arg His His Ala Trp
385                 390                 395                 400

Met Thr Tyr Glu Ala Val Val Ser Gly Leu Phe Pro Phe Phe Val Ala
                405                 410                 415

Ala Thr Val Leu Arg Leu Phe Tyr Ala Gly Arg Pro Trp Ala Leu Leu
            420                 425                 430

Trp Val Leu Leu Cys Val Gln Gly Val Ala Leu Ala Lys Ala Ala Phe
        435                 440                 445

Ala Ala Trp Leu Arg Gly Cys Leu Arg Met Val Leu Leu Ser Leu Tyr
    450                 455                 460

Ala Pro Leu Tyr Met Cys Gly Leu Leu Pro Ala Lys Phe Leu Ala Leu
465                 470                 475                 480

Val Thr Met Asn Gln Ser Gly Trp Gly Thr Ser Gly Arg Arg Lys Leu
                485                 490                 495

Ala Ala Asn Tyr Val Pro Leu Leu Pro Leu Ala Leu Trp Ala Leu Leu
            500                 505                 510

Leu Leu Gly Gly Leu Val Arg Ser Val Ala His Glu Ala Arg Ala Asp
        515                 520                 525

Trp Ser Gly Pro Ser Arg Ala Ala Glu Ala Tyr His Leu Ala Ala Gly
    530                 535                 540

Ala Gly Ala Tyr Val Gly Tyr Trp Val Ala Met Leu Thr Leu Tyr Trp
545                 550                 555                 560

Val Gly Val Arg Arg Leu Cys Arg Arg Arg Thr Gly Gly Tyr Arg Val
                565                 570                 575

Gln Val
```

<210> 154
<211> 577
<212> PRT
<213> Homo sapiens

<400> 154

```
Met Arg Gln Asp Ala Pro Lys Pro Thr Pro Ala Ala Cys Arg Cys Ser
1               5                  10                  15

Gly Leu Ala Arg Arg Val Leu Thr Ile Ala Phe Ala Leu Leu Ile Leu
            20                  25                  30

Gly Leu Met Thr Trp Ala Tyr Ala Ala Gly Val Pro Leu Ala Ser Asp
        35                  40                  45

Arg Tyr Gly Leu Leu Ala Phe Gly Leu Tyr Gly Ala Phe Leu Ser Ala
    50                  55                  60

His Leu Val Ala Gln Ser Leu Phe Ala Tyr Leu Glu His Arg Arg Val
65                  70                  75                  80

Ala Ala Ala Ala Arg Gly Pro Leu Asp Ala Ala Thr Ala Arg Ser Val
                85                  90                  95

Ala Leu Thr Ile Ser Ala Tyr Gln Glu Asp Pro Ala Tyr Leu Arg Gln
            100                 105                 110

Cys Leu Ala Ser Ala Arg Ala Leu Leu Tyr Pro Arg Ala Arg Leu Arg
        115                 120                 125

Val Leu Met Val Val Asp Gly Asn Arg Ala Glu Asp Leu Tyr Met Val
    130                 135                 140

Asp Met Phe Arg Glu Val Phe Ala Asp Glu Asp Pro Ala Thr Tyr Val
145                 150                 155                 160

Trp Asp Gly Asn Tyr His Gln Pro Trp Glu Pro Ala Ala Ala Gly Ala
                165                 170                 175

Val Gly Ala Gly Ala Tyr Arg Glu Val Glu Ala Glu Asp Pro Gly Arg
            180                 185                 190

Leu Ala Val Glu Ala Leu Val Arg Thr Arg Arg Cys Val Cys Val Ala
        195                 200                 205

Gln Arg Trp Gly Gly Lys Arg Glu Val Met Tyr Thr Ala Phe Lys Ala
    210                 215                 220

Leu Gly Asp Ser Val Asp Tyr Val Gln Val Cys Asp Ser Asp Thr Arg
225                 230                 235                 240
```

```
Leu Asp Pro Met Ala Leu Leu Glu Leu Val Arg Val Leu Asp Glu Asp
                245                 250                 255

Pro Arg Val Gly Ala Val Gly Gly Asp Val Arg Ile Leu Asn Pro Leu
            260                 265                 270

Asp Ser Trp Val Ser Phe Leu Ser Ser Leu Arg Tyr Trp Val Ala Phe
        275                 280                 285

Asn Val Glu Arg Ala Cys Gln Ser Tyr Phe His Cys Val Ser Cys Ile
    290                 295                 300

Ser Gly Pro Leu Gly Leu Tyr Arg Asn Asn Leu Leu Gln Gln Phe Leu
305                 310                 315                 320

Glu Ala Trp Tyr Asn Gln Lys Phe Leu Gly Thr His Cys Thr Phe Gly
                325                 330                 335

Asp Asp Arg His Leu Thr Asn Arg Met Leu Ser Met Gly Tyr Ala Thr
            340                 345                 350

Lys Tyr Thr Ser Arg Ser Arg Cys Tyr Ser Glu Thr Pro Ser Ser Phe
        355                 360                 365

Leu Arg Trp Leu Ser Gln Gln Thr Arg Trp Ser Lys Ser Tyr Phe Arg
    370                 375                 380

Glu Trp Leu Tyr Asn Ala Leu Trp Trp His Arg His His Ala Trp Met
385                 390                 395                 400

Thr Tyr Glu Ala Val Val Ser Gly Leu Phe Pro Phe Phe Val Ala Ala
                405                 410                 415

Thr Val Leu Arg Leu Phe Tyr Ala Gly Arg Pro Trp Ala Leu Leu Trp
            420                 425                 430

Val Leu Leu Cys Val Gln Gly Val Ala Leu Ala Lys Ala Ala Phe Ala
        435                 440                 445

Ala Trp Leu Arg Gly Cys Leu Arg Met Val Leu Leu Ser Leu Tyr Ala
    450                 455                 460

Pro Leu Tyr Met Cys Gly Leu Leu Pro Ala Lys Phe Leu Ala Leu Val
465                 470                 475                 480

Thr Met Asn Gln Ser Gly Trp Gly Thr Ser Gly Arg Arg Lys Leu Ala
                485                 490                 495

Ala Asn Tyr Val Pro Leu Leu Pro Leu Ala Leu Trp Ala Leu Leu Leu
            500                 505                 510
```

```
Leu Gly Gly Leu Val Arg Ser Val Ala His Glu Ala Arg Ala Asp Trp
        515                 520                 525

Ser Gly Pro Ser Arg Ala Ala Glu Ala Tyr His Leu Ala Ala Gly Ala
    530                 535                 540

Gly Ala Tyr Val Gly Tyr Trp Val Ala Met Leu Thr Leu Tyr Trp Val
545                 550                 555                 560

Gly Val Arg Arg Leu Cys Arg Arg Arg Thr Gly Gly Tyr Arg Val Gln
                565                 570                 575

Val
```

<210> 155
<211> 552
<212> PRT
<213> Homo sapiens

<400> 155

```
Met His Cys Glu Arg Phe Leu Cys Ile Leu Arg Ile Ile Gly Thr Thr
1               5                   10                  15

Leu Phe Gly Val Ser Leu Leu Leu Gly Ile Thr Ala Ala Tyr Ile Val
            20                  25                  30

Gly Tyr Gln Phe Ile Gln Thr Asp Asn Tyr Tyr Phe Ser Phe Gly Leu
        35                  40                  45

Tyr Gly Ala Phe Leu Ala Ser His Leu Ile Ile Gln Ser Leu Phe Ala
    50                  55                  60

Phe Leu Glu His Arg Lys Met Lys Lys Ser Leu Glu Thr Pro Ile Lys
65                  70                  75                  80

Leu Asn Lys Thr Val Ala Leu Cys Ile Ala Ala Tyr Gln Glu Asp Pro
                85                  90                  95

Asp Tyr Leu Arg Lys Cys Leu Gln Ser Val Lys Arg Leu Thr Tyr Pro
            100                 105                 110

Gly Ile Lys Val Val Met Val Ile Asp Gly Asn Ser Glu Asp Asp Leu
        115                 120                 125

Tyr Met Met Asp Ile Phe Ser Glu Val Met Gly Arg Asp Lys Ser Ala
    130                 135                 140

Thr Tyr Ile Trp Lys Asn Asn Phe His Glu Lys Gly Pro Gly Glu Thr
145                 150                 155                 160

Asp Glu Ser His Lys Glu Ser Ser Gln His Val Thr Gln Leu Val Leu
```

165 170 175

Ser Asn Lys Ser Ile Cys Ile Met Gln Lys Trp Gly Gly Lys Arg Glu
180 185 190

Val Met Tyr Thr Ala Phe Arg Ala Leu Gly Arg Ser Val Asp Tyr Val
195 200 205

Gln Val Cys Asp Ser Asp Thr Met Leu Asp Pro Ala Ser Ser Val Glu
210 215 220

Met Val Lys Val Leu Glu Glu Asp Pro Met Val Gly Gly Val Gly Gly
225 230 235 240

Asp Val Gln Ile Leu Asn Lys Tyr Asp Ser Trp Ile Ser Phe Leu Ser
245 250 255

Ser Val Arg Tyr Trp Met Ala Phe Asn Ile Glu Arg Ala Cys Gln Ser
260 265 270

Tyr Phe Gly Cys Val Gln Cys Ile Ser Gly Pro Leu Gly Met Tyr Arg
275 280 285

Asn Ser Leu Leu His Glu Phe Val Glu Asp Trp Tyr Asn Gln Glu Phe
290 295 300

Met Gly Asn Gln Cys Ser Phe Gly Asp Asp Arg His Leu Thr Asn Arg
305 310 315 320

Val Leu Ser Leu Gly Tyr Ala Thr Lys Tyr Thr Ala Arg Ser Lys Cys
325 330 335

Leu Thr Glu Thr Pro Ile Glu Tyr Leu Arg Trp Leu Asn Gln Gln Thr
340 345 350

Arg Trp Ser Lys Ser Tyr Phe Arg Glu Trp Leu Tyr Asn Ala Met Trp
355 360 365

Phe His Lys His His Leu Trp Met Thr Tyr Glu Ala Ile Ile Thr Gly
370 375 380

Phe Phe Pro Phe Phe Leu Ile Ala Thr Val Ile Gln Leu Phe Tyr Arg
385 390 395 400

Gly Lys Ile Trp Asn Ile Leu Leu Phe Leu Leu Thr Val Gln Leu Val
405 410 415

Gly Leu Ile Lys Ser Ser Phe Ala Ser Cys Leu Arg Gly Asn Ile Val
420 425 430

Met Val Phe Met Ser Leu Tyr Ser Val Leu Tyr Met Ser Ser Leu Leu

435 440 445

Pro Ala Lys Met Phe Ala Ile Ala Thr Ile Asn Lys Ala Gly Trp Gly
450 455 460

Thr Ser Gly Arg Lys Thr Ile Val Val Asn Phe Ile Gly Leu Ile Pro
465 470 475 480

Val Ser Val Trp Phe Thr Ile Leu Leu Gly Gly Val Ile Phe Thr Ile
485 490 495

Tyr Lys Glu Ser Lys Arg Pro Phe Ser Glu Ser Lys Gln Thr Val Leu
500 505 510

Ile Val Gly Thr Leu Leu Tyr Ala Cys Tyr Trp Val Met Leu Leu Thr
515 520 525

Leu Tyr Val Val Leu Ile Asn Lys Cys Gly Arg Arg Lys Lys Gly Gln
530 535 540

Gln Tyr Asp Met Val Leu Asp Val
545 550

<210> 156
<211> 553
<212> PRT
<213> Homo sapiens

<400> 156

Met Pro Val Gln Leu Thr Thr Ala Leu Arg Val Val Gly Thr Ser Leu
1 5 10 15

Phe Ala Leu Ala Val Leu Gly Gly Ile Leu Ala Ala Tyr Val Thr Gly
20 25 30

Tyr Gln Phe Ile His Thr Glu Lys His Tyr Leu Ser Phe Gly Leu Tyr
35 40 45

Gly Ala Ile Leu Gly Leu His Leu Leu Ile Gln Ser Leu Phe Ala Phe
50 55 60

Leu Glu His Arg Arg Met Arg Arg Ala Gly Gln Ala Leu Lys Leu Pro
65 70 75 80

Ser Pro Arg Arg Gly Ser Val Ala Leu Cys Ile Ala Ala Tyr Gln Glu
85 90 95

Asp Pro Asp Tyr Leu Arg Lys Cys Leu Arg Ser Ala Gln Arg Ile Ser
100 105 110

Phe Pro Asp Leu Lys Val Val Met Val Val Asp Gly Asn Arg Gln Glu
115 120 125

```
Asp Ala Tyr Met Leu Asp Ile Phe His Glu Val Leu Gly Gly Thr Glu
    130                 135                 140

Gln Ala Gly Phe Phe Val Trp Arg Ser Asn Phe His Glu Ala Gly Glu
145                 150                 155                 160

Gly Glu Thr Glu Ala Ser Leu Gln Glu Gly Met Asp Arg Val Arg Asp
                165                 170                 175

Val Val Arg Ala Ser Thr Phe Ser Cys Ile Met Gln Lys Trp Gly Gly
            180                 185                 190

Lys Arg Glu Val Met Tyr Thr Ala Phe Lys Ala Leu Gly Asp Ser Val
        195                 200                 205

Asp Tyr Ile Gln Val Cys Asp Ser Asp Thr Val Leu Asp Pro Ala Cys
    210                 215                 220

Thr Ile Glu Met Leu Arg Val Leu Glu Glu Asp Pro Gln Val Gly Gly
225                 230                 235                 240

Val Gly Gly Asp Val Gln Ile Leu Asn Lys Tyr Asp Ser Trp Ile Ser
                245                 250                 255

Phe Leu Ser Ser Val Arg Tyr Trp Met Ala Phe Asn Val Glu Arg Ala
            260                 265                 270

Cys Gln Ser Tyr Phe Gly Cys Val Gln Cys Ile Ser Gly Pro Leu Gly
        275                 280                 285

Met Tyr Arg Asn Ser Leu Leu Gln Gln Phe Leu Glu Asp Trp Tyr His
    290                 295                 300

Gln Lys Phe Leu Gly Ser Lys Cys Ser Phe Gly Asp Asp Arg His Leu
305                 310                 315                 320

Thr Asn Arg Val Leu Ser Leu Gly Tyr Arg Thr Lys Tyr Thr Ala Arg
                325                 330                 335

Ser Lys Cys Leu Thr Glu Thr Pro Thr Lys Tyr Leu Arg Trp Leu Asn
            340                 345                 350

Gln Gln Thr Arg Trp Ser Lys Ser Tyr Phe Arg Glu Trp Leu Tyr Asn
        355                 360                 365

Ser Leu Trp Phe His Lys His His Leu Trp Met Thr Tyr Glu Ser Val
    370                 375                 380

Val Thr Gly Phe Phe Pro Phe Phe Leu Ile Ala Thr Val Ile Gln Leu
385                 390                 395                 400
```

```
Phe Tyr Arg Gly Arg Ile Trp Asn Ile Leu Leu Phe Leu Leu Thr Val
                405                 410                 415

Gln Leu Val Gly Ile Ile Lys Ala Thr Tyr Ala Cys Phe Leu Arg Gly
            420                 425                 430

Asn Ala Glu Met Ile Phe Met Ser Leu Tyr Ser Leu Leu Tyr Met Ser
        435                 440                 445

Ser Leu Leu Pro Ala Lys Ile Phe Ala Ile Ala Thr Ile Asn Lys Ser
    450                 455                 460

Gly Trp Gly Thr Ser Gly Arg Lys Thr Ile Val Val Asn Phe Ile Gly
465                 470                 475                 480

Leu Ile Pro Val Ser Ile Trp Val Ala Val Leu Leu Gly Gly Leu Ala
                485                 490                 495

Tyr Thr Ala Tyr Cys Gln Asp Leu Phe Ser Glu Thr Glu Leu Ala Phe
            500                 505                 510

Leu Val Ser Gly Ala Ile Leu Tyr Gly Cys Tyr Trp Val Ala Leu Leu
        515                 520                 525

Met Leu Tyr Leu Ala Ile Ile Ala Arg Arg Cys Gly Lys Lys Pro Glu
    530                 535                 540

Gln Tyr Ser Leu Ala Phe Ala Glu Val
545                 550


<210>  157
<211>  281
<212>  PRT
<213>  Homo sapiens

<400>  157

Met Pro Val Gln Leu Thr Thr Ala Leu Arg Val Val Gly Thr Ser Leu
1               5                   10                  15

Phe Ala Leu Ala Val Leu Gly Gly Ile Leu Ala Ala Tyr Val Thr Gly
            20                  25                  30

Tyr Gln Phe Ile His Thr Glu Lys His Tyr Leu Ser Phe Gly Leu Tyr
        35                  40                  45

Gly Ala Ile Leu Gly Leu His Leu Leu Ile Gln Ser Leu Phe Ala Phe
    50                  55                  60

Leu Glu His Arg Arg Met Arg Arg Ala Gly Gln Ala Leu Lys Leu Pro
65                  70                  75                  80
```

```
Ser Pro Arg Arg Gly Ser Val Ala Leu Cys Ile Ala Ala Tyr Gln Glu
                85                  90                  95

Asp Pro Asp Tyr Leu Arg Lys Cys Leu Arg Ser Ala Gln Arg Ile Ser
            100                 105                 110

Phe Pro Asp Leu Lys Val Val Met Val Val Asp Gly Asn Arg Gln Glu
        115                 120                 125

Asp Ala Tyr Met Leu Asp Ile Phe His Glu Val Leu Gly Gly Thr Glu
    130                 135                 140

Gln Ala Gly Phe Phe Val Trp Arg Ser Asn Phe His Glu Ala Gly Glu
145                 150                 155                 160

Gly Glu Thr Glu Ala Ser Leu Gln Glu Gly Met Asp Arg Val Arg Asp
                165                 170                 175

Val Val Arg Ala Ser Thr Phe Ser Cys Ile Met Gln Lys Trp Gly Gly
            180                 185                 190

Lys Arg Glu Val Met Tyr Thr Ala Phe Lys Ala Leu Gly Asp Ser Val
        195                 200                 205

Asp Tyr Ile Gln Val Cys Asp Ser Asp Thr Val Leu Asp Pro Ala Cys
    210                 215                 220

Thr Ile Glu Met Leu Arg Val Leu Glu Glu Asp Pro Gln Val Gly Gly
225                 230                 235                 240

Val Gly Gly Asp Val Gln Pro Pro Gly Lys Gly Met Ala Val Glu Asp
                245                 250                 255

Asp Gln Val Gln Ala Ala Gln Val Arg Ala Thr Glu Ala Trp Ser Val
            260                 265                 270

His Gln Arg His Val Ser Arg Glu Gln
        275                 280


<210>  158
<211>  267
<212>  PRT
<213>  Homo sapiens

<400>  158

Met Pro Arg Ser Cys Cys Ser Arg Ser Gly Ala Leu Leu Leu Ala Leu
1               5                   10                  15

Leu Leu Gln Ala Ser Met Glu Val Arg Gly Trp Cys Leu Glu Ser Ser
            20                  25                  30
```

```
Gln Cys Gln Asp Leu Thr Thr Glu Ser Asn Leu Leu Glu Cys Ile Arg
        35                  40                  45

Ala Cys Lys Pro Asp Leu Ser Ala Glu Thr Pro Met Phe Pro Gly Asn
    50                  55                  60

Gly Asp Glu Gln Pro Leu Thr Glu Asn Pro Arg Lys Tyr Val Met Gly
65                  70                  75                  80

His Phe Arg Trp Asp Arg Phe Gly Arg Arg Asn Ser Ser Ser Ser Gly
                85                  90                  95

Ser Ser Gly Ala Gly Gln Lys Arg Glu Asp Val Ser Ala Gly Glu Asp
            100                 105                 110

Cys Gly Pro Leu Pro Glu Gly Gly Pro Glu Pro Arg Ser Asp Gly Ala
        115                 120                 125

Lys Pro Gly Pro Arg Glu Gly Lys Arg Ser Tyr Ser Met Glu His Phe
    130                 135                 140

Arg Trp Gly Lys Pro Val Gly Lys Lys Arg Arg Pro Val Lys Val Tyr
145                 150                 155                 160

Pro Asn Gly Ala Glu Asp Glu Ser Ala Glu Ala Phe Pro Leu Glu Phe
                165                 170                 175

Lys Arg Glu Leu Thr Gly Gln Arg Leu Arg Glu Gly Asp Gly Pro Asp
            180                 185                 190

Gly Pro Ala Asp Asp Gly Ala Gly Ala Gln Ala Asp Leu Glu His Ser
        195                 200                 205

Leu Leu Val Ala Ala Glu Lys Lys Asp Glu Gly Pro Tyr Arg Met Glu
    210                 215                 220

His Phe Arg Trp Gly Ser Pro Pro Lys Asp Lys Arg Tyr Gly Gly Phe
225                 230                 235                 240

Met Thr Ser Glu Lys Ser Gln Thr Pro Leu Val Thr Leu Phe Lys Asn
                245                 250                 255

Ala Ile Ile Lys Asn Ala Tyr Lys Lys Gly Glu
            260                 265
```

<210> 159
<211> 726
<212> PRT
<213> Homo sapiens

<400> 159

```
Met Asn His Ser Pro Leu Lys Thr Ala Leu Ala Tyr Glu Cys Phe Gln
```

```
1               5                   10                  15

Asp Gln Asp Asn Ser Thr Leu Ala Leu Pro Ser Asp Gln Lys Met Lys
            20                  25                  30

Thr Gly Thr Ser Gly Arg Gln Arg Val Gln Glu Gln Val Met Met Thr
        35                  40                  45

Val Lys Arg Gln Lys Ser Lys Ser Ser Gln Ser Ser Thr Leu Ser His
    50                  55                  60

Ser Asn Arg Gly Ser Met Tyr Asp Gly Leu Ala Asp Asn Tyr Asn Tyr
65                  70                  75                  80

Gly Thr Thr Ser Arg Ser Ser Tyr Tyr Ser Lys Phe Gln Ala Gly Asn
                85                  90                  95

Gly Ser Trp Gly Tyr Pro Ile Tyr Asn Gly Thr Leu Lys Arg Glu Pro
            100                 105                 110

Asp Asn Arg Arg Phe Ser Ser Tyr Ser Gln Met Glu Asn Trp Ser Arg
        115                 120                 125

His Tyr Pro Arg Gly Ser Cys Asn Thr Thr Gly Ala Gly Ser Asp Ile
    130                 135                 140

Cys Phe Met Gln Lys Ile Lys Ala Ser Arg Ser Glu Pro Asp Leu Tyr
145                 150                 155                 160

Cys Asp Pro Arg Gly Thr Leu Arg Lys Gly Thr Leu Gly Ser Lys Gly
                165                 170                 175

Gln Lys Thr Thr Gln Asn Arg Tyr Ser Phe Tyr Ser Thr Cys Ser Gly
            180                 185                 190

Gln Lys Ala Ile Lys Lys Cys Pro Val Arg Pro Pro Ser Cys Ala Ser
        195                 200                 205

Lys Gln Asp Pro Val Tyr Ile Pro Pro Ile Ser Cys Asn Lys Asp Leu
    210                 215                 220

Ser Phe Gly His Ser Arg Ala Ser Ser Lys Ile Cys Ser Glu Asp Ile
225                 230                 235                 240

Glu Cys Ser Gly Leu Thr Ile Pro Lys Ala Val Gln Tyr Leu Ser Ser
                245                 250                 255

Gln Asp Glu Lys Tyr Gln Ala Ile Gly Ala Tyr Tyr Ile Gln His Thr
            260                 265                 270

Cys Phe Gln Asp Glu Ser Ala Lys Gln Gln Val Tyr Gln Leu Gly Gly
```

275 280 285

Ile Cys Lys Leu Val Asp Leu Leu Arg Ser Pro Asn Gln Asn Val Gln
290 295 300

Gln Ala Ala Ala Gly Ala Leu Arg Asn Leu Val Phe Arg Ser Thr Thr
305 310 315 320

Asn Lys Leu Glu Thr Arg Arg Gln Asn Gly Ile Arg Glu Ala Val Ser
325 330 335

Leu Leu Arg Arg Thr Gly Asn Ala Glu Ile Gln Lys Gln Leu Thr Gly
340 345 350

Leu Leu Trp Asn Leu Ser Ser Thr Asp Glu Leu Lys Glu Glu Leu Ile
355 360 365

Ala Asp Ala Leu Pro Val Leu Ala Asp Arg Val Ile Ile Pro Phe Ser
370 375 380

Gly Trp Cys Asp Gly Asn Ser Asn Met Ser Arg Glu Val Val Asp Pro
385 390 395 400

Glu Val Phe Phe Asn Ala Thr Gly Cys Leu Arg Asn Leu Ser Ser Ala
405 410 415

Asp Ala Gly Arg Gln Thr Met Arg Asn Tyr Ser Gly Leu Ile Asp Ser
420 425 430

Leu Met Ala Tyr Val Gln Asn Cys Val Ala Ala Ser Arg Cys Asp Asp
435 440 445

Lys Ser Val Glu Asn Cys Met Cys Val Leu His Asn Leu Ser Tyr Arg
450 455 460

Leu Asp Ala Glu Val Pro Thr Arg Tyr Arg Gln Leu Glu Tyr Asn Ala
465 470 475 480

Arg Asn Ala Tyr Thr Glu Lys Ser Ser Thr Gly Cys Phe Ser Asn Lys
485 490 495

Ser Asp Lys Met Met Asn Asn Asn Tyr Asp Cys Pro Leu Pro Glu Glu
500 505 510

Glu Thr Asn Pro Lys Gly Ser Gly Trp Leu Tyr His Ser Asp Ala Ile
515 520 525

Arg Thr Tyr Leu Asn Leu Met Gly Lys Ser Lys Lys Asp Ala Thr Leu
530 535 540

Glu Ala Cys Ala Gly Ala Leu Gln Asn Leu Thr Ala Ser Lys Gly Leu

545 550 555 560

Met Ser Ser Gly Met Ser Gln Leu Ile Gly Leu Lys Glu Lys Gly Leu
565 570 575

Pro Gln Ile Ala Arg Leu Leu Gln Ser Gly Asn Ser Asp Val Val Arg
580 585 590

Ser Gly Ala Ser Leu Leu Ser Asn Met Ser Arg His Pro Leu Leu His
595 600 605

Arg Val Met Gly Asn Gln Val Phe Pro Glu Val Thr Arg Leu Leu Thr
610 615 620

Ser His Thr Gly Asn Thr Ser Asn Ser Glu Asp Ile Leu Ser Ser Ala
625 630 635 640

Cys Tyr Thr Val Arg Asn Leu Met Ala Ser Gln Pro Gln Leu Ala Lys
645 650 655

Gln Tyr Phe Ser Ser Ser Met Leu Asn Asn Ile Ile Asn Leu Cys Arg
660 665 670

Ser Ser Ala Ser Pro Lys Ala Ala Glu Ala Ala Arg Leu Leu Leu Ser
675 680 685

Asp Met Trp Ser Ser Lys Glu Leu Gln Gly Val Leu Arg Gln Gln Gly
690 695 700

Phe Asp Arg Asn Met Leu Gly Thr Leu Ala Gly Ala Asn Ser Leu Arg
705 710 715 720

Asn Phe Thr Ser Arg Phe
725

<210> 160
<211> 747
<212> PRT
<213> Homo sapiens

<400> 160

Met Asn His Ser Pro Leu Lys Thr Ala Leu Ala Tyr Glu Cys Phe Gln
1 5 10 15

Asp Gln Asp Asn Ser Thr Leu Ala Leu Pro Ser Asp Gln Lys Met Lys
20 25 30

Thr Gly Thr Ser Gly Arg Gln Arg Val Gln Glu Gln Val Met Met Thr
35 40 45

Val Lys Arg Gln Lys Ser Lys Ser Ser Gln Ser Ser Thr Leu Ser His
50 55 60

```
Ser Asn Arg Gly Ser Met Tyr Asp Gly Leu Ala Asp Asn Tyr Asn Tyr
65                  70                  75                  80

Gly Thr Thr Ser Arg Ser Ser Tyr Tyr Ser Lys Phe Gln Ala Gly Asn
                85                  90                  95

Gly Ser Trp Gly Tyr Pro Ile Tyr Asn Gly Thr Leu Lys Arg Glu Pro
            100                 105                 110

Asp Asn Arg Arg Phe Ser Ser Tyr Ser Gln Met Glu Asn Trp Ser Arg
        115                 120                 125

His Tyr Pro Arg Gly Ser Cys Asn Thr Thr Gly Ala Gly Ser Asp Ile
    130                 135                 140

Cys Phe Met Gln Lys Ile Lys Ala Ser Arg Ser Glu Pro Asp Leu Tyr
145                 150                 155                 160

Cys Asp Pro Arg Gly Thr Leu Arg Lys Gly Thr Leu Gly Ser Lys Gly
                165                 170                 175

Gln Lys Thr Thr Gln Asn Arg Tyr Ser Phe Tyr Ser Thr Cys Ser Gly
            180                 185                 190

Gln Lys Ala Ile Lys Lys Cys Pro Val Arg Pro Pro Ser Cys Ala Ser
        195                 200                 205

Lys Gln Asp Pro Val Tyr Ile Pro Pro Ile Ser Cys Asn Lys Asp Leu
    210                 215                 220

Ser Phe Gly His Ser Arg Ala Ser Ser Lys Ile Cys Ser Glu Asp Ile
225                 230                 235                 240

Glu Cys Ser Gly Leu Thr Ile Pro Lys Ala Val Gln Tyr Leu Ser Ser
                245                 250                 255

Gln Asp Glu Lys Tyr Gln Ala Ile Gly Ala Tyr Tyr Ile Gln His Thr
            260                 265                 270

Cys Phe Gln Asp Glu Ser Ala Lys Gln Gln Val Tyr Gln Leu Gly Gly
        275                 280                 285

Ile Cys Lys Leu Val Asp Leu Leu Arg Ser Pro Asn Gln Asn Val Gln
    290                 295                 300

Gln Ala Ala Ala Gly Ala Leu Arg Asn Leu Val Phe Arg Ser Thr Thr
305                 310                 315                 320

Asn Lys Leu Glu Thr Arg Arg Gln Asn Gly Ile Arg Glu Ala Val Ser
                325                 330                 335
```

```
Leu Leu Arg Arg Thr Gly Asn Ala Glu Ile Gln Lys Gln Leu Thr Gly
            340                 345                 350

Leu Leu Trp Asn Leu Ser Ser Thr Asp Glu Leu Lys Glu Glu Leu Ile
        355                 360                 365

Ala Asp Ala Leu Pro Val Leu Ala Asp Arg Val Ile Ile Pro Phe Ser
    370                 375                 380

Gly Trp Cys Asp Gly Asn Ser Asn Met Ser Arg Glu Val Val Asp Pro
385                 390                 395                 400

Glu Val Phe Phe Asn Ala Thr Gly Cys Leu Arg Lys Arg Leu Gly Met
                405                 410                 415

Arg Glu Leu Leu Ala Leu Val Pro Gln Arg Ala Thr Ser Ser Arg Val
            420                 425                 430

Asn Leu Ser Ser Ala Asp Ala Gly Arg Gln Thr Met Arg Asn Tyr Ser
        435                 440                 445

Gly Leu Ile Asp Ser Leu Met Ala Tyr Val Gln Asn Cys Val Ala Ala
    450                 455                 460

Ser Arg Cys Asp Asp Lys Ser Val Glu Asn Cys Met Cys Val Leu His
465                 470                 475                 480

Asn Leu Ser Tyr Arg Leu Asp Ala Glu Val Pro Thr Arg Tyr Arg Gln
                485                 490                 495

Leu Glu Tyr Asn Ala Arg Asn Ala Tyr Thr Glu Lys Ser Ser Thr Gly
            500                 505                 510

Cys Phe Ser Asn Lys Ser Asp Lys Met Met Asn Asn Asn Tyr Asp Cys
        515                 520                 525

Pro Leu Pro Glu Glu Glu Thr Asn Pro Lys Gly Ser Gly Trp Leu Tyr
    530                 535                 540

His Ser Asp Ala Ile Arg Thr Tyr Leu Asn Leu Met Gly Lys Ser Lys
545                 550                 555                 560

Lys Asp Ala Thr Leu Glu Ala Cys Ala Gly Ala Leu Gln Asn Leu Thr
                565                 570                 575

Ala Ser Lys Gly Leu Met Ser Ser Gly Met Ser Gln Leu Ile Gly Leu
            580                 585                 590

Lys Glu Lys Gly Leu Pro Gln Ile Ala Arg Leu Leu Gln Ser Gly Asn
        595                 600                 605
```

```
Ser Asp Val Val Arg Ser Gly Ala Ser Leu Leu Ser Asn Met Ser Arg
    610                 615                 620

His Pro Leu Leu His Arg Val Met Gly Asn Gln Val Phe Pro Glu Val
625                 630                 635                 640

Thr Arg Leu Leu Thr Ser His Thr Gly Asn Thr Ser Asn Ser Glu Asp
                645                 650                 655

Ile Leu Ser Ser Ala Cys Tyr Thr Val Arg Asn Leu Met Ala Ser Gln
            660                 665                 670

Pro Gln Leu Ala Lys Gln Tyr Phe Ser Ser Ser Met Leu Asn Asn Ile
        675                 680                 685

Ile Asn Leu Cys Arg Ser Ser Ala Ser Pro Lys Ala Ala Glu Ala Ala
    690                 695                 700

Arg Leu Leu Leu Ser Asp Met Trp Ser Ser Lys Glu Leu Gln Gly Val
705                 710                 715                 720

Leu Arg Gln Gln Gly Phe Asp Arg Asn Met Leu Gly Thr Leu Ala Gly
                725                 730                 735

Ala Asn Ser Leu Arg Asn Phe Thr Ser Arg Phe
            740                 745
```

<210> 161
<211> 341
<212> PRT
<213> Homo sapiens

<400> 161

```
Met Asn Ile Val Val Glu Phe Phe Val Val Thr Phe Lys Val Leu Trp
1               5                   10                  15

Ala Phe Val Leu Ala Ala Ala Arg Trp Leu Val Arg Pro Lys Glu Lys
            20                  25                  30

Ser Val Ala Gly Gln Val Cys Leu Ile Thr Gly Ala Gly Ser Gly Leu
        35                  40                  45

Gly Arg Leu Phe Ala Leu Glu Phe Ala Arg Arg Arg Ala Leu Leu Val
    50                  55                  60

Leu Trp Asp Ile Asn Thr Gln Ser Asn Glu Glu Thr Ala Gly Met Val
65                  70                  75                  80

Arg His Ile Tyr Arg Asp Leu Glu Ala Ala Asp Ala Ala Ala Leu Gln
                85                  90                  95
```

```
Ala Gly Asn Gly Glu Glu Glu Ile Leu Pro His Cys Asn Leu Gln Val
            100                 105                 110

Phe Thr Tyr Thr Cys Asp Val Gly Lys Arg Glu Asn Val Tyr Leu Thr
        115                 120                 125

Ala Glu Arg Val Arg Lys Glu Val Gly Glu Val Ser Val Leu Val Asn
    130                 135                 140

Asn Ala Gly Val Val Ser Gly His His Leu Leu Glu Cys Pro Asp Glu
145                 150                 155                 160

Leu Ile Glu Arg Thr Met Met Val Asn Cys His Ala His Phe Trp Thr
                165                 170                 175

Thr Lys Ala Phe Leu Pro Thr Met Leu Glu Ile Asn His Gly His Ile
            180                 185                 190

Val Thr Val Ala Ser Ser Leu Gly Leu Phe Ser Thr Ala Gly Val Glu
        195                 200                 205

Asp Tyr Cys Ala Ser Lys Phe Gly Val Val Gly Phe His Glu Ser Leu
    210                 215                 220

Ser His Glu Leu Lys Ala Ala Glu Lys Asp Gly Ile Lys Thr Thr Leu
225                 230                 235                 240

Val Cys Pro Tyr Leu Val Asp Thr Gly Met Phe Arg Gly Cys Arg Ile
                245                 250                 255

Arg Lys Glu Ile Glu Pro Phe Leu Pro Pro Leu Lys Pro Asp Tyr Cys
            260                 265                 270

Val Lys Gln Ala Met Lys Ala Ile Leu Thr Asp Gln Pro Met Ile Cys
        275                 280                 285

Thr Pro Arg Leu Met Tyr Ile Val Thr Phe Met Lys Ser Ile Leu Pro
    290                 295                 300

Phe Glu Ala Val Val Cys Met Tyr Arg Phe Leu Gly Ala Asp Lys Cys
305                 310                 315                 320

Met Tyr Pro Phe Ile Ala Gln Arg Lys Gln Ala Thr Asn Asn Asn Glu
                325                 330                 335

Ala Lys Asn Gly Ile
            340

<210>  162
<211>  307
<212>  PRT
```

<213> Homo sapiens

<400> 162

```
Met Gly Gly Leu Thr Ala Ser Asp Val His Pro Thr Leu Gly Val Gln
1               5                  10                  15

Leu Phe Ser Ala Gly Ile Ala Ala Cys Leu Ala Asp Val Ile Thr Phe
            20                  25                  30

Pro Leu Asp Thr Ala Lys Val Arg Leu Gln Val Gln Gly Glu Cys Pro
        35                  40                  45

Thr Ser Ser Val Ile Arg Tyr Lys Gly Val Leu Gly Thr Ile Thr Ala
    50                  55                  60

Val Val Lys Thr Glu Gly Arg Met Lys Leu Tyr Ser Gly Leu Pro Ala
65                  70                  75                  80

Gly Leu Gln Arg Gln Ile Ser Ser Ala Ser Leu Arg Ile Gly Leu Tyr
                85                  90                  95

Asp Thr Val Gln Glu Phe Leu Thr Ala Gly Lys Glu Thr Ala Pro Ser
            100                 105                 110

Leu Gly Ser Lys Ile Leu Ala Gly Leu Thr Thr Gly Gly Val Ala Val
        115                 120                 125

Phe Ile Gly Gln Pro Thr Glu Val Val Lys Val Arg Leu Gln Ala Gln
    130                 135                 140

Ser His Leu His Gly Ile Lys Pro Arg Tyr Thr Gly Thr Tyr Asn Ala
145                 150                 155                 160

Tyr Arg Ile Ile Ala Thr Thr Glu Gly Leu Thr Gly Leu Trp Lys Gly
                165                 170                 175

Thr Thr Pro Asn Leu Met Arg Ser Val Ile Ile Asn Cys Thr Glu Leu
            180                 185                 190

Val Thr Tyr Asp Leu Met Lys Glu Ala Phe Val Lys Asn Asn Ile Leu
        195                 200                 205

Ala Asp Asp Val Pro Cys His Leu Val Ser Ala Leu Ile Ala Gly Phe
    210                 215                 220

Cys Ala Thr Ala Met Ser Ser Pro Val Asp Val Val Lys Thr Arg Phe
225                 230                 235                 240

Ile Asn Ser Pro Pro Gly Gln Tyr Lys Ser Val Pro Asn Cys Ala Met
                245                 250                 255
```

Lys Val Phe Thr Asn Glu Gly Pro Thr Ala Phe Phe Lys Gly Leu Val
260 265 270

Pro Ser Phe Leu Arg Leu Gly Ser Trp Asn Val Ile Met Phe Val Cys
275 280 285

Phe Glu Gln Leu Lys Arg Glu Leu Ser Lys Ser Arg Gln Thr Met Asp
290 295 300

Cys Ala Thr
305

<210> 163
<211> 529
<212> PRT
<213> Homo sapiens

<400> 163

Met Leu Leu Ala Val Leu Tyr Cys Leu Leu Trp Ser Phe Gln Thr Ser
1 5 10 15

Ala Gly His Phe Pro Arg Ala Cys Val Ser Ser Lys Asn Leu Met Glu
20 25 30

Lys Glu Cys Cys Pro Pro Trp Ser Gly Asp Arg Ser Pro Cys Gly Gln
35 40 45

Leu Ser Gly Arg Gly Ser Cys Gln Asn Ile Leu Leu Ser Asn Ala Pro
50 55 60

Leu Gly Pro Gln Phe Pro Phe Thr Gly Val Asp Asp Arg Glu Ser Trp
65 70 75 80

Pro Ser Val Phe Tyr Asn Arg Thr Cys Gln Cys Ser Gly Asn Phe Met
85 90 95

Gly Phe Asn Cys Gly Asn Cys Lys Phe Gly Phe Trp Gly Pro Asn Cys
100 105 110

Thr Glu Arg Arg Leu Leu Val Arg Arg Asn Ile Phe Asp Leu Ser Ala
115 120 125

Pro Glu Lys Asp Lys Phe Phe Ala Tyr Leu Thr Leu Ala Lys His Thr
130 135 140

Ile Ser Ser Asp Tyr Val Ile Pro Ile Gly Thr Tyr Gly Gln Met Lys
145 150 155 160

Asn Gly Ser Thr Pro Met Phe Asn Asp Ile Asn Ile Tyr Asp Leu Phe
165 170 175

Val Trp Met His Tyr Tyr Val Ser Met Asp Ala Leu Leu Gly Gly Ser

180 185 190

Glu Ile Trp Arg Asp Ile Asp Phe Ala His Glu Ala Pro Ala Phe Leu
195 200 205

Pro Trp His Arg Leu Phe Leu Leu Arg Trp Glu Gln Glu Ile Gln Lys
210 215 220

Leu Thr Gly Asp Glu Asn Phe Thr Ile Pro Tyr Trp Asp Trp Arg Asp
225 230 235 240

Ala Glu Lys Cys Asp Ile Cys Thr Asp Glu Tyr Met Gly Gly Gln His
245 250 255

Pro Thr Asn Pro Asn Leu Leu Ser Pro Ala Ser Phe Phe Ser Ser Trp
260 265 270

Gln Ile Val Cys Ser Arg Leu Glu Glu Tyr Asn Ser His Gln Ser Leu
275 280 285

Cys Asn Gly Thr Pro Glu Gly Pro Leu Arg Arg Asn Pro Gly Asn His
290 295 300

Asp Lys Ser Arg Thr Pro Arg Leu Pro Ser Ser Ala Asp Val Glu Phe
305 310 315 320

Cys Leu Ser Leu Thr Gln Tyr Glu Ser Gly Ser Met Asp Lys Ala Ala
325 330 335

Asn Phe Ser Phe Arg Asn Thr Leu Glu Gly Phe Ala Ser Pro Leu Thr
340 345 350

Gly Ile Ala Asp Ala Ser Gln Ser Ser Met His Asn Ala Leu His Ile
355 360 365

Tyr Met Asn Gly Thr Met Ser Gln Val Gln Gly Ser Ala Asn Asp Pro
370 375 380

Ile Phe Leu Leu His His Ala Phe Val Asp Ser Ile Phe Glu Gln Trp
385 390 395 400

Leu Arg Arg His Arg Pro Leu Gln Glu Val Tyr Pro Glu Ala Asn Ala
405 410 415

Pro Ile Gly His Asn Arg Glu Ser Tyr Met Val Pro Phe Ile Pro Leu
420 425 430

Tyr Arg Asn Gly Asp Phe Phe Ile Ser Ser Lys Asp Leu Gly Tyr Asp
435 440 445

Tyr Ser Tyr Leu Gln Asp Ser Asp Pro Asp Ser Phe Gln Asp Tyr Ile

450 455 460

Lys Ser Tyr Leu Glu Gln Ala Ser Arg Ile Trp Ser Trp Leu Leu Gly
465 470 475 480

Ala Ala Met Val Gly Ala Val Leu Thr Ala Leu Leu Ala Gly Leu Val
485 490 495

Ser Leu Leu Cys Arg His Lys Arg Lys Gln Leu Pro Glu Glu Lys Gln
500 505 510

Pro Leu Leu Met Glu Lys Glu Asp Tyr His Ser Leu Tyr Gln Ser His
515 520 525

Leu

<210> 164
<211> 193
<212> PRT
<213> Homo sapiens

<400> 164

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
1 5 10 15

Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
20 25 30

Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
35 40 45

Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu
50 55 60

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg
65 70 75 80

Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu
85 90 95

Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser
100 105 110

Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
115 120 125

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu
130 135 140

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
145 150 155 160

```
Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu
                165                 170                 175

Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp
            180                 185                 190

Arg
```

<210> 165
<211> 166
<212> PRT
<213> Homo sapiens

<400> 165

```
Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu
1               5                   10                  15

Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His
            20                  25                  30

Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe
        35                  40                  45

Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp
    50                  55                  60

Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu
65                  70                  75                  80

Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp
                85                  90                  95

Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu
            100                 105                 110

Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala
        115                 120                 125

Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val
    130                 135                 140

Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala
145                 150                 155                 160

Cys Arg Thr Gly Asp Arg
                165
```

<210> 166
<211> 193
<212> PRT

<213> Homo sapiens

<400> 166

```
Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
1               5                  10                  15

Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
            20                  25                  30

Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
        35                  40                  45

Ala Glu Asn Ile Thr Thr Gly Cys Asn Glu Thr Cys Ser Leu Asn Glu
    50                  55                  60

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg
65                  70                  75                  80

Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu
                85                  90                  95

Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser
            100                 105                 110

Gln Val Asn Glu Thr Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
        115                 120                 125

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu
    130                 135                 140

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
145                 150                 155                 160

Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu
                165                 170                 175

Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp
            180                 185                 190

Arg
```

<210> 167
<211> 166
<212> PRT
<213> Homo sapiens

<400> 167

```
Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu
1               5                  10                  15

Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Asn Glu Thr
```

20 25 30

Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe
35 40 45

Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp
50 55 60

Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu
65 70 75 80

Leu Val Asn Ser Ser Gln Val Asn Glu Thr Leu Gln Leu His Val Asp
85 90 95

Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu
100 105 110

Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala
115 120 125

Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val
130 135 140

Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala
145 150 155 160

Cys Arg Thr Gly Asp Arg
165

<210> 168
<211> 794
<212> RNA
<213> Homo sapiens

<400> 168
uaauacgacu cacuauaggg acauuugcuu cugacacaac uguguucacu agcaaccuca 60

aacagcuagc caccaugggg gugcacgaau guccugccug gcuguggcuu cuccuguccc 120

ugcugucgcu cccucugggc cucccagucc ugggcgcccc accacgccuc aucugugaca 180

gccgaguccu ggagagguac cucuuggagg ccaaggaggc cgagaauauc acgacgggcu 240

guaaugaaac cugcagcuug aaugagaaua ucacuguccc agacaccaaa guuaauuucu 300

augccuggaa gaggauggag gucgggcagc aggccguaga agucuggcag ggccuggccc 360

ugcugucgga agcuguccug cggggccagg cccuguuggu caacucuucc caggugaacg 420

agacccugca gcugcaugug gauaaagccg ucaguggccu ucgcagccuc accacucugc 480

uucgggcucu gggagcccag aaggaagcca ucuccccucc agaugcggcc ucagcugcuc 540

cacuccgaac aaucacugcu gacacuuucc gcaaacucuu ccgagucuac uccaauuucc 600

uccggggaaa gcugaagcug uacacagggg aggccugcag gacaggggac agaugaaccg 660

gugcucgcuu ucuugcuguc caauuucuau uaaagguucc uuuguucccu aaguccaacu 720

acuaaacugg gggauauuau gaagggccuu gagcaucugg auucugccua auaaaaaaca 780

uuuauuuuca uugc 794

<210> 169
<211> 986
<212> PRT
<213> Homo sapiens

<400> 169

Met Pro Gly Val Ala Arg Leu Pro Leu Leu Leu Gly Leu Leu Leu Leu
1 5 10 15

Pro Arg Pro Gly Arg Pro Leu Asp Leu Ala Asp Tyr Thr Tyr Asp Leu
20 25 30

Ala Glu Glu Asp Asp Ser Glu Pro Leu Asn Tyr Lys Asp Pro Cys Lys
35 40 45

Ala Ala Ala Phe Leu Gly Asp Ile Ala Leu Asp Glu Glu Asp Leu Arg
50 55 60

Ala Phe Gln Val Gln Gln Ala Val Asp Leu Arg Arg His Thr Ala Arg
65 70 75 80

Lys Ser Ser Ile Lys Ala Ala Val Pro Gly Asn Thr Ser Thr Pro Ser
85 90 95

Cys Gln Ser Thr Asn Gly Gln Pro Gln Arg Gly Ala Cys Gly Arg Trp
100 105 110

Arg Gly Arg Ser Arg Ser Arg Arg Ala Ala Thr Ser Arg Pro Glu Arg
115 120 125

Val Trp Pro Asp Gly Val Ile Pro Phe Val Ile Gly Gly Asn Phe Thr
130 135 140

Gly Ser Gln Arg Ala Val Phe Arg Gln Ala Met Arg His Trp Glu Lys
145 150 155 160

His Thr Cys Val Thr Phe Leu Glu Arg Thr Asp Glu Asp Ser Tyr Ile
165 170 175

Val Phe Thr Tyr Arg Pro Cys Gly Cys Cys Ser Tyr Val Gly Arg Arg
180 185 190

Gly Gly Gly Pro Gln Ala Ile Ser Ile Gly Lys Asn Cys Asp Lys Phe
195 200 205

Gly Ile Val Val His Glu Leu Gly His Val Val Gly Phe Trp His Glu
210 215 220

```
His Thr Arg Pro Asp Arg Asp Arg His Val Ser Ile Val Arg Glu Asn
225                 230                 235                 240

Ile Gln Pro Gly Gln Glu Tyr Asn Phe Leu Lys Met Glu Pro Gln Glu
                245                 250                 255

Val Glu Ser Leu Gly Glu Thr Tyr Asp Phe Asp Ser Ile Met His Tyr
            260                 265                 270

Ala Arg Asn Thr Phe Ser Arg Gly Ile Phe Leu Asp Thr Ile Val Pro
        275                 280                 285

Lys Tyr Glu Val Asn Gly Val Lys Pro Pro Ile Gly Gln Arg Thr Arg
    290                 295                 300

Leu Ser Lys Gly Asp Ile Ala Gln Ala Arg Lys Leu Tyr Lys Cys Pro
305                 310                 315                 320

Ala Cys Gly Glu Thr Leu Gln Asp Ser Thr Gly Asn Phe Ser Ser Pro
                325                 330                 335

Glu Tyr Pro Asn Gly Tyr Ser Ala His Met His Cys Val Trp Arg Ile
            340                 345                 350

Ser Val Thr Pro Gly Glu Lys Ile Ile Leu Asn Phe Thr Ser Leu Asp
        355                 360                 365

Leu Tyr Arg Ser Arg Leu Cys Trp Tyr Asp Tyr Val Glu Val Arg Asp
    370                 375                 380

Gly Phe Trp Arg Lys Ala Pro Leu Arg Gly Arg Phe Cys Gly Ser Lys
385                 390                 395                 400

Leu Pro Glu Pro Ile Val Ser Thr Asp Ser Arg Leu Trp Val Glu Phe
                405                 410                 415

Arg Ser Ser Ser Asn Trp Val Gly Lys Gly Phe Phe Ala Val Tyr Glu
            420                 425                 430

Ala Ile Cys Gly Gly Asp Val Lys Lys Asp Tyr Gly His Ile Gln Ser
        435                 440                 445

Pro Asn Tyr Pro Asp Asp Tyr Arg Pro Ser Lys Val Cys Ile Trp Arg
    450                 455                 460

Ile Gln Val Ser Glu Gly Phe His Val Gly Leu Thr Phe Gln Ser Phe
465                 470                 475                 480

Glu Ile Glu Arg His Asp Ser Cys Ala Tyr Asp Tyr Leu Glu Val Arg
                485                 490                 495
```

```
Asp Gly His Ser Glu Ser Ser Thr Leu Ile Gly Arg Tyr Cys Gly Tyr
            500                 505                 510

Glu Lys Pro Asp Asp Ile Lys Ser Thr Ser Ser Arg Leu Trp Leu Lys
        515                 520                 525

Phe Val Ser Asp Gly Ser Ile Asn Lys Ala Gly Phe Ala Val Asn Phe
    530                 535                 540

Phe Lys Glu Val Asp Glu Cys Ser Arg Pro Asn Arg Gly Gly Cys Glu
545                 550                 555                 560

Gln Arg Cys Leu Asn Thr Leu Gly Ser Tyr Lys Cys Ser Cys Asp Pro
                565                 570                 575

Gly Tyr Glu Leu Ala Pro Asp Lys Arg Arg Cys Glu Ala Ala Cys Gly
            580                 585                 590

Gly Phe Leu Thr Lys Leu Asn Gly Ser Ile Thr Ser Pro Gly Trp Pro
        595                 600                 605

Lys Glu Tyr Pro Pro Asn Lys Asn Cys Ile Trp Gln Leu Val Ala Pro
    610                 615                 620

Thr Gln Tyr Arg Ile Ser Leu Gln Phe Asp Phe Phe Glu Thr Glu Gly
625                 630                 635                 640

Asn Asp Val Cys Lys Tyr Asp Phe Val Glu Val Arg Ser Gly Leu Thr
                645                 650                 655

Ala Asp Ser Lys Leu His Gly Lys Phe Cys Gly Ser Glu Lys Pro Glu
            660                 665                 670

Val Ile Thr Ser Gln Tyr Asn Asn Met Arg Val Glu Phe Lys Ser Asp
        675                 680                 685

Asn Thr Val Ser Lys Lys Gly Phe Lys Ala His Phe Phe Ser Asp Lys
    690                 695                 700

Asp Glu Cys Ser Lys Asp Asn Gly Gly Cys Gln Gln Asp Cys Val Asn
705                 710                 715                 720

Thr Phe Gly Ser Tyr Glu Cys Gln Cys Arg Ser Gly Phe Val Leu His
                725                 730                 735

Asp Asn Lys His Asp Cys Lys Glu Ala Gly Cys Asp His Lys Val Thr
            740                 745                 750

Ser Thr Ser Gly Thr Ile Thr Ser Pro Asn Trp Pro Asp Lys Tyr Pro
        755                 760                 765
```

```
Ser Lys Lys Glu Cys Thr Trp Ala Ile Ser Ser Thr Pro Gly His Arg
    770                 775                 780

Val Lys Leu Thr Phe Met Glu Met Asp Ile Glu Ser Gln Pro Glu Cys
785                 790                 795                 800

Ala Tyr Asp His Leu Glu Val Phe Asp Gly Arg Asp Ala Lys Ala Pro
                805                 810                 815

Val Leu Gly Arg Phe Cys Gly Ser Lys Lys Pro Glu Pro Val Leu Ala
            820                 825                 830

Thr Gly Ser Arg Met Phe Leu Arg Phe Tyr Ser Asp Asn Ser Val Gln
        835                 840                 845

Arg Lys Gly Phe Gln Ala Ser His Ala Thr Glu Cys Gly Gly Gln Val
    850                 855                 860

Arg Ala Asp Val Lys Thr Lys Asp Leu Tyr Ser His Ala Gln Phe Gly
865                 870                 875                 880

Asp Asn Asn Tyr Pro Gly Gly Val Asp Cys Glu Trp Val Ile Val Ala
                885                 890                 895

Glu Glu Gly Tyr Gly Val Glu Leu Val Phe Gln Thr Phe Glu Val Glu
            900                 905                 910

Glu Glu Thr Asp Cys Gly Tyr Asp Tyr Met Glu Leu Phe Asp Gly Tyr
        915                 920                 925

Asp Ser Thr Ala Pro Arg Leu Gly Arg Tyr Cys Gly Ser Gly Pro Pro
    930                 935                 940

Glu Glu Val Tyr Ser Ala Gly Asp Ser Val Leu Val Lys Phe His Ser
945                 950                 955                 960

Asp Asp Thr Ile Thr Lys Lys Gly Phe His Leu Arg Tyr Thr Ser Thr
                965                 970                 975

Lys Phe Gln Asp Thr Leu His Ser Arg Lys
            980                 985


<210>  170
<211>  396
<212>  PRT
<213>  Homo sapiens

<400>  170

Met Val Ala Gly Thr Arg Cys Leu Leu Ala Leu Leu Leu Pro Gln Val
1               5                   10                  15
```

```
Leu Leu Gly Gly Ala Ala Gly Leu Val Pro Glu Leu Gly Arg Arg Lys
            20                  25                  30

Phe Ala Ala Ala Ser Ser Gly Arg Pro Ser Ser Gln Pro Ser Asp Glu
        35                  40                  45

Val Leu Ser Glu Phe Glu Leu Arg Leu Leu Ser Met Phe Gly Leu Lys
    50                  55                  60

Gln Arg Pro Thr Pro Ser Arg Asp Ala Val Val Pro Pro Tyr Met Leu
65                  70                  75                  80

Asp Leu Tyr Arg Arg His Ser Gly Gln Pro Gly Ser Pro Ala Pro Asp
                85                  90                  95

His Arg Leu Glu Arg Ala Ala Ser Arg Ala Asn Thr Val Arg Ser Phe
            100                 105                 110

His His Glu Glu Ser Leu Glu Glu Leu Pro Glu Thr Ser Gly Lys Thr
        115                 120                 125

Thr Arg Arg Phe Phe Phe Asn Leu Ser Ser Ile Pro Thr Glu Glu Phe
    130                 135                 140

Ile Thr Ser Ala Glu Leu Gln Val Phe Arg Glu Gln Met Gln Asp Ala
145                 150                 155                 160

Leu Gly Asn Asn Ser Ser Phe His His Arg Ile Asn Ile Tyr Glu Ile
                165                 170                 175

Ile Lys Pro Ala Thr Ala Asn Ser Lys Phe Pro Val Thr Arg Leu Leu
            180                 185                 190

Asp Thr Arg Leu Val Asn Gln Asn Ala Ser Arg Trp Glu Ser Phe Asp
        195                 200                 205

Val Thr Pro Ala Val Met Arg Trp Thr Ala Gln Gly His Ala Asn His
    210                 215                 220

Gly Phe Val Val Glu Val Ala His Leu Glu Glu Lys Gln Gly Val Ser
225                 230                 235                 240

Lys Arg His Val Arg Ile Ser Arg Ser Leu His Gln Asp Glu His Ser
                245                 250                 255

Trp Ser Gln Ile Arg Pro Leu Leu Val Thr Phe Gly His Asp Gly Lys
            260                 265                 270

Gly His Pro Leu His Lys Arg Glu Lys Arg Gln Ala Lys His Lys Gln
        275                 280                 285
```

Arg Lys Arg Leu Lys Ser Ser Cys Lys Arg His Pro Leu Tyr Val Asp
290 295 300

Phe Ser Asp Val Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr
305 310 315 320

His Ala Phe Tyr Cys His Gly Glu Cys Pro Phe Pro Leu Ala Asp His
325 330 335

Leu Asn Ser Thr Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val
340 345 350

Asn Ser Lys Ile Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala
355 360 365

Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu Lys Val Val Leu Lys Asn
370 375 380

Tyr Gln Asp Met Val Val Glu Gly Cys Gly Cys Arg
385 390 395

<210> 171
<211> 408
<212> PRT
<213> Homo sapiens

<400> 171

Met Ile Pro Gly Asn Arg Met Leu Met Val Val Leu Leu Cys Gln Val
1 5 10 15

Leu Leu Gly Gly Ala Ser His Ala Ser Leu Ile Pro Glu Thr Gly Lys
20 25 30

Lys Lys Val Ala Glu Ile Gln Gly His Ala Gly Gly Arg Arg Ser Gly
35 40 45

Gln Ser His Glu Leu Leu Arg Asp Phe Glu Ala Thr Leu Leu Gln Met
50 55 60

Phe Gly Leu Arg Arg Arg Pro Gln Pro Ser Lys Ser Ala Val Ile Pro
65 70 75 80

Asp Tyr Met Arg Asp Leu Tyr Arg Leu Gln Ser Gly Glu Glu Glu Glu
85 90 95

Glu Gln Ile His Ser Thr Gly Leu Glu Tyr Pro Glu Arg Pro Ala Ser
100 105 110

Arg Ala Asn Thr Val Arg Ser Phe His His Glu Glu His Leu Glu Asn
115 120 125

Ile Pro Gly Thr Ser Glu Asn Ser Ala Phe Arg Phe Leu Phe Asn Leu

```
    130                 135                 140

Ser Ser Ile Pro Glu Asn Glu Val Ile Ser Ser Ala Glu Leu Arg Leu
145                 150                 155                 160

Phe Arg Glu Gln Val Asp Gln Gly Pro Asp Trp Glu Arg Gly Phe His
                165                 170                 175

Arg Ile Asn Ile Tyr Glu Val Met Lys Pro Pro Ala Glu Val Val Pro
            180                 185                 190

Gly His Leu Ile Thr Arg Leu Leu Asp Thr Arg Leu Val His His Asn
        195                 200                 205

Val Thr Arg Trp Glu Thr Phe Asp Val Ser Pro Ala Val Leu Arg Trp
    210                 215                 220

Thr Arg Glu Lys Gln Pro Asn Tyr Gly Leu Ala Ile Glu Val Thr His
225                 230                 235                 240

Leu His Gln Thr Arg Thr His Gln Gly Gln His Val Arg Ile Ser Arg
                245                 250                 255

Ser Leu Pro Gln Gly Ser Gly Asn Trp Ala Gln Leu Arg Pro Leu Leu
            260                 265                 270

Val Thr Phe Gly His Asp Gly Arg Gly His Ala Leu Thr Arg Arg Arg
        275                 280                 285

Arg Ala Lys Arg Ser Pro Lys His His Ser Gln Arg Ala Arg Lys Lys
    290                 295                 300

Asn Lys Asn Cys Arg Arg His Ser Leu Tyr Val Asp Phe Ser Asp Val
305                 310                 315                 320

Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr Gln Ala Phe Tyr
                325                 330                 335

Cys His Gly Asp Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr
            340                 345                 350

Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile
        355                 360                 365

Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu
    370                 375                 380

Tyr Leu Asp Glu Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met
385                 390                 395                 400

Val Val Glu Gly Cys Gly Cys Arg
```

405

<210> 172
<211> 408
<212> PRT
<213> Homo sapiens

<400> 172

Met Ile Pro Gly Asn Arg Met Leu Met Val Val Leu Leu Cys Gln Val
1 5 10 15

Leu Leu Gly Gly Ala Ser His Ala Ser Leu Ile Pro Glu Thr Gly Lys
20 25 30

Lys Lys Val Ala Glu Ile Gln Gly His Ala Gly Gly Arg Arg Ser Gly
35 40 45

Gln Ser His Glu Leu Leu Arg Asp Phe Glu Ala Thr Leu Leu Gln Met
50 55 60

Phe Gly Leu Arg Arg Arg Pro Gln Pro Ser Lys Ser Ala Val Ile Pro
65 70 75 80

Asp Tyr Met Arg Asp Leu Tyr Arg Leu Gln Ser Gly Glu Glu Glu Glu
85 90 95

Glu Gln Ile His Ser Thr Gly Leu Glu Tyr Pro Glu Arg Pro Ala Ser
100 105 110

Arg Ala Asn Thr Val Arg Ser Phe His His Glu Glu His Leu Glu Asn
115 120 125

Ile Pro Gly Thr Ser Glu Asn Ser Ala Phe Arg Phe Leu Phe Asn Leu
130 135 140

Ser Ser Ile Pro Glu Asn Glu Val Ile Ser Ser Ala Glu Leu Arg Leu
145 150 155 160

Phe Arg Glu Gln Val Asp Gln Gly Pro Asp Trp Glu Arg Gly Phe His
165 170 175

Arg Ile Asn Ile Tyr Glu Val Met Lys Pro Pro Ala Glu Val Val Pro
180 185 190

Gly His Leu Ile Thr Arg Leu Leu Asp Thr Arg Leu Val His His Asn
195 200 205

Val Thr Arg Trp Glu Thr Phe Asp Val Ser Pro Ala Val Leu Arg Trp
210 215 220

Thr Arg Glu Lys Gln Pro Asn Tyr Gly Leu Ala Ile Glu Val Thr His
225 230 235 240

```
Leu His Gln Thr Arg Thr His Gln Gly Gln His Val Arg Ile Ser Arg
                245                 250                 255

Ser Leu Pro Gln Gly Ser Gly Asn Trp Ala Gln Leu Arg Pro Leu Leu
            260                 265                 270

Val Thr Phe Gly His Asp Gly Arg Gly His Ala Leu Thr Arg Arg Arg
        275                 280                 285

Arg Ala Lys Arg Ser Pro Lys His His Ser Gln Arg Ala Arg Lys Lys
    290                 295                 300

Asn Lys Asn Cys Arg Arg His Ser Leu Tyr Val Asp Phe Ser Asp Val
305                 310                 315                 320

Gly Trp Asn Asp Trp Ile Val Ala Pro Pro Gly Tyr Gln Ala Phe Tyr
                325                 330                 335

Cys His Gly Asp Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr
            340                 345                 350

Asn His Ala Ile Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile
        355                 360                 365

Pro Lys Ala Cys Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu
    370                 375                 380

Tyr Leu Asp Glu Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met
385                 390                 395                 400

Val Val Glu Gly Cys Gly Cys Arg
                405
```

<210> 173
<211> 454
<212> PRT
<213> Homo sapiens

<400> 173

```
Met His Leu Thr Val Phe Leu Leu Lys Gly Ile Val Gly Phe Leu Trp
1               5                   10                  15

Ser Cys Trp Val Leu Val Gly Tyr Ala Lys Gly Gly Leu Gly Asp Asn
            20                  25                  30

His Val His Ser Ser Phe Ile Tyr Arg Arg Leu Arg Asn His Glu Arg
        35                  40                  45

Arg Glu Ile Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu Pro His Arg
    50                  55                  60
```

```
Pro Arg Pro Phe Ser Pro Gly Lys Gln Ala Ser Ser Ala Pro Leu Phe
65                  70                  75                  80

Met Leu Asp Leu Tyr Asn Ala Met Thr Asn Glu Glu Asn Pro Glu Glu
                85                  90                  95

Ser Glu Tyr Ser Val Arg Ala Ser Leu Ala Glu Glu Thr Arg Gly Ala
            100                 105                 110

Arg Lys Gly Tyr Pro Ala Ser Pro Asn Gly Tyr Pro Arg Arg Ile Gln
        115                 120                 125

Leu Ser Arg Thr Thr Pro Leu Thr Thr Gln Ser Pro Pro Leu Ala Ser
    130                 135                 140

Leu His Asp Thr Asn Phe Leu Asn Asp Ala Asp Met Val Met Ser Phe
145                 150                 155                 160

Val Asn Leu Val Glu Arg Asp Lys Asp Phe Ser His Gln Arg Arg His
                165                 170                 175

Tyr Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile Pro His Gly Glu Ala
            180                 185                 190

Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Asp Arg Ser Asn Asn Arg
        195                 200                 205

Phe Glu Asn Glu Thr Ile Lys Ile Ser Ile Tyr Gln Ile Ile Lys Glu
    210                 215                 220

Tyr Thr Asn Arg Asp Ala Asp Leu Phe Leu Leu Asp Thr Arg Lys Ala
225                 230                 235                 240

Gln Ala Leu Asp Val Gly Trp Leu Val Phe Asp Ile Thr Val Thr Ser
                245                 250                 255

Asn His Trp Val Ile Asn Pro Gln Asn Asn Leu Gly Leu Gln Leu Cys
            260                 265                 270

Ala Glu Thr Gly Asp Gly Arg Ser Ile Asn Val Lys Ser Ala Gly Leu
        275                 280                 285

Val Gly Arg Gln Gly Pro Gln Ser Lys Gln Pro Phe Met Val Ala Phe
    290                 295                 300

Phe Lys Ala Ser Glu Val Leu Leu Arg Ser Val Arg Ala Ala Asn Lys
305                 310                 315                 320

Arg Lys Asn Gln Asn Arg Asn Lys Ser Ser Ser His Gln Asp Ser Ser
                325                 330                 335
```

```
Arg Met Ser Ser Val Gly Asp Tyr Asn Thr Ser Glu Gln Lys Gln Ala
            340                 345                 350

Cys Lys Lys His Glu Leu Tyr Val Ser Phe Arg Asp Leu Gly Trp Gln
        355                 360                 365

Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala Phe Tyr Cys Asp Gly
    370                 375                 380

Glu Cys Ser Phe Pro Leu Asn Ala His Met Asn Ala Thr Asn His Ala
385                 390                 395                 400

Ile Val Gln Thr Leu Val His Leu Met Phe Pro Asp His Val Pro Lys
                405                 410                 415

Pro Cys Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe
            420                 425                 430

Asp Asp Ser Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val
        435                 440                 445

Arg Ser Cys Gly Cys His
    450
```

<210> 174
<211> 513
<212> PRT
<213> Homo sapiens

<400> 174

```
Met Pro Gly Leu Gly Arg Arg Ala Gln Trp Leu Cys Trp Trp Trp Gly
1               5                   10                  15

Leu Leu Cys Ser Cys Cys Gly Pro Pro Pro Leu Arg Pro Pro Leu Pro
            20                  25                  30

Ala Ala Ala Ala Ala Ala Ala Gly Gly Gln Leu Leu Gly Asp Gly Gly
        35                  40                  45

Ser Pro Gly Arg Thr Glu Gln Pro Pro Pro Ser Pro Gln Ser Ser Ser
    50                  55                  60

Gly Phe Leu Tyr Arg Arg Leu Lys Thr Gln Glu Lys Arg Glu Met Gln
65                  70                  75                  80

Lys Glu Ile Leu Ser Val Leu Gly Leu Pro His Arg Pro Arg Pro Leu
                85                  90                  95

His Gly Leu Gln Gln Pro Gln Pro Pro Ala Leu Arg Gln Gln Glu Glu
            100                 105                 110
```

```
Gln Gln Gln Gln Gln Gln Leu Pro Arg Gly Glu Pro Pro Pro Gly Arg
        115                 120                 125

Leu Lys Ser Ala Pro Leu Phe Met Leu Asp Leu Tyr Asn Ala Leu Ser
    130                 135                 140

Ala Asp Asn Asp Glu Asp Gly Ala Ser Glu Gly Glu Arg Gln Gln Ser
145                 150                 155                 160

Trp Pro His Glu Ala Ala Ser Ser Ser Gln Arg Arg Gln Pro Pro Pro
                165                 170                 175

Gly Ala Ala His Pro Leu Asn Arg Lys Ser Leu Leu Ala Pro Gly Ser
            180                 185                 190

Gly Ser Gly Gly Ala Ser Pro Leu Thr Ser Ala Gln Asp Ser Ala Phe
        195                 200                 205

Leu Asn Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu Tyr
    210                 215                 220

Asp Lys Glu Phe Ser Pro Arg Gln Arg His His Lys Glu Phe Lys Phe
225                 230                 235                 240

Asn Leu Ser Gln Ile Pro Glu Gly Glu Val Val Thr Ala Ala Glu Phe
                245                 250                 255

Arg Ile Tyr Lys Asp Cys Val Met Gly Ser Phe Lys Asn Gln Thr Phe
            260                 265                 270

Leu Ile Ser Ile Tyr Gln Val Leu Gln Glu His Gln His Arg Asp Ser
        275                 280                 285

Asp Leu Phe Leu Leu Asp Thr Arg Val Val Trp Ala Ser Glu Glu Gly
    290                 295                 300

Trp Leu Glu Phe Asp Ile Thr Ala Thr Ser Asn Leu Trp Val Val Thr
305                 310                 315                 320

Pro Gln His Asn Met Gly Leu Gln Leu Ser Val Val Thr Arg Asp Gly
                325                 330                 335

Val His Val His Pro Arg Ala Ala Gly Leu Val Gly Arg Asp Gly Pro
            340                 345                 350

Tyr Asp Lys Gln Pro Phe Met Val Ala Phe Phe Lys Val Ser Glu Val
        355                 360                 365

His Val Arg Thr Thr Arg Ser Ala Ser Ser Arg Arg Arg Gln Gln Ser
    370                 375                 380
```

```
Arg Asn Arg Ser Thr Gln Ser Gln Asp Val Ala Arg Val Ser Ser Ala
385                 390                 395                 400

Ser Asp Tyr Asn Ser Ser Glu Leu Lys Thr Ala Cys Arg Lys His Glu
                405                 410                 415

Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala
            420                 425                 430

Pro Lys Gly Tyr Ala Ala Asn Tyr Cys Asp Gly Glu Cys Ser Phe Pro
        435                 440                 445

Leu Asn Ala His Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu
    450                 455                 460

Val His Leu Met Asn Pro Glu Tyr Val Pro Lys Pro Cys Cys Ala Pro
465                 470                 475                 480

Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Asn Ser Asn
                485                 490                 495

Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys
            500                 505                 510

His
```

<210> 175
<211> 431
<212> PRT
<213> Homo sapiens

<400> 175

```
Met His Val Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala
1               5                   10                  15

Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser
            20                  25                  30

Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser
        35                  40                  45

Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu
    50                  55                  60

Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro
65                  70                  75                  80

Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly
                85                  90                  95

Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser
```

100 105 110

Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr
115 120 125

Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys
130 135 140

Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu
145 150 155 160

Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile
165 170 175

Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile
180 185 190

Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu
195 200 205

Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu
210 215 220

Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg
225 230 235 240

His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser
245 250 255

Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn
260 265 270

Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe
275 280 285

Arg Ser Ile Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser
290 295 300

Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu
305 310 315 320

Asn Ser Ser Ser Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr
325 330 335

Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu
340 345 350

Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn
355 360 365

Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His

370 375 380

Phe Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln
385 390 395 400

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile
405 410 415

Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys His
420 425 430

<210> 176
<211> 402
<212> PRT
<213> Homo sapiens

<400> 176

Met Thr Ala Leu Pro Gly Pro Leu Trp Leu Leu Gly Leu Ala Leu Cys
1 5 10 15

Ala Leu Gly Gly Gly Gly Pro Gly Leu Arg Pro Pro Pro Gly Cys Pro
20 25 30

Gln Arg Arg Leu Gly Ala Arg Glu Arg Arg Asp Val Gln Arg Glu Ile
35 40 45

Leu Ala Val Leu Gly Leu Pro Gly Arg Pro Arg Pro Arg Ala Pro Pro
50 55 60

Ala Ala Ser Arg Leu Pro Ala Ser Ala Pro Leu Phe Met Leu Asp Leu
65 70 75 80

Tyr His Ala Met Ala Gly Asp Asp Asp Glu Asp Gly Ala Pro Ala Glu
85 90 95

Arg Arg Leu Gly Arg Ala Asp Leu Val Met Ser Phe Val Asn Met Val
100 105 110

Glu Arg Asp Arg Ala Leu Gly His Gln Glu Pro His Trp Lys Glu Phe
115 120 125

Arg Phe Asp Leu Thr Gln Ile Pro Ala Gly Glu Ala Val Thr Ala Ala
130 135 140

Glu Phe Arg Ile Tyr Lys Val Pro Ser Ile His Leu Leu Asn Arg Thr
145 150 155 160

Leu His Val Ser Met Phe Gln Val Val Gln Glu Gln Ser Asn Arg Glu
165 170 175

Ser Asp Leu Phe Phe Leu Asp Leu Gln Thr Leu Arg Ala Gly Asp Glu
180 185 190

```
Gly Trp Leu Val Leu Asp Val Thr Ala Ala Ser Asp Cys Trp Leu Leu
        195                 200                 205

Lys Arg His Lys Asp Leu Gly Leu Arg Leu Tyr Val Glu Thr Glu Asp
    210                 215                 220

Gly His Ser Val Asp Pro Gly Leu Ala Gly Leu Leu Gly Gln Arg Ala
225                 230                 235                 240

Pro Arg Ser Gln Gln Pro Phe Val Val Thr Phe Phe Arg Ala Ser Pro
                245                 250                 255

Ser Pro Ile Arg Thr Pro Arg Ala Val Arg Pro Leu Arg Arg Arg Gln
            260                 265                 270

Pro Lys Lys Ser Asn Glu Leu Pro Gln Ala Asn Arg Leu Pro Gly Ile
        275                 280                 285

Phe Asp Asp Val His Gly Ser His Gly Arg Gln Val Cys Arg Arg His
    290                 295                 300

Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Leu Asp Trp Val Ile
305                 310                 315                 320

Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys Ser Phe
                325                 330                 335

Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu Gln Ser
            340                 345                 350

Leu Val His Leu Met Met Pro Asp Ala Val Pro Lys Ala Cys Cys Ala
        355                 360                 365

Pro Thr Lys Leu Ser Ala Thr Ser Val Leu Tyr Tyr Asp Ser Ser Asn
    370                 375                 380

Asn Val Ile Leu Arg Lys His Arg Asn Met Val Val Lys Ala Cys Gly
385                 390                 395                 400

Cys His
```

<210> 177
<211> 372
<212> PRT
<213> Homo sapiens

<400> 177

```
Met Pro Pro Pro Gln Gln Gly Pro Cys Gly His His Leu Leu Leu Leu
1               5                   10                  15
```

```
Leu Ala Leu Leu Leu Pro Ser Leu Pro Leu Thr Arg Ala Pro Val Pro
            20                  25                  30

Pro Gly Pro Ala Ala Ala Leu Leu Gln Ala Leu Gly Leu Arg Asp Glu
        35                  40                  45

Pro Gln Gly Ala Pro Arg Leu Arg Pro Val Pro Pro Val Met Trp Arg
    50                  55                  60

Leu Phe Arg Arg Arg Asp Pro Gln Glu Thr Arg Ser Gly Ser Arg Arg
65                  70                  75                  80

Thr Ser Pro Gly Val Thr Leu Gln Pro Cys His Val Glu Glu Leu Gly
                85                  90                  95

Val Ala Gly Asn Ile Val Arg His Ile Pro Asp Arg Gly Ala Pro Thr
            100                 105                 110

Arg Ala Ser Glu Pro Ala Ser Ala Ala Gly His Cys Pro Glu Trp Thr
        115                 120                 125

Val Val Phe Asp Leu Ser Ala Val Glu Pro Ala Glu Arg Pro Ser Arg
    130                 135                 140

Ala Arg Leu Glu Leu Arg Phe Ala Ala Ala Ala Ala Ala Ala Pro Glu
145                 150                 155                 160

Gly Gly Trp Glu Leu Ser Val Ala Gln Ala Gly Gln Gly Ala Gly Ala
                165                 170                 175

Asp Pro Gly Pro Val Leu Leu Arg Gln Leu Val Pro Ala Leu Gly Pro
            180                 185                 190

Pro Val Arg Ala Glu Leu Leu Gly Ala Ala Trp Ala Arg Asn Ala Ser
        195                 200                 205

Trp Pro Arg Ser Leu Arg Leu Ala Leu Ala Leu Arg Pro Arg Ala Pro
    210                 215                 220

Ala Ala Cys Ala Arg Leu Ala Glu Ala Ser Leu Leu Leu Val Thr Leu
225                 230                 235                 240

Asp Pro Arg Leu Cys His Pro Leu Ala Arg Pro Arg Arg Asp Ala Glu
                245                 250                 255

Pro Val Leu Gly Gly Gly Pro Gly Gly Ala Cys Arg Ala Arg Arg Leu
            260                 265                 270

Tyr Val Ser Phe Arg Glu Val Gly Trp His Arg Trp Val Ile Ala Pro
        275                 280                 285
```

```
Arg Gly Phe Leu Ala Asn Tyr Cys Gln Gly Gln Cys Ala Leu Pro Val
    290                 295                 300

Ala Leu Ser Gly Ser Gly Gly Pro Pro Ala Leu Asn His Ala Val Leu
305                 310                 315                 320

Arg Ala Leu Met His Ala Ala Ala Pro Gly Ala Ala Asp Leu Pro Cys
                325                 330                 335

Cys Val Pro Ala Arg Leu Ser Pro Ile Ser Val Leu Phe Phe Asp Asn
            340                 345                 350

Ser Asp Asn Val Val Leu Arg Gln Tyr Glu Asp Met Val Val Asp Glu
        355                 360                 365

Cys Gly Cys Arg
    370


<210>  178
<211>  429
<212>  PRT
<213>  Homo sapiens

<400>  178

Met Cys Pro Gly Ala Leu Trp Val Ala Leu Pro Leu Leu Ser Leu Leu
1               5                   10                  15

Ala Gly Ser Leu Gln Gly Lys Pro Leu Gln Ser Trp Gly Arg Gly Ser
            20                  25                  30

Ala Gly Gly Asn Ala His Ser Pro Leu Gly Val Pro Gly Gly Gly Leu
        35                  40                  45

Pro Glu His Thr Phe Asn Leu Lys Met Phe Leu Glu Asn Val Lys Val
    50                  55                  60

Asp Phe Leu Arg Ser Leu Asn Leu Ser Gly Val Pro Ser Gln Asp Lys
65                  70                  75                  80

Thr Arg Val Glu Pro Pro Gln Tyr Met Ile Asp Leu Tyr Asn Arg Tyr
                85                  90                  95

Thr Ser Asp Lys Ser Thr Thr Pro Ala Ser Asn Ile Val Arg Ser Phe
            100                 105                 110

Ser Met Glu Asp Ala Ile Ser Ile Thr Ala Thr Glu Asp Phe Pro Phe
        115                 120                 125

Gln Lys His Ile Leu Leu Phe Asn Ile Ser Ile Pro Arg His Glu Gln
    130                 135                 140
```

```
Ile Thr Arg Ala Glu Leu Arg Leu Tyr Val Ser Cys Gln Asn His Val
145                 150                 155                 160

Asp Pro Ser His Asp Leu Lys Gly Ser Val Val Ile Tyr Asp Val Leu
                165                 170                 175

Asp Gly Thr Asp Ala Trp Asp Ser Ala Thr Glu Thr Lys Thr Phe Leu
            180                 185                 190

Val Ser Gln Asp Ile Gln Asp Glu Gly Trp Glu Thr Leu Glu Val Ser
        195                 200                 205

Ser Ala Val Lys Arg Trp Val Arg Ser Asp Ser Thr Lys Ser Lys Asn
    210                 215                 220

Lys Leu Glu Val Thr Val Glu Ser His Arg Lys Gly Cys Asp Thr Leu
225                 230                 235                 240

Asp Ile Ser Val Pro Pro Gly Ser Arg Asn Leu Pro Phe Phe Val Val
                245                 250                 255

Phe Ser Asn Asp His Ser Ser Gly Thr Lys Glu Thr Arg Leu Glu Leu
            260                 265                 270

Arg Glu Met Ile Ser His Glu Gln Glu Ser Val Leu Lys Lys Leu Ser
        275                 280                 285

Lys Asp Gly Ser Thr Glu Ala Gly Glu Ser Ser His Glu Glu Asp Thr
    290                 295                 300

Asp Gly His Val Ala Ala Gly Ser Thr Leu Ala Arg Arg Lys Arg Ser
305                 310                 315                 320

Ala Gly Ala Gly Ser His Cys Gln Lys Thr Ser Leu Arg Val Asn Phe
                325                 330                 335

Glu Asp Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Lys Glu Tyr Glu
            340                 345                 350

Ala Tyr Glu Cys Lys Gly Gly Cys Phe Phe Pro Leu Ala Asp Asp Val
        355                 360                 365

Thr Pro Thr Lys His Ala Ile Val Gln Thr Leu Val His Leu Lys Phe
    370                 375                 380

Pro Thr Lys Val Gly Lys Ala Cys Cys Val Pro Thr Lys Leu Ser Pro
385                 390                 395                 400

Ile Ser Val Leu Tyr Lys Asp Asp Met Gly Val Pro Thr Leu Lys Tyr
                405                 410                 415
```

His Tyr Glu Gly Met Ser Val Ala Glu Cys Gly Cys Arg
420 425

<210> 179
<211> 424
<212> PRT
<213> Homo sapiens

<400> 179

Met Gly Ser Leu Val Leu Thr Leu Cys Ala Leu Phe Cys Leu Ala Ala
1 5 10 15

Tyr Leu Val Ser Gly Ser Pro Ile Met Asn Leu Glu Gln Ser Pro Leu
20 25 30

Glu Glu Asp Met Ser Leu Phe Gly Asp Val Phe Ser Glu Gln Asp Gly
35 40 45

Val Asp Phe Asn Thr Leu Leu Gln Ser Met Lys Asp Glu Phe Leu Lys
50 55 60

Thr Leu Asn Leu Ser Asp Ile Pro Thr Gln Asp Ser Ala Lys Val Asp
65 70 75 80

Pro Pro Glu Tyr Met Leu Glu Leu Tyr Asn Lys Phe Ala Thr Asp Arg
85 90 95

Thr Ser Met Pro Ser Ala Asn Ile Ile Arg Ser Phe Lys Asn Glu Asp
100 105 110

Leu Phe Ser Gln Pro Val Ser Phe Asn Gly Leu Arg Lys Tyr Pro Leu
115 120 125

Leu Phe Asn Val Ser Ile Pro His His Glu Glu Val Ile Met Ala Glu
130 135 140

Leu Arg Leu Tyr Thr Leu Val Gln Arg Asp Arg Met Ile Tyr Asp Gly
145 150 155 160

Val Asp Arg Lys Ile Thr Ile Phe Glu Val Leu Glu Ser Lys Gly Asp
165 170 175

Asn Glu Gly Glu Arg Asn Met Leu Val Leu Val Ser Gly Glu Ile Tyr
180 185 190

Gly Thr Asn Ser Glu Trp Glu Thr Phe Asp Val Thr Asp Ala Ile Arg
195 200 205

Arg Trp Gln Lys Ser Gly Ser Ser Thr His Gln Leu Glu Val His Ile
210 215 220

Glu Ser Lys His Asp Glu Ala Glu Asp Ala Ser Ser Gly Arg Leu Glu

225 230 235 240

Ile Asp Thr Ser Ala Gln Asn Lys His Asn Pro Leu Leu Ile Val Phe
245 250 255

Ser Asp Asp Gln Ser Ser Asp Lys Glu Arg Lys Glu Glu Leu Asn Glu
260 265 270

Met Ile Ser His Glu Gln Leu Pro Glu Leu Asp Asn Leu Gly Leu Asp
275 280 285

Ser Phe Ser Ser Gly Pro Gly Glu Glu Ala Leu Leu Gln Met Arg Ser
290 295 300

Asn Ile Ile Tyr Asp Ser Thr Ala Arg Ile Arg Arg Asn Ala Lys Gly
305 310 315 320

Asn Tyr Cys Lys Arg Thr Pro Leu Tyr Ile Asp Phe Lys Glu Ile Gly
325 330 335

Trp Asp Ser Trp Ile Ile Ala Pro Pro Gly Tyr Glu Ala Tyr Glu Cys
340 345 350

Arg Gly Val Cys Asn Tyr Pro Leu Ala Glu His Leu Thr Pro Thr Lys
355 360 365

His Ala Ile Ile Gln Ala Leu Val His Leu Lys Asn Ser Gln Lys Ala
370 375 380

Ser Lys Ala Cys Cys Val Pro Thr Lys Leu Glu Pro Ile Ser Ile Leu
385 390 395 400

Tyr Leu Asp Lys Gly Val Val Thr Tyr Lys Phe Lys Tyr Glu Gly Met
405 410 415

Ala Val Ser Glu Cys Gly Cys Arg
420

<210> 180
<211> 450
<212> PRT
<213> Homo sapiens

<400> 180

Met Asp Leu Ser Ala Ala Ala Ala Leu Cys Leu Trp Leu Leu Ser Ala
1 5 10 15

Cys Arg Pro Arg Asp Gly Leu Glu Ala Ala Ala Val Leu Arg Ala Ala
20 25 30

Gly Ala Gly Pro Val Arg Ser Pro Gly Gly Gly Gly Gly Gly Gly Gly
35 40 45

```
Gly Gly Arg Thr Leu Ala Gln Ala Ala Gly Ala Ala Ala Val Pro Ala
    50                  55                  60

Ala Ala Val Pro Arg Ala Arg Ala Ala Arg Arg Ala Ala Gly Ser Gly
65                  70                  75                  80

Phe Arg Asn Gly Ser Val Val Pro His His Phe Met Met Ser Leu Tyr
                85                  90                  95

Arg Ser Leu Ala Gly Arg Ala Pro Ala Gly Ala Ala Ala Val Ser Ala
            100                 105                 110

Ser Gly His Gly Arg Ala Asp Thr Ile Thr Gly Phe Thr Asp Gln Ala
        115                 120                 125

Thr Gln Asp Glu Ser Ala Ala Glu Thr Gly Gln Ser Phe Leu Phe Asp
    130                 135                 140

Val Ser Ser Leu Asn Asp Ala Asp Glu Val Val Gly Ala Glu Leu Arg
145                 150                 155                 160

Val Leu Arg Arg Gly Ser Pro Glu Ser Gly Pro Gly Ser Trp Thr Ser
                165                 170                 175

Pro Pro Leu Leu Leu Leu Ser Thr Cys Pro Gly Ala Ala Arg Ala Pro
            180                 185                 190

Arg Leu Leu Tyr Ser Arg Ala Ala Glu Pro Leu Val Gly Gln Arg Trp
        195                 200                 205

Glu Ala Phe Asp Val Ala Asp Ala Met Arg Arg His Arg Arg Glu Pro
    210                 215                 220

Arg Pro Pro Arg Ala Phe Cys Leu Leu Leu Arg Ala Val Ala Gly Pro
225                 230                 235                 240

Val Pro Ser Pro Leu Ala Leu Arg Arg Leu Gly Phe Gly Trp Pro Gly
                245                 250                 255

Gly Gly Gly Ser Ala Ala Glu Glu Arg Ala Val Leu Val Val Ser Ser
            260                 265                 270

Arg Thr Gln Arg Lys Glu Ser Leu Phe Arg Glu Ile Arg Ala Gln Ala
        275                 280                 285

Arg Ala Leu Gly Ala Ala Leu Ala Ser Glu Pro Leu Pro Asp Pro Gly
    290                 295                 300

Thr Gly Thr Ala Ser Pro Arg Ala Val Ile Gly Gly Arg Arg Arg Arg
305                 310                 315                 320
```

```
Arg Thr Ala Leu Ala Gly Thr Arg Thr Ala Gln Gly Ser Gly Gly Gly
                325                 330                 335

Ala Gly Arg Gly His Gly Arg Arg Gly Arg Ser Arg Cys Ser Arg Lys
            340                 345                 350

Pro Leu His Val Asp Phe Lys Glu Leu Gly Trp Asp Asp Trp Ile Ile
        355                 360                 365

Ala Pro Leu Asp Tyr Glu Ala Tyr His Cys Glu Gly Leu Cys Asp Phe
    370                 375                 380

Pro Leu Arg Ser His Leu Glu Pro Thr Asn His Ala Ile Ile Gln Thr
385                 390                 395                 400

Leu Leu Asn Ser Met Ala Pro Asp Ala Ala Pro Ala Ser Cys Cys Val
                405                 410                 415

Pro Ala Arg Leu Ser Pro Ile Ser Ile Leu Tyr Ile Asp Ala Ala Asn
            420                 425                 430

Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu Ala Cys Gly
        435                 440                 445

Cys Arg
    450
```

<210> 181
<211> 392
<212> PRT
<213> Homo sapiens

<400> 181

```
Met Val Leu Leu Ser Ile Leu Arg Ile Leu Phe Leu Cys Glu Leu Val
1               5                   10                  15

Leu Phe Met Glu His Arg Ala Gln Met Ala Glu Gly Gly Gln Ser Ser
            20                  25                  30

Ile Ala Leu Leu Ala Glu Ala Pro Thr Leu Pro Leu Ile Glu Glu Leu
        35                  40                  45

Leu Glu Glu Ser Pro Gly Glu Gln Pro Arg Lys Pro Arg Leu Leu Gly
    50                  55                  60

His Ser Leu Arg Tyr Met Leu Glu Leu Tyr Arg Arg Ser Ala Asp Ser
65                  70                  75                  80

His Gly His Pro Arg Glu Asn Arg Thr Ile Gly Ala Thr Met Val Arg
                85                  90                  95
```

```
Leu Val Lys Pro Leu Thr Asn Val Ala Arg Pro His Arg Gly Thr Trp
            100                 105                 110

His Ile Gln Ile Leu Gly Phe Pro Leu Arg Pro Asn Arg Gly Leu Tyr
        115                 120                 125

Gln Leu Val Arg Ala Thr Val Val Tyr Arg His His Leu Gln Leu Thr
    130                 135                 140

Arg Phe Asn Leu Ser Cys His Val Glu Pro Trp Val Gln Lys Asn Pro
145                 150                 155                 160

Thr Asn His Phe Pro Ser Ser Glu Gly Asp Ser Ser Lys Pro Ser Leu
                165                 170                 175

Met Ser Asn Ala Trp Lys Glu Met Asp Ile Thr Gln Leu Val Gln Gln
            180                 185                 190

Arg Phe Trp Asn Asn Lys Gly His Arg Ile Leu Arg Leu Arg Phe Met
        195                 200                 205

Cys Gln Gln Gln Lys Asp Ser Gly Gly Leu Glu Leu Trp His Gly Thr
    210                 215                 220

Ser Ser Leu Asp Ile Ala Phe Leu Leu Leu Tyr Phe Asn Asp Thr His
225                 230                 235                 240

Lys Ser Ile Arg Lys Ala Lys Phe Leu Pro Arg Gly Met Glu Glu Phe
                245                 250                 255

Met Glu Arg Glu Ser Leu Leu Arg Arg Thr Arg Gln Ala Asp Gly Ile
            260                 265                 270

Ser Ala Glu Val Thr Ala Ser Ser Ser Lys His Ser Gly Pro Glu Asn
        275                 280                 285

Asn Gln Cys Ser Leu His Pro Phe Gln Ile Ser Phe Arg Gln Leu Gly
    290                 295                 300

Trp Asp His Trp Ile Ile Ala Pro Pro Phe Tyr Thr Pro Asn Tyr Cys
305                 310                 315                 320

Lys Gly Thr Cys Leu Arg Val Leu Arg Asp Gly Leu Asn Ser Pro Asn
                325                 330                 335

His Ala Ile Ile Gln Asn Leu Ile Asn Gln Leu Val Asp Gln Ser Val
            340                 345                 350

Pro Arg Pro Ser Cys Val Pro Tyr Lys Tyr Val Pro Ile Ser Val Leu
        355                 360                 365
```

Met Ile Glu Ala Asn Gly Ser Ile Leu Tyr Lys Glu Tyr Glu Gly Met
370 375 380

Ile Ala Glu Ser Cys Thr Cys Arg
385 390

<210> 182
<211> 366
<212> PRT
<213> Homo sapiens

<400> 182

Met Gln Pro Leu Trp Leu Cys Trp Ala Leu Trp Val Leu Pro Leu Ala
1 5 10 15

Ser Pro Gly Ala Ala Leu Thr Gly Glu Gln Leu Leu Gly Ser Leu Leu
20 25 30

Arg Gln Leu Gln Leu Lys Glu Val Pro Thr Leu Asp Arg Ala Asp Met
35 40 45

Glu Glu Leu Val Ile Pro Thr His Val Arg Ala Gln Tyr Val Ala Leu
50 55 60

Leu Gln Arg Ser His Gly Asp Arg Ser Arg Gly Lys Arg Phe Ser Gln
65 70 75 80

Ser Phe Arg Glu Val Ala Gly Arg Phe Leu Ala Leu Glu Ala Ser Thr
85 90 95

His Leu Leu Val Phe Gly Met Glu Gln Arg Leu Pro Pro Asn Ser Glu
100 105 110

Leu Val Gln Ala Val Leu Arg Leu Phe Gln Glu Pro Val Pro Lys Ala
115 120 125

Ala Leu His Arg His Gly Arg Leu Ser Pro Arg Ser Ala Arg Ala Arg
130 135 140

Val Thr Val Glu Trp Leu Arg Val Arg Asp Asp Gly Ser Asn Arg Thr
145 150 155 160

Ser Leu Ile Asp Ser Arg Leu Val Ser Val His Glu Ser Gly Trp Lys
165 170 175

Ala Phe Asp Val Thr Glu Ala Val Asn Phe Trp Gln Gln Leu Ser Arg
180 185 190

Pro Arg Gln Pro Leu Leu Leu Gln Val Ser Val Gln Arg Glu His Leu
195 200 205

```
Gly Pro Leu Ala Ser Gly Ala His Lys Leu Val Arg Phe Ala Ser Gln
    210                 215                 220

Gly Ala Pro Ala Gly Leu Gly Glu Pro Gln Leu Glu Leu His Thr Leu
225                 230                 235                 240

Asp Leu Gly Asp Tyr Gly Ala Gln Gly Asp Cys Asp Pro Glu Ala Pro
                245                 250                 255

Met Thr Glu Gly Thr Arg Cys Cys Arg Gln Glu Met Tyr Ile Asp Leu
            260                 265                 270

Gln Gly Met Lys Trp Ala Glu Asn Trp Val Leu Glu Pro Pro Gly Phe
        275                 280                 285

Leu Ala Tyr Glu Cys Val Gly Thr Cys Arg Gln Pro Pro Glu Ala Leu
    290                 295                 300

Ala Phe Lys Trp Pro Phe Leu Gly Pro Arg Gln Cys Ile Ala Ser Glu
305                 310                 315                 320

Thr Ala Ser Leu Pro Met Ile Val Ser Ile Lys Glu Gly Gly Arg Thr
                325                 330                 335

Arg Pro Gln Val Val Ser Leu Pro Asn Met Arg Val Gln Lys Cys Ser
            340                 345                 350

Cys Ala Ser Asp Gly Ala Leu Val Pro Arg Arg Leu Gln Pro
        355                 360                 365


<210>  183
<211>  366
<212>  PRT
<213>  Homo sapiens

<400>  183

Met Trp Pro Leu Trp Leu Cys Trp Ala Leu Trp Val Leu Pro Leu Ala
1               5                   10                  15

Gly Pro Gly Ala Ala Leu Thr Glu Glu Gln Leu Leu Gly Ser Leu Leu
            20                  25                  30

Arg Gln Leu Gln Leu Ser Glu Val Pro Val Leu Asp Arg Ala Asp Met
        35                  40                  45

Glu Lys Leu Val Ile Pro Ala His Val Arg Ala Gln Tyr Val Val Leu
    50                  55                  60

Leu Arg Arg Ser His Gly Asp Arg Ser Arg Gly Lys Arg Phe Ser Gln
65                  70                  75                  80

Ser Phe Arg Glu Val Ala Gly Arg Phe Leu Ala Ser Glu Ala Ser Thr
```

85 90 95

His Leu Leu Val Phe Gly Met Glu Gln Arg Leu Pro Pro Asn Ser Glu
100 105 110

Leu Val Gln Ala Val Leu Arg Leu Phe Gln Glu Pro Val Pro Lys Ala
115 120 125

Ala Leu His Arg His Gly Arg Leu Ser Pro Arg Ser Ala Gln Ala Arg
130 135 140

Val Thr Val Glu Trp Leu Arg Val Arg Asp Asp Gly Ser Asn Arg Thr
145 150 155 160

Ser Leu Ile Asp Ser Arg Leu Val Ser Val His Glu Ser Gly Trp Lys
165 170 175

Ala Phe Asp Val Thr Glu Ala Val Asn Phe Trp Gln Gln Leu Ser Arg
180 185 190

Pro Arg Gln Pro Leu Leu Leu Gln Val Ser Val Gln Arg Glu His Leu
195 200 205

Gly Pro Leu Ala Ser Gly Ala His Lys Leu Val Arg Phe Ala Ser Gln
210 215 220

Gly Ala Pro Ala Gly Leu Gly Glu Pro Gln Leu Glu Leu His Thr Leu
225 230 235 240

Asp Leu Arg Asp Tyr Gly Ala Gln Gly Asp Cys Asp Pro Glu Ala Pro
245 250 255

Met Thr Glu Gly Thr Arg Cys Cys Arg Gln Glu Met Tyr Ile Asp Leu
260 265 270

Gln Gly Met Lys Trp Ala Lys Asn Trp Val Leu Glu Pro Pro Gly Phe
275 280 285

Leu Ala Tyr Glu Cys Val Gly Thr Cys Gln Gln Pro Pro Glu Ala Leu
290 295 300

Ala Phe Asn Trp Pro Phe Leu Gly Pro Arg Gln Cys Ile Ala Ser Glu
305 310 315 320

Thr Ala Ser Leu Pro Met Ile Val Ser Ile Lys Glu Gly Gly Arg Thr
325 330 335

Arg Pro Gln Val Val Ser Leu Pro Asn Met Arg Val Gln Lys Cys Ser
340 345 350

Cys Ala Ser Asp Gly Ala Leu Val Pro Arg Arg Leu Gln Pro

355 360 365

<210> 184
<211> 366
<212> PRT
<213> Homo sapiens

<400> 184

Met Val Leu His Leu Leu Leu Phe Leu Leu Leu Thr Pro Gln Gly Gly
1 5 10 15

His Ser Cys Gln Gly Leu Glu Leu Ala Arg Glu Leu Val Leu Ala Lys
20 25 30

Val Arg Ala Leu Phe Leu Asp Ala Leu Gly Pro Pro Ala Val Thr Arg
35 40 45

Glu Gly Gly Asp Pro Gly Val Arg Arg Leu Pro Arg Arg His Ala Leu
50 55 60

Gly Gly Phe Thr His Arg Gly Ser Glu Pro Glu Glu Glu Glu Asp Val
65 70 75 80

Ser Gln Ala Ile Leu Phe Pro Ala Thr Asp Ala Ser Cys Glu Asp Lys
85 90 95

Ser Ala Ala Arg Gly Leu Ala Gln Glu Ala Glu Glu Gly Leu Phe Arg
100 105 110

Tyr Met Phe Arg Pro Ser Gln His Thr Arg Ser Arg Gln Val Thr Ser
115 120 125

Ala Gln Leu Trp Phe His Thr Gly Leu Asp Arg Gln Gly Thr Ala Ala
130 135 140

Ser Asn Ser Ser Glu Pro Leu Leu Gly Leu Leu Ala Leu Ser Pro Gly
145 150 155 160

Gly Pro Val Ala Val Pro Met Ser Leu Gly His Ala Pro Pro His Trp
165 170 175

Ala Val Leu His Leu Ala Thr Ser Ala Leu Ser Leu Leu Thr His Pro
180 185 190

Val Leu Val Leu Leu Leu Arg Cys Pro Leu Cys Thr Cys Ser Ala Arg
195 200 205

Pro Glu Ala Thr Pro Phe Leu Val Ala His Thr Arg Thr Arg Pro Pro
210 215 220

Ser Gly Gly Glu Arg Ala Arg Arg Ser Thr Pro Leu Met Ser Trp Pro
225 230 235 240

```
Trp Ser Pro Ser Ala Leu Arg Leu Leu Gln Arg Pro Pro Glu Glu Pro
                245                 250                 255

Ala Ala His Ala Asn Cys His Arg Val Ala Leu Asn Ile Ser Phe Gln
            260                 265                 270

Glu Leu Gly Trp Glu Arg Trp Ile Val Tyr Pro Pro Ser Phe Ile Phe
        275                 280                 285

His Tyr Cys His Gly Gly Cys Gly Leu His Ile Pro Pro Asn Leu Ser
    290                 295                 300

Leu Pro Val Pro Gly Ala Pro Pro Thr Pro Ala Gln Pro Tyr Ser Leu
305                 310                 315                 320

Leu Pro Gly Ala Gln Pro Cys Cys Ala Ala Leu Pro Gly Thr Met Arg
                325                 330                 335

Pro Leu His Val Arg Thr Thr Ser Asp Gly Gly Tyr Ser Phe Lys Tyr
            340                 345                 350

Glu Thr Val Pro Asn Leu Leu Thr Gln His Cys Ala Cys Ile
        355                 360                 365


<210>  185
<211>  426
<212>  PRT
<213>  Homo sapiens

<400>  185

Met Pro Leu Leu Trp Leu Arg Gly Phe Leu Leu Ala Ser Cys Trp Ile
1               5                   10                  15

Ile Val Arg Ser Ser Pro Thr Pro Gly Ser Glu Gly His Ser Ala Ala
            20                  25                  30

Pro Asp Cys Pro Ser Cys Ala Leu Ala Ala Leu Pro Lys Asp Val Pro
        35                  40                  45

Asn Ser Gln Pro Glu Met Val Glu Ala Val Lys Lys His Ile Leu Asn
    50                  55                  60

Met Leu His Leu Lys Lys Arg Pro Asp Val Thr Gln Pro Val Pro Lys
65                  70                  75                  80

Ala Ala Leu Leu Asn Ala Ile Arg Lys Leu His Val Gly Lys Val Gly
                85                  90                  95

Glu Asn Gly Tyr Val Glu Ile Glu Asp Asp Ile Gly Arg Arg Ala Glu
            100                 105                 110
```

```
Met Asn Glu Leu Met Glu Gln Thr Ser Glu Ile Ile Thr Phe Ala Glu
        115                 120                 125

Ser Gly Thr Ala Arg Lys Thr Leu His Phe Glu Ile Ser Lys Glu Gly
    130                 135                 140

Ser Asp Leu Ser Val Val Glu Arg Ala Glu Val Trp Leu Phe Leu Lys
145                 150                 155                 160

Val Pro Lys Ala Asn Arg Thr Arg Thr Lys Val Thr Ile Arg Leu Phe
                165                 170                 175

Gln Gln Gln Lys His Pro Gln Gly Ser Leu Asp Thr Gly Glu Glu Ala
            180                 185                 190

Glu Glu Val Gly Leu Lys Gly Glu Arg Ser Glu Leu Leu Leu Ser Glu
        195                 200                 205

Lys Val Val Asp Ala Arg Lys Ser Thr Trp His Val Phe Pro Val Ser
    210                 215                 220

Ser Ser Ile Gln Arg Leu Leu Asp Gln Gly Lys Ser Ser Leu Asp Val
225                 230                 235                 240

Arg Ile Ala Cys Glu Gln Cys Gln Glu Ser Gly Ala Ser Leu Val Leu
                245                 250                 255

Leu Gly Lys Lys Lys Lys Lys Glu Glu Glu Gly Glu Gly Lys Lys Lys
            260                 265                 270

Gly Gly Gly Glu Gly Gly Ala Gly Ala Asp Glu Glu Lys Glu Gln Ser
        275                 280                 285

His Arg Pro Phe Leu Met Leu Gln Ala Arg Gln Ser Glu Asp His Pro
    290                 295                 300

His Arg Arg Arg Arg Arg Gly Leu Glu Cys Asp Gly Lys Val Asn Ile
305                 310                 315                 320

Cys Cys Lys Lys Gln Phe Phe Val Ser Phe Lys Asp Ile Gly Trp Asn
                325                 330                 335

Asp Trp Ile Ile Ala Pro Ser Gly Tyr His Ala Asn Tyr Cys Glu Gly
            340                 345                 350

Glu Cys Pro Ser His Ile Ala Gly Thr Ser Gly Ser Ser Leu Ser Phe
        355                 360                 365

His Ser Thr Val Ile Asn His Tyr Arg Met Arg Gly His Ser Pro Phe
    370                 375                 380
```

```
Ala Asn Leu Lys Ser Cys Cys Val Pro Thr Lys Leu Arg Pro Met Ser
385                 390                 395                 400


Met Leu Tyr Tyr Asp Asp Gly Gln Asn Ile Ile Lys Lys Asp Ile Gln
                405                 410                 415


Asn Met Ile Val Glu Glu Cys Gly Cys Ser
            420                 425


<210>  186
<211>  407
<212>  PRT
<213>  Homo sapiens

<400>  186

Met Asp Gly Leu Pro Gly Arg Ala Leu Gly Ala Ala Cys Leu Leu Leu
1               5                   10                  15


Leu Ala Ala Gly Trp Leu Gly Pro Glu Ala Trp Gly Ser Pro Thr Pro
            20                  25                  30


Pro Pro Thr Pro Ala Ala Pro Pro Pro Pro Pro Pro Pro Gly Ser Pro
        35                  40                  45


Gly Gly Ser Gln Asp Thr Cys Thr Ser Cys Gly Gly Phe Arg Arg Pro
    50                  55                  60


Glu Glu Leu Gly Arg Val Asp Gly Asp Phe Leu Glu Ala Val Lys Arg
65                  70                  75                  80


His Ile Leu Ser Arg Leu Gln Met Arg Gly Arg Pro Asn Ile Thr His
                85                  90                  95


Ala Val Pro Lys Ala Ala Met Val Thr Ala Leu Arg Lys Leu His Ala
            100                 105                 110


Gly Lys Val Arg Glu Asp Gly Arg Val Glu Ile Pro His Leu Asp Gly
        115                 120                 125


His Ala Ser Pro Gly Ala Asp Gly Gln Glu Arg Val Ser Glu Ile Ile
    130                 135                 140


Ser Phe Ala Glu Thr Asp Gly Leu Ala Ser Ser Arg Val Arg Leu Tyr
145                 150                 155                 160


Phe Phe Ile Ser Asn Glu Gly Asn Gln Asn Leu Phe Val Val Gln Ala
                165                 170                 175


Ser Leu Trp Leu Tyr Leu Lys Leu Leu Pro Tyr Val Leu Glu Lys Gly
            180                 185                 190
```

```
Ser Arg Arg Lys Val Arg Val Lys Val Tyr Phe Gln Glu Gln Gly His
        195                 200                 205

Gly Asp Arg Trp Asn Met Val Glu Lys Arg Val Asp Leu Lys Arg Ser
    210                 215                 220

Gly Trp His Thr Phe Pro Leu Thr Glu Ala Ile Gln Ala Leu Phe Glu
225                 230                 235                 240

Arg Gly Glu Arg Arg Leu Asn Leu Asp Val Gln Cys Asp Ser Cys Gln
                245                 250                 255

Glu Leu Ala Val Val Pro Val Phe Val Asp Pro Gly Glu Glu Ser His
            260                 265                 270

Arg Pro Phe Val Val Val Gln Ala Arg Leu Gly Asp Ser Arg His Arg
        275                 280                 285

Ile Arg Lys Arg Gly Leu Glu Cys Asp Gly Arg Thr Asn Leu Cys Cys
    290                 295                 300

Arg Gln Gln Phe Phe Ile Asp Phe Arg Leu Ile Gly Trp Asn Asp Trp
305                 310                 315                 320

Ile Ile Ala Pro Thr Gly Tyr Tyr Gly Asn Tyr Cys Glu Gly Ser Cys
                325                 330                 335

Pro Ala Tyr Leu Ala Gly Val Pro Gly Ser Ala Ser Ser Phe His Thr
            340                 345                 350

Ala Val Val Asn Gln Tyr Arg Met Arg Gly Leu Asn Pro Gly Thr Val
        355                 360                 365

Asn Ser Cys Cys Ile Pro Thr Lys Leu Ser Thr Met Ser Met Leu Tyr
    370                 375                 380

Phe Asp Asp Glu Tyr Asn Ile Val Lys Arg Asp Val Pro Asn Met Ile
385                 390                 395                 400

Val Glu Glu Cys Gly Cys Ala
                405

<210>  187
<211>  267
<212>  PRT
<213>  Homo sapiens

<400>  187

Met His Leu Leu Leu Phe Gln Leu Leu Val Leu Leu Pro Leu Gly Lys
1               5                   10                  15

Thr Thr Arg His Gln Asp Gly Arg Gln Asn Gln Ser Ser Leu Ser Pro
```

20 25 30

Val Leu Leu Pro Arg Asn Gln Arg Glu Leu Pro Thr Gly Asn His Glu
35 40 45

Glu Ala Glu Glu Lys Pro Asp Leu Phe Val Ala Val Pro His Leu Val
50 55 60

Ala Thr Ser Pro Ala Gly Glu Gly Gln Arg Gln Arg Glu Lys Met Leu
65 70 75 80

Ser Arg Phe Gly Arg Phe Trp Lys Lys Pro Glu Arg Glu Met His Pro
85 90 95

Ser Arg Asp Ser Asp Ser Glu Pro Phe Pro Pro Gly Thr Gln Ser Leu
100 105 110

Ile Gln Pro Ile Asp Gly Met Lys Met Glu Lys Ser Pro Leu Arg Glu
115 120 125

Glu Ala Lys Lys Phe Trp His His Phe Met Phe Arg Lys Thr Pro Ala
130 135 140

Ser Gln Gly Val Ile Leu Pro Ile Lys Ser His Glu Val His Trp Glu
145 150 155 160

Thr Cys Arg Thr Val Pro Phe Ser Gln Thr Ile Thr His Glu Gly Cys
165 170 175

Glu Lys Val Val Val Gln Asn Asn Leu Cys Phe Gly Lys Cys Gly Ser
180 185 190

Val His Phe Pro Gly Ala Ala Gln His Ser His Thr Ser Cys Ser His
195 200 205

Cys Leu Pro Ala Lys Phe Thr Thr Met His Leu Pro Leu Asn Cys Thr
210 215 220

Glu Leu Ser Ser Val Ile Lys Val Val Met Leu Val Glu Glu Cys Gln
225 230 235 240

Cys Lys Val Lys Thr Glu His Glu Asp Gly His Ile Leu His Ala Gly
245 250 255

Ser Gln Asp Ser Phe Ile Pro Gly Val Ser Ala
260 265

<210> 188
<211> 1038
<212> PRT
<213> Homo sapiens

<400> 188

```
Met Thr Ser Ser Leu Gln Arg Pro Trp Arg Val Pro Trp Leu Pro Trp
1               5                  10                  15

Thr Ile Leu Leu Val Ser Thr Ala Ala Ala Ser Gln Asn Gln Glu Arg
            20                  25                  30

Leu Cys Ala Phe Lys Asp Pro Tyr Gln Gln Asp Leu Gly Ile Gly Glu
        35                  40                  45

Ser Arg Ile Ser His Glu Asn Gly Thr Ile Leu Cys Ser Lys Gly Ser
    50                  55                  60

Thr Cys Tyr Gly Leu Trp Glu Lys Ser Lys Gly Asp Ile Asn Leu Val
65                  70                  75                  80

Lys Gln Gly Cys Trp Ser His Ile Gly Asp Pro Gln Glu Cys His Tyr
                85                  90                  95

Glu Glu Cys Val Val Thr Thr Thr Pro Pro Ser Ile Gln Asn Gly Thr
            100                 105                 110

Tyr Arg Phe Cys Cys Cys Ser Thr Asp Leu Cys Asn Val Asn Phe Thr
        115                 120                 125

Glu Asn Phe Pro Pro Pro Asp Thr Thr Pro Leu Ser Pro Pro His Ser
    130                 135                 140

Phe Asn Arg Asp Glu Thr Ile Ile Ile Ala Leu Ala Ser Val Ser Val
145                 150                 155                 160

Leu Ala Val Leu Ile Val Ala Leu Cys Phe Gly Tyr Arg Met Leu Thr
                165                 170                 175

Gly Asp Arg Lys Gln Gly Leu His Ser Met Asn Met Met Glu Ala Ala
            180                 185                 190

Ala Ser Glu Pro Ser Leu Asp Leu Asp Asn Leu Lys Leu Leu Glu Leu
        195                 200                 205

Ile Gly Arg Gly Arg Tyr Gly Ala Val Tyr Lys Gly Ser Leu Asp Glu
    210                 215                 220

Arg Pro Val Ala Val Lys Val Phe Ser Phe Ala Asn Arg Gln Asn Phe
225                 230                 235                 240

Ile Asn Glu Lys Asn Ile Tyr Arg Val Pro Leu Met Glu His Asp Asn
                245                 250                 255

Ile Ala Arg Phe Ile Val Gly Asp Glu Arg Val Thr Ala Asp Gly Arg
            260                 265                 270
```

```
Met Glu Tyr Leu Leu Val Met Glu Tyr Tyr Pro Asn Gly Ser Leu Cys
        275                 280                 285

Lys Tyr Leu Ser Leu His Thr Ser Asp Trp Val Ser Ser Cys Arg Leu
    290                 295                 300

Ala His Ser Val Thr Arg Gly Leu Ala Tyr Leu His Thr Glu Leu Pro
305                 310                 315                 320

Arg Gly Asp His Tyr Lys Pro Ala Ile Ser His Arg Asp Leu Asn Ser
                325                 330                 335

Arg Asn Val Leu Val Lys Asn Asp Gly Thr Cys Val Ile Ser Asp Phe
            340                 345                 350

Gly Leu Ser Met Arg Leu Thr Gly Asn Arg Leu Val Arg Pro Gly Glu
        355                 360                 365

Glu Asp Asn Ala Ala Ile Ser Glu Val Gly Thr Ile Arg Tyr Met Ala
    370                 375                 380

Pro Glu Val Leu Glu Gly Ala Val Asn Leu Arg Asp Cys Glu Ser Ala
385                 390                 395                 400

Leu Lys Gln Val Asp Met Tyr Ala Leu Gly Leu Ile Tyr Trp Glu Ile
                405                 410                 415

Phe Met Arg Cys Thr Asp Leu Phe Pro Gly Glu Ser Val Pro Glu Tyr
            420                 425                 430

Gln Met Ala Phe Gln Thr Glu Val Gly Asn His Pro Thr Phe Glu Asp
        435                 440                 445

Met Gln Val Leu Val Ser Arg Glu Lys Gln Arg Pro Lys Phe Pro Glu
    450                 455                 460

Ala Trp Lys Glu Asn Ser Leu Ala Val Arg Ser Leu Lys Glu Thr Ile
465                 470                 475                 480

Glu Asp Cys Trp Asp Gln Asp Ala Glu Ala Arg Leu Thr Ala Gln Cys
                485                 490                 495

Ala Glu Glu Arg Met Ala Glu Leu Met Met Ile Trp Glu Arg Asn Lys
            500                 505                 510

Ser Val Ser Pro Thr Val Asn Pro Met Ser Thr Ala Met Gln Asn Glu
        515                 520                 525

Arg Asn Leu Ser His Asn Arg Arg Val Pro Lys Ile Gly Pro Tyr Pro
    530                 535                 540
```

```
Asp Tyr Ser Ser Ser Ser Tyr Ile Glu Asp Ser Ile His His Thr Asp
545                 550                 555                 560

Ser Ile Val Lys Asn Ile Ser Ser Glu His Ser Met Ser Ser Thr Pro
                565                 570                 575

Leu Thr Ile Gly Glu Lys Asn Arg Asn Ser Ile Asn Tyr Glu Arg Gln
            580                 585                 590

Gln Ala Gln Ala Arg Ile Pro Ser Pro Glu Thr Ser Val Thr Ser Leu
        595                 600                 605

Ser Thr Asn Thr Thr Thr Thr Asn Thr Thr Gly Leu Thr Pro Ser Thr
    610                 615                 620

Gly Met Thr Thr Ile Ser Glu Met Pro Tyr Pro Asp Glu Thr Asn Leu
625                 630                 635                 640

His Thr Thr Asn Val Ala Gln Ser Ile Gly Pro Thr Pro Val Cys Leu
                645                 650                 655

Gln Leu Thr Glu Glu Asp Leu Glu Thr Asn Lys Leu Asp Pro Lys Glu
            660                 665                 670

Val Asp Lys Asn Leu Lys Glu Ser Ser Asp Glu Asn Leu Met Glu His
        675                 680                 685

Ser Leu Lys Gln Phe Ser Gly Pro Asp Pro Leu Ser Ser Thr Ser Ser
    690                 695                 700

Ser Leu Leu Tyr Pro Leu Ile Lys Leu Ala Val Glu Ala Thr Gly Gln
705                 710                 715                 720

Gln Asp Phe Thr Gln Thr Ala Asn Gly Gln Ala Cys Leu Ile Pro Asp
                725                 730                 735

Val Leu Pro Thr Gln Ile Tyr Pro Leu Pro Lys Gln Gln Asn Leu Pro
            740                 745                 750

Lys Arg Pro Thr Ser Leu Pro Leu Asn Thr Lys Asn Ser Thr Lys Glu
        755                 760                 765

Pro Arg Leu Lys Phe Gly Ser Lys His Lys Ser Asn Leu Lys Gln Val
    770                 775                 780

Glu Thr Gly Val Ala Lys Met Asn Thr Ile Asn Ala Ala Glu Pro His
785                 790                 795                 800

Val Val Thr Val Thr Met Asn Gly Val Ala Gly Arg Asn His Ser Val
                805                 810                 815
```

```
Asn Ser His Ala Ala Thr Thr Gln Tyr Ala Asn Gly Thr Val Leu Ser
            820                 825                 830

Gly Gln Thr Thr Asn Ile Val Thr His Arg Ala Gln Glu Met Leu Gln
        835                 840                 845

Asn Gln Phe Ile Gly Glu Asp Thr Arg Leu Asn Ile Asn Ser Ser Pro
    850                 855                 860

Asp Glu His Glu Pro Leu Leu Arg Arg Glu Gln Gln Ala Gly His Asp
865                 870                 875                 880

Glu Gly Val Leu Asp Arg Leu Val Asp Arg Arg Glu Arg Pro Leu Glu
                885                 890                 895

Gly Gly Arg Thr Asn Ser Asn Asn Asn Asn Ser Asn Pro Cys Ser Glu
            900                 905                 910

Gln Asp Val Leu Ala Gln Gly Val Pro Ser Thr Ala Ala Asp Pro Gly
        915                 920                 925

Pro Ser Lys Pro Arg Arg Ala Gln Arg Pro Asn Ser Leu Asp Leu Ser
    930                 935                 940

Ala Thr Asn Val Leu Asp Gly Ser Ser Ile Gln Ile Gly Glu Ser Thr
945                 950                 955                 960

Gln Asp Gly Lys Ser Gly Ser Gly Glu Lys Ile Lys Lys Arg Val Lys
                965                 970                 975

Thr Pro Tyr Ser Leu Lys Arg Trp Arg Pro Ser Thr Trp Val Ile Ser
            980                 985                 990

Thr Glu Ser Leu Asp Cys Glu Val  Asn Asn Asn Gly Ser  Asn Arg Ala
        995                 1000                1005

Val His  Ser Lys Ser Ser Thr  Ala Val Tyr Leu Ala  Glu Gly Gly
    1010                1015                1020

Thr Ala  Thr Thr Met Val Ser  Lys Asp Ile Gly Met  Asn Cys Leu
    1025                1030                1035


<210>  189
<211>  794
<212>  PRT
<213>  Homo sapiens

<400>  189

Met Glu Leu Arg Pro Trp Leu Leu Trp Val Val Ala Ala Thr Gly Thr
1               5                   10                  15
```

```
Leu Val Leu Leu Ala Ala Asp Ala Gln Gly Gln Lys Val Phe Thr Asn
            20                  25                  30

Thr Trp Ala Val Arg Ile Pro Gly Gly Pro Ala Val Ala Asn Ser Val
        35                  40                  45

Ala Arg Lys His Gly Phe Leu Asn Leu Gly Gln Ile Phe Gly Asp Tyr
    50                  55                  60

Tyr His Phe Trp His Arg Gly Val Thr Lys Arg Ser Leu Ser Pro His
65                  70                  75                  80

Arg Pro Arg His Ser Arg Leu Gln Arg Glu Pro Gln Val Gln Trp Leu
                85                  90                  95

Glu Gln Gln Val Ala Lys Arg Arg Thr Lys Arg Asp Val Tyr Gln Glu
            100                 105                 110

Pro Thr Asp Pro Lys Phe Pro Gln Gln Trp Tyr Leu Ser Gly Val Thr
        115                 120                 125

Gln Arg Asp Leu Asn Val Lys Ala Ala Trp Ala Gln Gly Tyr Thr Gly
    130                 135                 140

His Gly Ile Val Val Ser Ile Leu Asp Asp Gly Ile Glu Lys Asn His
145                 150                 155                 160

Pro Asp Leu Ala Gly Asn Tyr Asp Pro Gly Ala Ser Phe Asp Val Asn
                165                 170                 175

Asp Gln Asp Pro Asp Pro Gln Pro Arg Tyr Thr Gln Met Asn Asp Asn
            180                 185                 190

Arg His Gly Thr Arg Cys Ala Gly Glu Val Ala Ala Val Ala Asn Asn
        195                 200                 205

Gly Val Cys Gly Val Gly Val Ala Tyr Asn Ala Arg Ile Gly Gly Val
    210                 215                 220

Arg Met Leu Asp Gly Glu Val Thr Asp Ala Val Glu Ala Arg Ser Leu
225                 230                 235                 240

Gly Leu Asn Pro Asn His Ile His Ile Tyr Ser Ala Ser Trp Gly Pro
                245                 250                 255

Glu Asp Asp Gly Lys Thr Val Asp Gly Pro Ala Arg Leu Ala Glu Glu
            260                 265                 270

Ala Phe Phe Arg Gly Val Ser Gln Gly Arg Gly Gly Leu Gly Ser Ile
        275                 280                 285
```

```
Phe Val Trp Ala Ser Gly Asn Gly Gly Arg Glu His Asp Ser Cys Asn
    290                 295                 300

Cys Asp Gly Tyr Thr Asn Ser Ile Tyr Thr Leu Ser Ile Ser Ser Ala
305                 310                 315                 320

Thr Gln Phe Gly Asn Val Pro Trp Tyr Ser Glu Ala Cys Ser Ser Thr
                325                 330                 335

Leu Ala Thr Thr Tyr Ser Ser Gly Asn Gln Asn Glu Lys Gln Ile Val
            340                 345                 350

Thr Thr Asp Leu Arg Gln Lys Cys Thr Glu Ser His Thr Gly Thr Ser
        355                 360                 365

Ala Ser Ala Pro Leu Ala Ala Gly Ile Ile Ala Leu Thr Leu Glu Ala
    370                 375                 380

Asn Lys Asn Leu Thr Trp Arg Asp Met Gln His Leu Val Val Gln Thr
385                 390                 395                 400

Ser Lys Pro Ala His Leu Asn Ala Asn Asp Trp Ala Thr Asn Gly Val
                405                 410                 415

Gly Arg Lys Val Ser His Ser Tyr Gly Tyr Gly Leu Leu Asp Ala Gly
            420                 425                 430

Ala Met Val Ala Leu Ala Gln Asn Trp Thr Thr Val Ala Pro Gln Arg
        435                 440                 445

Lys Cys Ile Ile Asp Ile Leu Thr Glu Pro Lys Asp Ile Gly Lys Arg
    450                 455                 460

Leu Glu Val Arg Lys Thr Val Thr Ala Cys Leu Gly Glu Pro Asn His
465                 470                 475                 480

Ile Thr Arg Leu Glu His Ala Gln Ala Arg Leu Thr Leu Ser Tyr Asn
                485                 490                 495

Arg Arg Gly Asp Leu Ala Ile His Leu Val Ser Pro Met Gly Thr Arg
            500                 505                 510

Ser Thr Leu Leu Ala Ala Arg Pro His Asp Tyr Ser Ala Asp Gly Phe
        515                 520                 525

Asn Asp Trp Ala Phe Met Thr Thr His Ser Trp Asp Glu Asp Pro Ser
    530                 535                 540

Gly Glu Trp Val Leu Glu Ile Glu Asn Thr Ser Glu Ala Asn Asn Tyr
545                 550                 555                 560
```

```
Gly Thr Leu Thr Lys Phe Thr Leu Val Leu Tyr Gly Thr Ala Pro Glu
                565                 570                 575

Gly Leu Pro Val Pro Pro Glu Ser Ser Gly Cys Lys Thr Leu Thr Ser
            580                 585                 590

Ser Gln Ala Cys Val Val Cys Glu Glu Gly Phe Ser Leu His Gln Lys
        595                 600                 605

Ser Cys Val Gln His Cys Pro Pro Gly Phe Ala Pro Gln Val Leu Asp
    610                 615                 620

Thr His Tyr Ser Thr Glu Asn Asp Val Glu Thr Ile Arg Ala Ser Val
625                 630                 635                 640

Cys Ala Pro Cys His Ala Ser Cys Ala Thr Cys Gln Gly Pro Ala Leu
                645                 650                 655

Thr Asp Cys Leu Ser Cys Pro Ser His Ala Ser Leu Asp Pro Val Glu
            660                 665                 670

Gln Thr Cys Ser Arg Gln Ser Gln Ser Ser Arg Glu Ser Pro Pro Gln
        675                 680                 685

Gln Gln Pro Pro Arg Leu Pro Pro Glu Val Glu Ala Gly Gln Arg Leu
    690                 695                 700

Arg Ala Gly Leu Leu Pro Ser His Leu Pro Glu Val Val Ala Gly Leu
705                 710                 715                 720

Ser Cys Ala Phe Ile Val Leu Val Phe Val Thr Val Phe Leu Val Leu
                725                 730                 735

Gln Leu Arg Ser Gly Phe Ser Phe Arg Gly Val Lys Val Tyr Thr Met
            740                 745                 750

Asp Arg Gly Leu Ile Ser Tyr Lys Gly Leu Pro Pro Glu Ala Trp Gln
        755                 760                 765

Glu Glu Cys Pro Ser Asp Ser Glu Glu Asp Glu Gly Arg Gly Glu Arg
    770                 775                 780

Thr Ala Phe Ile Lys Asp Gln Ser Ala Leu
785                 790

<210>  190
<211>  390
<212>  PRT
<213>  Homo sapiens

<400>  190
```

```
Met Pro Pro Ser Gly Leu Arg Leu Leu Leu Leu Leu Pro Leu Leu
1               5                  10                  15

Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr
            20                  25                  30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala
        35                  40                  45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
    50                  55                  60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu
65                  70                  75                  80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Glu Pro Glu
                85                  90                  95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu
            100                 105                 110

Met Val Glu Thr His Asn Glu Ile Tyr Asp Lys Phe Lys Gln Ser Thr
        115                 120                 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Glu Leu Arg Glu Ala Val
    130                 135                 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu
145                 150                 155                 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn
                165                 170                 175

Asn Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser
            180                 185                 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu
        195                 200                 205

Ser Arg Gly Gly Glu Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser
    210                 215                 220

Cys Asp Ser Arg Asp Asn Thr Leu Gln Val Asp Ile Asn Gly Phe Thr
225                 230                 235                 240

Thr Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro
                245                 250                 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu Gln
            260                 265                 270
```

```
Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser
        275                 280                 285

Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys
    290                 295                 300

Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn
305                 310                 315                 320

Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr
                325                 330                 335

Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala
            340                 345                 350

Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr
        355                 360                 365

Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val
    370                 375                 380

Arg Ser Cys Lys Cys Ser
385                 390


<210>  191
<211>  414
<212>  PRT
<213>  Homo sapiens

<400>  191

Met His Tyr Cys Val Leu Ser Ala Phe Leu Ile Leu His Leu Val Thr
1               5                   10                  15

Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe
            20                  25                  30

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu
        35                  40                  45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Glu Glu Val Pro
    50                  55                  60

Pro Glu Val Ile Ser Ile Tyr Asn Ser Thr Arg Asp Leu Leu Gln Glu
65                  70                  75                  80

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Asp Glu
                85                  90                  95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Pro Phe Phe
            100                 105                 110

Pro Ser Glu Asn Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg
```

```
        115                 120                 125

Ile Val Arg Phe Asp Val Ser Ala Met Glu Lys Asn Ala Ser Asn Leu
    130                 135                 140

Val Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg
145                 150                 155                 160

Val Pro Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp
                165                 170                 175

Leu Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr
            180                 185                 190

Arg Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val His
        195                 200                 205

Glu Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu
    210                 215                 220

His Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro
225                 230                 235                 240

Asn Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr
                245                 250                 255

Ser Thr Tyr Thr Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys
            260                 265                 270

Lys Asn Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser
        275                 280                 285

Tyr Arg Leu Glu Ser Gln Gln Thr Asn Arg Arg Lys Lys Arg Ala Leu
    290                 295                 300

Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg
305                 310                 315                 320

Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His
                325                 330                 335

Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr
            340                 345                 350

Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu Tyr Asn
        355                 360                 365

Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp
    370                 375                 380

Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro Lys Ile
```

385 390 395 400

Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser
405 410

<210> 192
<211> 202
<212> PRT
<213> Homo sapiens

<400> 192

Met Leu Val Ala Gly Phe Leu Leu Ala Leu Pro Pro Ser Trp Ala Ala
1 5 10 15

Gly Ala Pro Arg Ala Gly Arg Arg Pro Ala Arg Pro Arg Gly Cys Ala
20 25 30

Asp Arg Pro Glu Glu Leu Leu Glu Gln Leu Tyr Gly Arg Leu Ala Ala
35 40 45

Gly Val Leu Ser Ala Phe His His Thr Leu Gln Leu Gly Pro Arg Glu
50 55 60

Gln Ala Arg Asn Ala Ser Cys Pro Ala Gly Gly Arg Pro Ala Asp Arg
65 70 75 80

Arg Phe Arg Pro Pro Thr Asn Leu Arg Ser Val Ser Pro Trp Ala Tyr
85 90 95

Arg Ile Ser Tyr Asp Pro Ala Arg Tyr Pro Arg Tyr Leu Pro Glu Ala
100 105 110

Tyr Cys Leu Cys Arg Gly Cys Leu Thr Gly Leu Phe Gly Glu Glu Asp
115 120 125

Val Arg Phe Arg Ser Ala Pro Val Tyr Met Pro Thr Val Val Leu Arg
130 135 140

Arg Thr Pro Ala Cys Ala Gly Gly Arg Ser Val Tyr Thr Glu Ala Tyr
145 150 155 160

Val Thr Ile Pro Val Gly Cys Thr Cys Val Pro Glu Pro Glu Lys Asp
165 170 175

Ala Asp Ser Ile Asn Ser Ser Ile Asp Lys Gln Gly Ala Lys Leu Leu
180 185 190

Leu Gly Pro Asn Asp Ala Pro Ala Gly Pro
195 200

<210> 193
<211> 1821

<212> PRT
<213> Homo sapiens

<400> 193

```
Met Arg Pro Arg Thr Lys Ala Arg Ser Pro Gly Arg Ala Leu Arg Asn
1               5                  10                  15

Pro Trp Arg Gly Phe Leu Pro Leu Thr Leu Ala Leu Phe Val Gly Ala
            20                  25                  30

Gly His Ala Gln Arg Asp Pro Val Gly Arg Tyr Glu Pro Ala Gly Gly
        35                  40                  45

Asp Ala Asn Arg Leu Arg Arg Pro Gly Gly Ser Tyr Pro Ala Ala Ala
    50                  55                  60

Ala Ala Lys Val Tyr Ser Leu Phe Arg Glu Gln Asp Ala Pro Val Ala
65                  70                  75                  80

Gly Leu Gln Pro Val Glu Arg Ala Gln Pro Gly Trp Gly Ser Pro Arg
                85                  90                  95

Arg Pro Thr Glu Ala Glu Ala Arg Arg Pro Ser Arg Ala Gln Gln Ser
            100                 105                 110

Arg Arg Val Gln Pro Pro Ala Gln Thr Arg Arg Ser Thr Pro Leu Gly
        115                 120                 125

Gln Gln Gln Pro Ala Pro Arg Thr Arg Ala Ala Pro Ala Leu Pro Arg
    130                 135                 140

Leu Gly Thr Pro Gln Arg Ser Gly Ala Ala Pro Pro Thr Pro Pro Arg
145                 150                 155                 160

Gly Arg Leu Thr Gly Arg Asn Val Cys Gly Gly Gln Cys Cys Pro Gly
                165                 170                 175

Trp Thr Thr Ala Asn Ser Thr Asn His Cys Ile Lys Pro Val Cys Glu
            180                 185                 190

Pro Pro Cys Gln Asn Arg Gly Ser Cys Ser Arg Pro Gln Leu Cys Val
        195                 200                 205

Cys Arg Ser Gly Phe Arg Gly Ala Arg Cys Glu Glu Val Ile Pro Asp
    210                 215                 220

Glu Glu Phe Asp Pro Gln Asn Ser Arg Leu Ala Pro Arg Arg Trp Ala
225                 230                 235                 240

Glu Arg Ser Pro Asn Leu Arg Arg Ser Ser Ala Ala Gly Glu Gly Thr
                245                 250                 255
```

```
Leu Ala Arg Ala Gln Pro Pro Ala Pro Gln Ser Pro Pro Ala Pro Gln
            260                 265                 270

Ser Pro Pro Ala Gly Thr Leu Ser Gly Leu Ser Gln Thr His Pro Ser
        275                 280                 285

Gln Gln His Val Gly Leu Ser Arg Thr Val Arg Leu His Pro Thr Ala
    290                 295                 300

Thr Ala Ser Ser Gln Leu Ser Ser Asn Ala Leu Pro Pro Gly Pro Gly
305                 310                 315                 320

Leu Glu Gln Arg Asp Gly Thr Gln Gln Ala Val Pro Leu Glu His Pro
                325                 330                 335

Ser Ser Pro Trp Gly Leu Asn Leu Thr Glu Lys Ile Lys Lys Ile Lys
            340                 345                 350

Ile Val Phe Thr Pro Thr Ile Cys Lys Gln Thr Cys Ala Arg Gly His
        355                 360                 365

Cys Ala Asn Ser Cys Glu Arg Gly Asp Thr Thr Thr Leu Tyr Ser Gln
    370                 375                 380

Gly Gly His Gly His Asp Pro Lys Ser Gly Phe Arg Ile Tyr Phe Cys
385                 390                 395                 400

Gln Ile Pro Cys Leu Asn Gly Gly Arg Cys Ile Gly Arg Asp Glu Cys
                405                 410                 415

Trp Cys Pro Ala Asn Ser Thr Gly Lys Phe Cys His Leu Pro Ile Pro
            420                 425                 430

Gln Pro Asp Arg Glu Pro Pro Gly Arg Gly Ser Arg Pro Arg Ala Leu
        435                 440                 445

Leu Glu Ala Pro Leu Lys Gln Ser Thr Phe Thr Leu Pro Leu Ser Asn
    450                 455                 460

Gln Leu Ala Ser Val Asn Pro Ser Leu Val Lys Val His Ile His His
465                 470                 475                 480

Pro Pro Glu Ala Ser Val Gln Ile His Gln Val Ala Gln Val Arg Gly
                485                 490                 495

Gly Val Glu Glu Ala Leu Val Glu Asn Ser Val Glu Thr Arg Pro Pro
            500                 505                 510

Pro Trp Leu Pro Ala Ser Pro Gly His Ser Leu Trp Asp Ser Asn Asn
        515                 520                 525
```

```
Ile Pro Ala Arg Ser Gly Glu Pro Pro Arg Pro Leu Pro Pro Ala Ala
    530                 535                 540

Pro Arg Pro Arg Gly Leu Leu Gly Arg Cys Tyr Leu Asn Thr Val Asn
545                 550                 555                 560

Gly Gln Cys Ala Asn Pro Leu Leu Glu Leu Thr Thr Gln Glu Asp Cys
                565                 570                 575

Cys Gly Ser Val Gly Ala Phe Trp Gly Val Thr Leu Cys Ala Pro Cys
            580                 585                 590

Pro Pro Arg Pro Ala Ser Pro Val Ile Glu Asn Gly Gln Leu Glu Cys
        595                 600                 605

Pro Gln Gly Tyr Lys Arg Leu Asn Leu Thr His Cys Gln Asp Ile Asn
    610                 615                 620

Glu Cys Leu Thr Leu Gly Leu Cys Lys Asp Ala Glu Cys Val Asn Thr
625                 630                 635                 640

Arg Gly Ser Tyr Leu Cys Thr Cys Arg Pro Gly Leu Met Leu Asp Pro
                645                 650                 655

Ser Arg Ser Arg Cys Val Ser Asp Lys Ala Ile Ser Met Leu Gln Gly
            660                 665                 670

Leu Cys Tyr Arg Ser Leu Gly Pro Gly Thr Cys Thr Leu Pro Leu Ala
        675                 680                 685

Gln Arg Ile Thr Lys Gln Ile Cys Cys Cys Ser Arg Val Gly Lys Ala
    690                 695                 700

Trp Gly Ser Glu Cys Glu Lys Cys Pro Leu Pro Gly Thr Glu Ala Phe
705                 710                 715                 720

Arg Glu Ile Cys Pro Ala Gly His Gly Tyr Thr Tyr Ala Ser Ser Asp
                725                 730                 735

Ile Arg Leu Ser Met Arg Lys Ala Glu Glu Glu Glu Leu Ala Arg Pro
            740                 745                 750

Pro Arg Glu Gln Gly Gln Arg Ser Ser Gly Ala Leu Pro Gly Pro Ala
        755                 760                 765

Glu Arg Gln Pro Leu Arg Val Val Thr Asp Thr Trp Leu Glu Ala Gly
    770                 775                 780

Thr Ile Pro Asp Lys Gly Asp Ser Gln Ala Gly Gln Val Thr Thr Ser
785                 790                 795                 800
```

```
Val Thr His Ala Pro Ala Trp Val Thr Gly Asn Ala Thr Thr Pro Pro
                805                 810                 815

Met Pro Glu Gln Gly Ile Ala Glu Ile Gln Glu Glu Gln Val Thr Pro
            820                 825                 830

Ser Thr Asp Val Leu Val Thr Leu Ser Thr Pro Gly Ile Asp Arg Cys
        835                 840                 845

Ala Ala Gly Ala Thr Asn Val Cys Gly Pro Gly Thr Cys Val Asn Leu
    850                 855                 860

Pro Asp Gly Tyr Arg Cys Val Cys Ser Pro Gly Tyr Gln Leu His Pro
865                 870                 875                 880

Ser Gln Ala Tyr Cys Thr Asp Asp Asn Glu Cys Leu Arg Asp Pro Cys
                885                 890                 895

Lys Gly Lys Gly Arg Cys Ile Asn Arg Val Gly Ser Tyr Ser Cys Phe
            900                 905                 910

Cys Tyr Pro Gly Tyr Thr Leu Ala Thr Ser Gly Ala Thr Gln Glu Cys
        915                 920                 925

Gln Asp Ile Asn Glu Cys Glu Gln Pro Gly Val Cys Ser Gly Gly Gln
    930                 935                 940

Cys Thr Asn Thr Glu Gly Ser Tyr His Cys Glu Cys Asp Gln Gly Tyr
945                 950                 955                 960

Ile Met Val Arg Lys Gly His Cys Gln Asp Ile Asn Glu Cys Arg His
                965                 970                 975

Pro Gly Thr Cys Pro Asp Gly Arg Cys Val Asn Ser Pro Gly Ser Tyr
            980                 985                 990

Thr Cys Leu Ala Cys Glu Glu Gly  Tyr Arg Gly Gln Ser  Gly Ser Cys
        995                 1000                1005

Val Asp  Val Asn Glu Cys Leu  Thr Pro Gly Val Cys  Ala His Gly
    1010                1015                1020

Lys Cys  Thr Asn Leu Glu Gly  Ser Phe Arg Cys Ser  Cys Glu Gln
    1025                1030                1035

Gly Tyr  Glu Val Thr Ser Asp  Glu Lys Gly Cys Gln  Asp Val Asp
    1040                1045                1050

Glu Cys  Ala Ser Arg Ala Ser  Cys Pro Thr Gly Leu  Cys Leu Asn
    1055                1060                1065
```

```
Thr Glu  Gly Ser Phe Ala Cys  Ser Ala Cys Glu Asn  Gly Tyr Trp
    1070                1075                1080

Val Asn  Glu Asp Gly Thr Ala  Cys Glu Asp Leu Asp  Glu Cys Ala
    1085                1090                1095

Phe Pro  Gly Val Cys Pro Ser  Gly Val Cys Thr Asn  Thr Ala Gly
    1100                1105                1110

Ser Phe  Ser Cys Lys Asp Cys  Asp Gly Gly Tyr Arg  Pro Ser Pro
    1115                1120                1125

Leu Gly  Asp Ser Cys Glu Asp  Val Asp Glu Cys Glu  Asp Pro Gln
    1130                1135                1140

Ser Ser  Cys Leu Gly Gly Glu  Cys Lys Asn Thr Val  Gly Ser Tyr
    1145                1150                1155

Gln Cys  Leu Cys Pro Gln Gly  Phe Gln Leu Ala Asn  Gly Thr Val
    1160                1165                1170

Cys Glu  Asp Val Asn Glu Cys  Met Gly Glu Glu His  Cys Ala Pro
    1175                1180                1185

His Gly  Glu Cys Leu Asn Ser  His Gly Ser Phe Phe  Cys Leu Cys
    1190                1195                1200

Ala Pro  Gly Phe Val Ser Ala  Glu Gly Gly Thr Ser  Cys Gln Asp
    1205                1210                1215

Val Asp  Glu Cys Ala Thr Thr  Asp Pro Cys Val Gly  Gly His Cys
    1220                1225                1230

Val Asn  Thr Glu Gly Ser Phe  Asn Cys Leu Cys Glu  Thr Gly Phe
    1235                1240                1245

Gln Pro  Ser Pro Glu Ser Gly  Glu Cys Val Asp Ile  Asp Glu Cys
    1250                1255                1260

Glu Asp  Tyr Gly Asp Pro Val  Cys Gly Thr Trp Lys  Cys Glu Asn
    1265                1270                1275

Ser Pro  Gly Ser Tyr Arg Cys  Val Leu Gly Cys Gln  Pro Gly Phe
    1280                1285                1290

His Met  Ala Pro Asn Gly Asp  Cys Ile Asp Ile Asp  Glu Cys Ala
    1295                1300                1305

Asn Asp  Thr Met Cys Gly Ser  His Gly Phe Cys Asp  Asn Thr Asp
    1310                1315                1320
```

```
Gly Ser  Phe Arg Cys Leu Cys  Asp Gln Gly Phe Glu  Ile Ser Pro
    1325                1330                1335

Ser Gly  Trp Asp Cys Val Asp  Val Asn Glu Cys Glu  Leu Met Leu
    1340                1345                1350

Ala Val  Cys Gly Ala Ala Leu  Cys Glu Asn Val Glu  Gly Ser Phe
    1355                1360                1365

Leu Cys  Leu Cys Ala Ser Asp  Leu Glu Glu Tyr Asp  Ala Gln Glu
    1370                1375                1380

Gly His  Cys Arg Pro Arg Gly  Ala Gly Gly Gln Ser  Met Ser Glu
    1385                1390                1395

Ala Pro  Thr Gly Asp His Ala  Pro Ala Pro Thr Arg  Met Asp Cys
    1400                1405                1410

Tyr Ser  Gly Gln Lys Gly His  Ala Pro Cys Ser Ser  Val Leu Gly
    1415                1420                1425

Arg Asn  Thr Thr Gln Ala Glu  Cys Cys Cys Thr Gln  Gly Ala Ser
    1430                1435                1440

Trp Gly  Asp Ala Cys Asp Leu  Cys Pro Ser Glu Asp  Ser Ala Glu
    1445                1450                1455

Phe Ser  Glu Ile Cys Pro Ser  Gly Lys Gly Tyr Ile  Pro Val Glu
    1460                1465                1470

Gly Ala  Trp Thr Phe Gly Gln  Thr Met Tyr Thr Asp  Ala Asp Glu
    1475                1480                1485

Cys Val  Ile Phe Gly Pro Gly  Leu Cys Pro Asn Gly  Arg Cys Leu
    1490                1495                1500

Asn Thr  Val Pro Gly Tyr Val  Cys Leu Cys Asn Pro  Gly Phe His
    1505                1510                1515

Tyr Asp  Ala Ser His Lys Lys  Cys Glu Asp His Asp  Glu Cys Gln
    1520                1525                1530

Asp Leu  Ala Cys Glu Asn Gly  Glu Cys Val Asn Thr  Glu Gly Ser
    1535                1540                1545

Phe His  Cys Phe Cys Ser Pro  Pro Leu Thr Leu Asp  Leu Ser Gln
    1550                1555                1560

Gln Arg  Cys Met Asn Ser Thr  Ser Ser Thr Glu Asp  Leu Pro Asp
    1565                1570                1575
```

```
His Asp  Ile His Met Asp Ile  Cys Trp Lys Lys Val  Thr Asn Asp
    1580                1585                1590

Val Cys  Ser Glu Pro Leu Arg  Gly His Arg Thr Thr  Tyr Thr Glu
    1595                1600                1605

Cys Cys  Cys Gln Asp Gly Glu  Ala Trp Ser Gln Gln  Cys Ala Leu
    1610                1615                1620

Cys Pro  Pro Arg Ser Ser Glu  Val Tyr Ala Gln Leu  Cys Asn Val
    1625                1630                1635

Ala Arg  Ile Glu Ala Glu Arg  Glu Ala Gly Val His  Phe Arg Pro
    1640                1645                1650

Gly Tyr  Glu Tyr Gly Pro Gly  Pro Asp Asp Leu His  Tyr Ser Ile
    1655                1660                1665

Tyr Gly  Pro Asp Gly Ala Pro  Phe Tyr Asn Tyr Leu  Gly Pro Glu
    1670                1675                1680

Asp Thr  Val Pro Glu Pro Ala  Phe Pro Asn Thr Ala  Gly His Ser
    1685                1690                1695

Ala Asp  Arg Thr Pro Ile Leu  Glu Ser Pro Leu Gln  Pro Ser Glu
    1700                1705                1710

Leu Gln  Pro His Tyr Val Ala  Ser His Pro Glu Pro  Pro Ala Gly
    1715                1720                1725

Phe Glu  Gly Leu Gln Ala Glu  Glu Cys Gly Ile Leu  Asn Gly Cys
    1730                1735                1740

Glu Asn  Gly Arg Cys Val Arg  Val Arg Glu Gly Tyr  Thr Cys Asp
    1745                1750                1755

Cys Phe  Glu Gly Phe Gln Leu  Asp Ala Ala His Met  Ala Cys Val
    1760                1765                1770

Asp Val  Asn Glu Cys Asp Asp  Leu Asn Gly Pro Ala  Val Leu Cys
    1775                1780                1785

Val His  Gly Tyr Cys Glu Asn  Thr Glu Gly Ser Tyr  Arg Cys His
    1790                1795                1800

Cys Ser  Pro Gly Tyr Val Ala  Glu Ala Gly Pro Pro  His Cys Thr
    1805                1810                1815

Ala Lys  Glu
    1820
```

<210> 194
<211> 501
<212> PRT
<213> Homo sapiens

<400> 194

```
Met Arg Leu Pro Lys Leu Leu Thr Phe Leu Leu Trp Tyr Leu Ala Trp
1               5                  10                  15

Leu Asp Leu Glu Phe Ile Cys Thr Val Leu Gly Ala Pro Asp Leu Gly
            20                  25                  30

Gln Arg Pro Gln Gly Thr Arg Pro Gly Leu Ala Lys Ala Glu Ala Lys
        35                  40                  45

Glu Arg Pro Pro Leu Ala Arg Asn Val Phe Arg Pro Gly Gly His Ser
    50                  55                  60

Tyr Gly Gly Gly Ala Thr Asn Ala Asn Ala Arg Ala Lys Gly Gly Thr
65                  70                  75                  80

Gly Gln Thr Gly Gly Leu Thr Gln Pro Lys Lys Asp Glu Pro Lys Lys
                85                  90                  95

Leu Pro Pro Arg Pro Gly Gly Pro Glu Pro Lys Pro Gly His Pro Pro
            100                 105                 110

Gln Thr Arg Gln Ala Thr Ala Arg Thr Val Thr Pro Lys Gly Gln Leu
        115                 120                 125

Pro Gly Gly Lys Ala Pro Pro Lys Ala Gly Ser Val Pro Ser Ser Phe
    130                 135                 140

Leu Leu Lys Lys Ala Arg Glu Pro Gly Pro Pro Arg Glu Pro Lys Glu
145                 150                 155                 160

Pro Phe Arg Pro Pro Pro Ile Thr Pro His Glu Tyr Met Leu Ser Leu
                165                 170                 175

Tyr Arg Thr Leu Ser Asp Ala Asp Arg Lys Gly Gly Asn Ser Ser Val
            180                 185                 190

Lys Leu Glu Ala Gly Leu Ala Asn Thr Ile Thr Ser Phe Ile Asp Lys
        195                 200                 205

Gly Gln Asp Asp Arg Gly Pro Val Val Arg Lys Gln Arg Tyr Val Phe
    210                 215                 220

Asp Ile Ser Ala Leu Glu Lys Asp Gly Leu Leu Gly Ala Glu Leu Arg
225                 230                 235                 240
```

```
Ile Leu Arg Lys Lys Pro Ser Asp Thr Ala Lys Pro Ala Ala Pro Gly
                245                 250                 255

Gly Gly Arg Ala Ala Gln Leu Lys Leu Ser Ser Cys Pro Ser Gly Arg
            260                 265                 270

Gln Pro Ala Ser Leu Leu Asp Val Arg Ser Val Pro Gly Leu Asp Gly
        275                 280                 285

Ser Gly Trp Glu Val Phe Asp Ile Trp Lys Leu Phe Arg Asn Phe Lys
    290                 295                 300

Asn Ser Ala Gln Leu Cys Leu Glu Leu Glu Ala Trp Glu Arg Gly Arg
305                 310                 315                 320

Ala Val Asp Leu Arg Gly Leu Gly Phe Asp Arg Ala Ala Arg Gln Val
                325                 330                 335

His Glu Lys Ala Leu Phe Leu Val Phe Gly Arg Thr Lys Lys Arg Asp
            340                 345                 350

Leu Phe Phe Asn Glu Ile Lys Ala Arg Ser Gly Gln Asp Asp Lys Thr
        355                 360                 365

Val Tyr Glu Tyr Leu Phe Ser Gln Arg Arg Lys Arg Arg Ala Pro Leu
    370                 375                 380

Ala Thr Arg Gln Gly Lys Arg Pro Ser Lys Asn Leu Lys Ala Arg Cys
385                 390                 395                 400

Ser Arg Lys Ala Leu His Val Asn Phe Lys Asp Met Gly Trp Asp Asp
                405                 410                 415

Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys Glu Gly Leu
            420                 425                 430

Cys Glu Phe Pro Leu Arg Ser His Leu Glu Pro Thr Asn His Ala Val
        435                 440                 445

Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr Pro Pro Thr
    450                 455                 460

Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu Phe Ile Asp
465                 470                 475                 480

Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu
                485                 490                 495

Ser Cys Gly Cys Arg
            500
```

<210> 195
<211> 184
<212> PRT
<213> Homo sapiens

<400> 195

Met Ser Arg Thr Ala Tyr Thr Val Gly Ala Leu Leu Leu Leu Leu Gly
1 5 10 15

Thr Leu Leu Pro Ala Ala Glu Gly Lys Lys Lys Gly Ser Gln Gly Ala
20 25 30

Ile Pro Pro Pro Asp Lys Ala Gln His Asn Asp Ser Glu Gln Thr Gln
35 40 45

Ser Pro Gln Gln Pro Gly Ser Arg Asn Arg Gly Arg Gly Gln Gly Arg
50 55 60

Gly Thr Ala Met Pro Gly Glu Glu Val Leu Glu Ser Ser Gln Glu Ala
65 70 75 80

Leu His Val Thr Glu Arg Lys Tyr Leu Lys Arg Asp Trp Cys Lys Thr
85 90 95

Gln Pro Leu Lys Gln Thr Ile His Glu Glu Gly Cys Asn Ser Arg Thr
100 105 110

Ile Ile Asn Arg Phe Cys Tyr Gly Gln Cys Asn Ser Phe Tyr Ile Pro
115 120 125

Arg His Ile Arg Lys Glu Glu Gly Ser Phe Gln Ser Cys Ser Phe Cys
130 135 140

Lys Pro Lys Lys Phe Thr Thr Met Met Val Thr Leu Asn Cys Pro Glu
145 150 155 160

Leu Gln Pro Pro Thr Lys Lys Lys Arg Val Thr Arg Val Lys Gln Cys
165 170 175

Arg Cys Ile Ser Ile Asp Leu Asp
180

<210> 196
<211> 108
<212> PRT
<213> Homo sapiens

<400> 196

Met Lys Ala Leu Cys Leu Leu Leu Leu Pro Val Leu Gly Leu Leu Val
1 5 10 15

Ser Ser Lys Thr Leu Cys Ser Met Glu Glu Ala Ile Asn Glu Arg Ile
20 25 30

```
Gln Glu Val Ala Gly Ser Leu Ile Phe Arg Ala Ile Ser Ser Ile Gly
        35                  40                  45

Leu Glu Cys Gln Ser Val Thr Ser Arg Gly Asp Leu Ala Thr Cys Pro
    50                  55                  60

Arg Gly Phe Ala Val Thr Gly Cys Thr Cys Gly Ser Ala Cys Gly Ser
65                  70                  75                  80

Trp Asp Val Arg Ala Glu Thr Thr Cys His Cys Gln Cys Ala Gly Met
                85                  90                  95

Asp Trp Thr Gly Ala Arg Cys Cys Arg Val Gln Pro
            100                 105


<210>  197
<211>  323
<212>  PRT
<213>  Homo sapiens

<400>  197

Met Ala Tyr Val Pro Ala Pro Gly Tyr Gln Pro Thr Tyr Asn Pro Thr
1               5                   10                  15

Leu Pro Tyr Tyr Gln Pro Ile Pro Gly Gly Leu Asn Val Gly Met Ser
            20                  25                  30

Val Tyr Ile Gln Gly Val Ala Ser Glu His Met Lys Arg Phe Phe Val
        35                  40                  45

Asn Phe Val Val Gly Gln Asp Pro Gly Ser Asp Val Ala Phe His Phe
    50                  55                  60

Asn Pro Arg Phe Asp Gly Trp Asp Lys Val Val Phe Asn Thr Leu Gln
65                  70                  75                  80

Gly Gly Lys Trp Gly Ser Glu Glu Arg Lys Arg Ser Met Pro Phe Lys
                85                  90                  95

Lys Gly Ala Ala Phe Glu Leu Val Phe Ile Val Leu Ala Glu His Tyr
            100                 105                 110

Lys Val Val Val Asn Gly Asn Pro Phe Tyr Glu Tyr Gly His Arg Leu
        115                 120                 125

Pro Leu Gln Met Val Thr His Leu Gln Val Asp Gly Asp Leu Gln Leu
    130                 135                 140

Gln Ser Ile Asn Phe Ile Gly Gly Gln Pro Leu Arg Pro Gln Gly Pro
145                 150                 155                 160
```

```
Pro Met Met Pro Pro Tyr Pro Gly Pro Gly His Cys His Gln Gln Leu
                165                 170                 175

Asn Ser Leu Pro Thr Met Glu Gly Pro Pro Thr Phe Asn Pro Pro Val
            180                 185                 190

Pro Tyr Phe Gly Arg Leu Gln Gly Gly Leu Thr Ala Arg Arg Thr Ile
        195                 200                 205

Ile Ile Lys Gly Tyr Val Pro Pro Thr Gly Lys Ser Phe Ala Ile Asn
    210                 215                 220

Phe Lys Val Gly Ser Ser Gly Asp Ile Ala Leu His Ile Asn Pro Arg
225                 230                 235                 240

Met Gly Asn Gly Thr Val Val Arg Asn Ser Leu Leu Asn Gly Ser Trp
                245                 250                 255

Gly Ser Glu Glu Lys Lys Ile Thr His Asn Pro Phe Gly Pro Gly Gln
            260                 265                 270

Phe Phe Asp Leu Ser Ile Arg Cys Gly Leu Asp Arg Phe Lys Val Tyr
        275                 280                 285

Ala Asn Gly Gln His Leu Phe Asp Phe Ala His Arg Leu Ser Ala Phe
    290                 295                 300

Gln Arg Val Asp Thr Leu Glu Ile Gln Gly Asp Val Thr Leu Ser Tyr
305                 310                 315                 320

Val Gln Ile
```

<210> 198
<211> 244
<212> PRT
<213> Homo sapiens

<400> 198

```
Met Leu Leu Leu Gly Ala Val Leu Leu Leu Ala Leu Pro Gly His
1               5                   10                  15

Asp Gln Glu Thr Thr Thr Gln Gly Pro Gly Val Leu Leu Pro Leu Pro
            20                  25                  30

Lys Gly Ala Cys Thr Gly Trp Met Ala Gly Ile Pro Gly His Pro Gly
        35                  40                  45

His Asn Gly Ala Pro Gly Arg Asp Gly Arg Asp Gly Thr Pro Gly Glu
    50                  55                  60
```

```
Lys Gly Glu Lys Gly Asp Pro Gly Leu Ile Gly Pro Lys Gly Asp Ile
65                  70                  75                  80

Gly Glu Thr Gly Val Pro Gly Ala Glu Gly Pro Arg Gly Phe Pro Gly
                85                  90                  95

Ile Gln Gly Arg Lys Gly Glu Pro Gly Glu Gly Ala Tyr Val Tyr Arg
            100                 105                 110

Ser Ala Phe Ser Val Gly Leu Glu Thr Tyr Val Thr Ile Pro Asn Met
        115                 120                 125

Pro Ile Arg Phe Thr Lys Ile Phe Tyr Asn Gln Gln Asn His Tyr Asp
    130                 135                 140

Gly Ser Thr Gly Lys Phe His Cys Asn Ile Pro Gly Leu Tyr Tyr Phe
145                 150                 155                 160

Ala Tyr His Ile Thr Val Tyr Met Lys Asp Val Lys Val Ser Leu Phe
                165                 170                 175

Lys Lys Asp Lys Ala Met Leu Phe Thr Tyr Asp Gln Tyr Gln Glu Asn
            180                 185                 190

Asn Val Asp Gln Ala Ser Gly Ser Val Leu Leu His Leu Glu Val Gly
        195                 200                 205

Asp Gln Val Trp Leu Gln Val Tyr Gly Glu Gly Glu Arg Asn Gly Leu
    210                 215                 220

Tyr Ala Asp Asn Asp Asn Asp Ser Thr Phe Thr Gly Phe Leu Leu Tyr
225                 230                 235                 240

His Asp Thr Asn
```

<210> 199
<211> 245
<212> PRT
<213> Homo sapiens

<400> 199

```
Met Asp Val Gly Pro Ser Ser Leu Pro His Leu Gly Leu Lys Leu Leu
1               5                   10                  15

Leu Leu Leu Leu Leu Leu Pro Leu Arg Gly Gln Ala Asn Thr Gly Cys
            20                  25                  30

Tyr Gly Ile Pro Gly Met Pro Gly Leu Pro Gly Ala Pro Gly Lys Asp
        35                  40                  45

Gly Tyr Asp Gly Leu Pro Gly Pro Lys Gly Glu Pro Gly Ile Pro Ala
```

50 55 60

Ile Pro Gly Ile Arg Gly Pro Lys Gly Gln Lys Gly Glu Pro Gly Leu
65 70 75 80

Pro Gly His Pro Gly Lys Asn Gly Pro Met Gly Pro Pro Gly Met Pro
85 90 95

Gly Val Pro Gly Pro Met Gly Ile Pro Gly Glu Pro Gly Glu Glu Gly
100 105 110

Arg Tyr Lys Gln Lys Phe Gln Ser Val Phe Thr Val Thr Arg Gln Thr
115 120 125

His Gln Pro Pro Ala Pro Asn Ser Leu Ile Arg Phe Asn Ala Val Leu
130 135 140

Thr Asn Pro Gln Gly Asp Tyr Asp Thr Ser Thr Gly Lys Phe Thr Cys
145 150 155 160

Lys Val Pro Gly Leu Tyr Tyr Phe Val Tyr His Ala Ser His Thr Ala
165 170 175

Asn Leu Cys Val Leu Leu Tyr Arg Ser Gly Val Lys Val Val Thr Phe
180 185 190

Cys Gly His Thr Ser Lys Thr Asn Gln Val Asn Ser Gly Gly Val Leu
195 200 205

Leu Arg Leu Gln Val Gly Glu Glu Val Trp Leu Ala Val Asn Asp Tyr
210 215 220

Tyr Asp Met Val Gly Ile Gln Gly Ser Asp Ser Val Phe Ser Gly Phe
225 230 235 240

Leu Leu Phe Pro Asp
245

<210> 200
<211> 672
<212> PRT
<213> Homo sapiens

<400> 200

Met Arg Ala Gly Arg Gly Ala Thr Pro Ala Arg Glu Leu Phe Arg Asp
1 5 10 15

Ala Ala Phe Pro Ala Ala Asp Ser Ser Leu Phe Cys Asp Leu Ser Thr
20 25 30

Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu
35 40 45

```
Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
    50                  55                  60

Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
65                  70                  75                  80

Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
                85                  90                  95

Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
            100                 105                 110

Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu
        115                 120                 125

Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp
    130                 135                 140

Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
145                 150                 155                 160

Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
                165                 170                 175

Leu Thr Gly Gly Leu Ala Glu Arg Trp Asn Leu Lys Gly Val Ala Gly
            180                 185                 190

Ser Gly Gly Gln Gln Asp Arg Pro Gly Arg Trp Glu His Arg Thr Cys
        195                 200                 205

Arg Gln Leu Leu His Leu Lys Asp Gln Cys Leu Ile Ser Cys Cys Val
    210                 215                 220

Leu Ser Pro Arg Ala Gly Ala Arg Glu Leu Gly Glu Phe His Ala Phe
225                 230                 235                 240

Ile Val Ser Asp Leu Arg Glu Leu Gln Gly Gln Ala Gly Gln Cys Ile
                245                 250                 255

Leu Leu Leu Arg Ile Gln Asn Pro Trp Gly Arg Arg Cys Trp Gln Gly
            260                 265                 270

Leu Trp Arg Glu Gly Gly Glu Gly Trp Ser Gln Val Asp Ala Ala Val
        275                 280                 285

Ala Ser Glu Leu Leu Ser Gln Leu Gln Glu Gly Glu Phe Trp Val Glu
    290                 295                 300

Glu Glu Glu Phe Leu Arg Glu Phe Asp Glu Leu Thr Val Gly Tyr Pro
305                 310                 315                 320
```

```
Val Thr Glu Ala Gly His Leu Gln Ser Leu Tyr Thr Glu Arg Leu Leu
                325                 330                 335

Cys His Thr Arg Ala Leu Pro Gly Ala Trp Val Lys Gly Gln Ser Ala
            340                 345                 350

Gly Gly Cys Arg Asn Asn Ser Gly Phe Pro Ser Asn Pro Lys Phe Trp
        355                 360                 365

Leu Arg Val Ser Glu Pro Ser Glu Val Tyr Ile Ala Val Leu Gln Arg
    370                 375                 380

Ser Arg Leu His Ala Ala Asp Trp Ala Gly Arg Ala Arg Ala Leu Val
385                 390                 395                 400

Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His
                405                 410                 415

Tyr Gln Ala Val Gly Leu His Leu Trp Lys Val Glu Lys Arg Arg Val
            420                 425                 430

Asn Leu Pro Arg Val Leu Ser Met Pro Pro Val Ala Gly Thr Ala Cys
        435                 440                 445

His Ala Tyr Asp Arg Glu Val His Leu Arg Cys Glu Leu Ser Pro Gly
    450                 455                 460

Tyr Tyr Leu Ala Val Pro Ser Thr Phe Leu Lys Asp Ala Pro Gly Glu
465                 470                 475                 480

Phe Leu Leu Arg Val Phe Ser Thr Gly Arg Val Ser Leu Ser Ala Ile
                485                 490                 495

Arg Ala Val Ala Lys Asn Thr Thr Pro Gly Ala Ala Leu Pro Ala Gly
            500                 505                 510

Glu Trp Gly Thr Val Gln Leu Arg Gly Ser Trp Arg Val Gly Gln Thr
        515                 520                 525

Ala Gly Gly Ser Arg Asn Phe Ala Ser Tyr Pro Thr Asn Pro Cys Phe
    530                 535                 540

Pro Phe Ser Val Pro Glu Gly Pro Gly Pro Arg Cys Val Arg Ile Thr
545                 550                 555                 560

Leu His Gln His Cys Arg Pro Ser Asp Thr Glu Phe His Pro Ile Gly
                565                 570                 575

Phe His Ile Phe Gln Val Pro Glu Gly Gly Arg Ser Gln Asp Ala Pro
            580                 585                 590
```

```
Pro Leu Leu Leu Gln Glu Pro Leu Leu Ser Cys Val Pro His Arg Tyr
        595                 600                 605


Ala Gln Glu Val Ser Arg Leu Cys Leu Leu Pro Ala Gly Thr Tyr Lys
    610                 615                 620


Val Val Pro Ser Thr Tyr Leu Pro Asp Thr Glu Gly Ala Phe Thr Val
625                 630                 635                 640


Thr Ile Ala Thr Arg Ile Asp Arg Pro Ser Ile His Ser Gln Glu Met
                645                 650                 655


Leu Gly Gln Phe Leu Gln Glu Val Ser Ile Met Ala Val Met Lys Thr
            660                 665                 670


<210>  201
<211>  544
<212>  PRT
<213>  Homo sapiens

<400>  201

Met Arg Ala Gly Arg Gly Ala Thr Pro Ala Arg Glu Leu Phe Arg Asp
1               5                   10                  15


Ala Ala Phe Pro Ala Ala Asp Ser Ser Leu Phe Cys Asp Leu Ser Thr
            20                  25                  30


Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu
        35                  40                  45


Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
    50                  55                  60


Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
65                  70                  75                  80


Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
                85                  90                  95


Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
            100                 105                 110


Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu
        115                 120                 125


Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp
    130                 135                 140


Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
145                 150                 155                 160
```

```
Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
                165                 170                 175

Leu Thr Gly Gly Leu Ala Glu Arg Trp Asn Leu Lys Gly Val Ala Gly
            180                 185                 190

Ser Gly Gly Gln Gln Asp Arg Pro Gly Arg Trp Glu His Arg Thr Cys
        195                 200                 205

Arg Gln Leu Leu His Leu Lys Asp Gln Cys Leu Ile Ser Cys Cys Val
    210                 215                 220

Leu Ser Pro Arg Ala Gly Ala Arg Glu Leu Gly Glu Phe His Ala Phe
225                 230                 235                 240

Ile Val Ser Asp Leu Arg Glu Leu Gln Gly Gln Ala Gly Gln Cys Ile
                245                 250                 255

Leu Leu Leu Arg Ile Gln Asn Pro Trp Gly Arg Arg Cys Trp Gln Gly
            260                 265                 270

Leu Trp Arg Glu Gly Gly Glu Gly Trp Ser Gln Val Asp Ala Ala Val
        275                 280                 285

Ala Ser Glu Leu Leu Ser Gln Leu Gln Glu Gly Glu Phe Trp Val Glu
    290                 295                 300

Glu Glu Glu Phe Leu Arg Glu Phe Asp Glu Leu Thr Val Gly Tyr Pro
305                 310                 315                 320

Val Thr Glu Ala Gly His Leu Gln Ser Leu Tyr Thr Glu Arg Leu Leu
                325                 330                 335

Cys His Thr Arg Ala Leu Pro Gly Ala Trp Val Lys Gly Gln Ser Ala
            340                 345                 350

Gly Gly Cys Arg Asn Asn Ser Gly Phe Pro Ser Asn Pro Lys Phe Trp
        355                 360                 365

Leu Arg Val Ser Glu Pro Ser Glu Val Tyr Ile Ala Val Leu Gln Arg
    370                 375                 380

Ser Arg Leu His Ala Ala Asp Trp Ala Gly Arg Ala Arg Ala Leu Val
385                 390                 395                 400

Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His
                405                 410                 415

Tyr Gln Ala Val Gly Leu His Leu Trp Lys Val Glu Lys Arg Arg Val
            420                 425                 430
```

```
Asn Leu Pro Arg Val Leu Ser Met Pro Pro Val Ala Gly Thr Ala Cys
        435                 440                 445

His Ala Tyr Asp Arg Glu Val His Leu Arg Cys Glu Leu Ser Pro Gly
    450                 455                 460

Tyr Tyr Leu Ala Val Pro Ser Thr Phe Leu Lys Asp Ala Pro Gly Glu
465                 470                 475                 480

Phe Leu Leu Arg Val Phe Ser Thr Gly Arg Val Ser Leu Arg Ala Leu
                485                 490                 495

Ala Pro Ala Ala Ser Ala Ser Leu Cys Ile Ser Thr Ala Gly Pro Val
            500                 505                 510

Thr Pro Ser Ser Thr Pro Ser Ala Ser Ile Ser Ser Arg Ser Gln Arg
        515                 520                 525

Val Glu Gly Ala Arg Thr His Pro His Cys Cys Cys Arg Ser Arg Cys
    530                 535                 540
```

<210> 202
<211> 517
<212> PRT
<213> Homo sapiens

<400> 202

```
Met Arg Ala Gly Arg Gly Ala Thr Pro Ala Arg Glu Leu Phe Arg Asp
1               5                   10                  15

Ala Ala Phe Pro Ala Ala Asp Ser Ser Leu Phe Cys Asp Leu Ser Thr
            20                  25                  30

Pro Leu Ala Gln Phe Arg Glu Asp Ile Thr Trp Arg Arg Pro Gln Glu
        35                  40                  45

Ile Cys Ala Thr Pro Arg Leu Phe Pro Asp Asp Pro Arg Glu Gly Gln
    50                  55                  60

Val Lys Gln Gly Leu Leu Gly Asp Cys Trp Phe Leu Cys Ala Cys Ala
65                  70                  75                  80

Ala Leu Gln Lys Ser Arg His Leu Leu Asp Gln Val Ile Pro Pro Gly
                85                  90                  95

Gln Pro Ser Trp Ala Asp Gln Glu Tyr Arg Gly Ser Phe Thr Cys Arg
            100                 105                 110

Ile Trp Gln Phe Gly Arg Trp Val Glu Val Thr Thr Asp Asp Arg Leu
        115                 120                 125
```

```
Pro Cys Leu Ala Gly Arg Leu Cys Phe Ser Arg Cys Gln Arg Glu Asp
    130                 135                 140

Val Phe Trp Leu Pro Leu Leu Glu Lys Val Tyr Ala Lys Val His Gly
145                 150                 155                 160

Ser Tyr Glu His Leu Trp Ala Gly Gln Val Ala Asp Ala Leu Val Asp
                165                 170                 175

Leu Thr Gly Gly Leu Ala Glu Arg Trp Asn Leu Lys Gly Val Ala Gly
            180                 185                 190

Ser Gly Gly Gln Gln Asp Arg Pro Gly Arg Trp Glu His Arg Thr Cys
        195                 200                 205

Arg Gln Leu Leu His Leu Lys Asp Gln Cys Leu Ile Ser Cys Cys Val
    210                 215                 220

Leu Ser Pro Arg Ala Gly Ala Arg Glu Leu Gly Glu Phe His Ala Phe
225                 230                 235                 240

Ile Val Ser Asp Leu Arg Glu Leu Gln Gly Gln Ala Gly Gln Cys Ile
                245                 250                 255

Leu Leu Leu Arg Ile Gln Asn Pro Trp Gly Arg Arg Cys Trp Gln Gly
            260                 265                 270

Leu Trp Arg Glu Gly Gly Glu Gly Trp Ser Gln Val Asp Ala Ala Val
        275                 280                 285

Ala Ser Glu Leu Leu Ser Gln Leu Gln Glu Gly Glu Phe Trp Val Glu
    290                 295                 300

Glu Glu Glu Phe Leu Arg Glu Phe Asp Glu Leu Thr Val Gly Tyr Pro
305                 310                 315                 320

Val Thr Glu Ala Gly His Leu Gln Ser Leu Tyr Thr Glu Arg Leu Leu
                325                 330                 335

Cys His Thr Arg Ala Leu Pro Gly Ala Trp Val Lys Gly Gln Ser Ala
            340                 345                 350

Gly Gly Cys Arg Asn Asn Ser Gly Phe Pro Ser Asn Pro Lys Phe Trp
        355                 360                 365

Leu Arg Val Ser Glu Pro Ser Glu Val Tyr Ile Ala Val Leu Gln Arg
    370                 375                 380

Ser Arg Leu His Ala Ala Asp Trp Ala Gly Arg Ala Arg Ala Leu Val
385                 390                 395                 400
```

Gly Asp Ser His Thr Ser Trp Ser Pro Ala Ser Ile Pro Gly Lys His
405 410 415

Tyr Gln Ala Val Gly Leu His Leu Trp Lys Val Pro Glu Gly Gly Arg
420 425 430

Ser Gln Asp Ala Pro Pro Leu Leu Leu Gln Glu Pro Leu Leu Ser Cys
435 440 445

Val Pro His Arg Tyr Ala Gln Glu Val Ser Arg Leu Cys Leu Leu Pro
450 455 460

Ala Gly Thr Tyr Lys Val Val Pro Ser Thr Tyr Leu Pro Asp Thr Glu
465 470 475 480

Gly Ala Phe Thr Val Thr Ile Ala Thr Arg Ile Asp Arg Pro Ser Ile
485 490 495

His Ser Gln Glu Met Leu Gly Gln Phe Leu Gln Glu Val Ser Ile Met
500 505 510

Ala Val Met Lys Thr
515

<210> 203
<211> 370
<212> PRT
<213> Homo sapiens

<400> 203

Met His Arg Leu Ile Phe Val Tyr Thr Leu Ile Cys Ala Asn Phe Cys
1 5 10 15

Ser Cys Arg Asp Thr Ser Ala Thr Pro Gln Ser Ala Ser Ile Lys Ala
20 25 30

Leu Arg Asn Ala Asn Leu Arg Arg Asp Glu Ser Asn His Leu Thr Asp
35 40 45

Leu Tyr Arg Arg Asp Glu Thr Ile Gln Val Lys Gly Asn Gly Tyr Val
50 55 60

Gln Ser Pro Arg Phe Pro Asn Ser Tyr Pro Arg Asn Leu Leu Leu Thr
65 70 75 80

Trp Arg Leu His Ser Gln Glu Asn Thr Arg Ile Gln Leu Val Phe Asp
85 90 95

Asn Gln Phe Gly Leu Glu Glu Ala Glu Asn Asp Ile Cys Arg Tyr Asp
100 105 110

Phe Val Glu Val Glu Asp Ile Ser Glu Thr Ser Thr Ile Ile Arg Gly

115 120 125

Arg Trp Cys Gly His Lys Glu Val Pro Pro Arg Ile Lys Ser Arg Thr
130 135 140

Asn Gln Ile Lys Ile Thr Phe Lys Ser Asp Asp Tyr Phe Val Ala Lys
145 150 155 160

Pro Gly Phe Lys Ile Tyr Tyr Ser Leu Leu Glu Asp Phe Gln Pro Ala
165 170 175

Ala Ala Ser Glu Thr Asn Trp Glu Ser Val Thr Ser Ser Ile Ser Gly
180 185 190

Val Ser Tyr Asn Ser Pro Ser Val Thr Asp Pro Thr Leu Ile Ala Asp
195 200 205

Ala Leu Asp Lys Lys Ile Ala Glu Phe Asp Thr Val Glu Asp Leu Leu
210 215 220

Lys Tyr Phe Asn Pro Glu Ser Trp Gln Glu Asp Leu Glu Asn Met Tyr
225 230 235 240

Leu Asp Thr Pro Arg Tyr Arg Gly Arg Ser Tyr His Asp Arg Lys Ser
245 250 255

Lys Val Asp Leu Asp Arg Leu Asn Asp Asp Ala Lys Arg Tyr Ser Cys
260 265 270

Thr Pro Arg Asn Tyr Ser Val Asn Ile Arg Glu Glu Leu Lys Leu Ala
275 280 285

Asn Val Val Phe Phe Pro Arg Cys Leu Leu Val Gln Arg Cys Gly Gly
290 295 300

Asn Cys Gly Cys Gly Thr Val Asn Trp Arg Ser Cys Thr Cys Asn Ser
305 310 315 320

Gly Lys Thr Val Lys Lys Tyr His Glu Val Leu Gln Phe Glu Pro Gly
325 330 335

His Ile Lys Arg Arg Gly Arg Ala Lys Thr Met Ala Leu Val Asp Ile
340 345 350

Gln Leu Asp His His Glu Arg Cys Asp Cys Ile Cys Ser Ser Arg Pro
355 360 365

Pro Arg
370

<210> 204

<211> 281
<212> PRT
<213> Homo sapiens

<400> 204

```
Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
1               5                  10                  15

Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
            20                  25                  30

Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
        35                  40                  45

Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Leu Pro
    50                  55                  60

Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
65                  70                  75                  80

Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
                85                  90                  95

Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
            100                 105                 110

Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu
        115                 120                 125

Lys Gln Ile Gly His Pro Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg
    130                 135                 140

Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu
145                 150                 155                 160

Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr
                165                 170                 175

Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr
            180                 185                 190

Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser
        195                 200                 205

His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met
    210                 215                 220

Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala
225                 230                 235                 240

Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His
                245                 250                 255
```

Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser
260 265 270

Gln Thr Phe Phe Gly Leu Tyr Lys Leu
275 280

<210> 205
<211> 1447
<212> PRT
<213> Homo sapiens

<400> 205

Met Ala Ser Ala Gly Asn Ala Ala Glu Pro Gln Asp Arg Gly Gly Gly
1 5 10 15

Gly Ser Gly Cys Ile Gly Ala Pro Gly Arg Pro Ala Gly Gly Gly Arg
20 25 30

Arg Arg Arg Thr Gly Gly Leu Arg Arg Ala Ala Ala Pro Asp Arg Asp
35 40 45

Tyr Leu His Arg Pro Ser Tyr Cys Asp Ala Ala Phe Ala Leu Glu Gln
50 55 60

Ile Ser Lys Gly Lys Ala Thr Gly Arg Lys Ala Pro Leu Trp Leu Arg
65 70 75 80

Ala Lys Phe Gln Arg Leu Leu Phe Lys Leu Gly Cys Tyr Ile Gln Lys
85 90 95

Asn Cys Gly Lys Phe Leu Val Val Gly Leu Leu Ile Phe Gly Ala Phe
100 105 110

Ala Val Gly Leu Lys Ala Ala Asn Leu Glu Thr Asn Val Glu Glu Leu
115 120 125

Trp Val Glu Val Gly Gly Arg Val Ser Arg Glu Leu Asn Tyr Thr Arg
130 135 140

Gln Lys Ile Gly Glu Glu Ala Met Phe Asn Pro Gln Leu Met Ile Gln
145 150 155 160

Thr Pro Lys Glu Glu Gly Ala Asn Val Leu Thr Thr Glu Ala Leu Leu
165 170 175

Gln His Leu Asp Ser Ala Leu Gln Ala Ser Arg Val His Val Tyr Met
180 185 190

Tyr Asn Arg Gln Trp Lys Leu Glu His Leu Cys Tyr Lys Ser Gly Glu
195 200 205

```
Leu Ile Thr Glu Thr Gly Tyr Met Asp Gln Ile Ile Glu Tyr Leu Tyr
    210                 215                 220

Pro Cys Leu Ile Ile Thr Pro Leu Asp Cys Phe Trp Glu Gly Ala Lys
225                 230                 235                 240

Leu Gln Ser Gly Thr Ala Tyr Leu Leu Gly Lys Pro Pro Leu Arg Trp
                245                 250                 255

Thr Asn Phe Asp Pro Leu Glu Phe Leu Glu Glu Leu Lys Lys Ile Asn
            260                 265                 270

Tyr Gln Val Asp Ser Trp Glu Glu Met Leu Asn Lys Ala Glu Val Gly
        275                 280                 285

His Gly Tyr Met Asp Arg Pro Cys Leu Asn Pro Ala Asp Pro Asp Cys
    290                 295                 300

Pro Ala Thr Ala Pro Asn Lys Asn Ser Thr Lys Pro Leu Asp Met Ala
305                 310                 315                 320

Leu Val Leu Asn Gly Gly Cys His Gly Leu Ser Arg Lys Tyr Met His
                325                 330                 335

Trp Gln Glu Glu Leu Ile Val Gly Gly Thr Val Lys Asn Ser Thr Gly
            340                 345                 350

Lys Leu Val Ser Ala His Ala Leu Gln Thr Met Phe Gln Leu Met Thr
        355                 360                 365

Pro Lys Gln Met Tyr Glu His Phe Lys Gly Tyr Glu Tyr Val Ser His
    370                 375                 380

Ile Asn Trp Asn Glu Asp Lys Ala Ala Ala Ile Leu Glu Ala Trp Gln
385                 390                 395                 400

Arg Thr Tyr Val Glu Val Val His Gln Ser Val Ala Gln Asn Ser Thr
                405                 410                 415

Gln Lys Val Leu Ser Phe Thr Thr Thr Thr Leu Asp Asp Ile Leu Lys
            420                 425                 430

Ser Phe Ser Asp Val Ser Val Ile Arg Val Ala Ser Gly Tyr Leu Leu
        435                 440                 445

Met Leu Ala Tyr Ala Cys Leu Thr Met Leu Arg Trp Asp Cys Ser Lys
    450                 455                 460

Ser Gln Gly Ala Val Gly Leu Ala Gly Val Leu Leu Val Ala Leu Ser
465                 470                 475                 480
```

```
Val Ala Ala Gly Leu Gly Leu Cys Ser Leu Ile Gly Ile Ser Phe Asn
                485                 490                 495

Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu Gly Val Gly Val
            500                 505                 510

Asp Asp Val Phe Leu Leu Ala His Ala Phe Ser Glu Thr Gly Gln Asn
        515                 520                 525

Lys Arg Ile Pro Phe Glu Asp Arg Thr Gly Glu Cys Leu Lys Arg Thr
    530                 535                 540

Gly Ala Ser Val Ala Leu Thr Ser Ile Ser Asn Val Thr Ala Phe Phe
545                 550                 555                 560

Met Ala Ala Leu Ile Pro Ile Pro Ala Leu Arg Ala Phe Ser Leu Gln
                565                 570                 575

Ala Ala Val Val Val Val Phe Asn Phe Ala Met Val Leu Leu Ile Phe
            580                 585                 590

Pro Ala Ile Leu Ser Met Asp Leu Tyr Arg Arg Glu Asp Arg Arg Leu
        595                 600                 605

Asp Ile Phe Cys Cys Phe Thr Ser Pro Cys Val Ser Arg Val Ile Gln
    610                 615                 620

Val Glu Pro Gln Ala Tyr Thr Asp Thr His Asp Asn Thr Arg Tyr Ser
625                 630                 635                 640

Pro Pro Pro Pro Tyr Ser Ser His Ser Phe Ala His Glu Thr Gln Ile
                645                 650                 655

Thr Met Gln Ser Thr Val Gln Leu Arg Thr Glu Tyr Asp Pro His Thr
            660                 665                 670

His Val Tyr Tyr Thr Thr Ala Glu Pro Arg Ser Glu Ile Ser Val Gln
        675                 680                 685

Pro Val Thr Val Thr Gln Asp Thr Leu Ser Cys Gln Ser Pro Glu Ser
    690                 695                 700

Thr Ser Ser Thr Arg Asp Leu Leu Ser Gln Phe Ser Asp Ser Ser Leu
705                 710                 715                 720

His Cys Leu Glu Pro Pro Cys Thr Lys Trp Thr Leu Ser Ser Phe Ala
                725                 730                 735

Glu Lys His Tyr Ala Pro Phe Leu Leu Lys Pro Lys Ala Lys Val Val
            740                 745                 750
```

```
Val Ile Phe Leu Phe Leu Gly Leu Leu Gly Val Ser Leu Tyr Gly Thr
        755                 760                 765

Thr Arg Val Arg Asp Gly Leu Asp Leu Thr Asp Ile Val Pro Arg Glu
    770                 775                 780

Thr Arg Glu Tyr Asp Phe Ile Ala Ala Gln Phe Lys Tyr Phe Ser Phe
785                 790                 795                 800

Tyr Asn Met Tyr Ile Val Thr Gln Lys Ala Asp Tyr Pro Asn Ile Gln
                805                 810                 815

His Leu Leu Tyr Asp Leu His Arg Ser Phe Ser Asn Val Lys Tyr Val
            820                 825                 830

Met Leu Glu Glu Asn Lys Gln Leu Pro Lys Met Trp Leu His Tyr Phe
        835                 840                 845

Arg Asp Trp Leu Gln Gly Leu Gln Asp Ala Phe Asp Ser Asp Trp Glu
    850                 855                 860

Thr Gly Lys Ile Met Pro Asn Asn Tyr Lys Asn Gly Ser Asp Asp Gly
865                 870                 875                 880

Val Leu Ala Tyr Lys Leu Leu Val Gln Thr Gly Ser Arg Asp Lys Pro
                885                 890                 895

Ile Asp Ile Ser Gln Leu Thr Lys Gln Arg Leu Val Asp Ala Asp Gly
            900                 905                 910

Ile Ile Asn Pro Ser Ala Phe Tyr Ile Tyr Leu Thr Ala Trp Val Ser
        915                 920                 925

Asn Asp Pro Val Ala Tyr Ala Ala Ser Gln Ala Asn Ile Arg Pro His
    930                 935                 940

Arg Pro Glu Trp Val His Asp Lys Ala Asp Tyr Met Pro Glu Thr Arg
945                 950                 955                 960

Leu Arg Ile Pro Ala Ala Glu Pro Ile Glu Tyr Ala Gln Phe Pro Phe
                965                 970                 975

Tyr Leu Asn Gly Leu Arg Asp Thr Ser Asp Phe Val Glu Ala Ile Glu
            980                 985                 990

Lys Val Arg Thr Ile Cys Ser Asn  Tyr Thr Ser Leu Gly  Leu Ser Ser
        995                 1000                1005

Tyr Pro  Asn Gly Tyr Pro Phe  Leu Phe Trp Glu Gln  Tyr Ile Gly
    1010                1015                1020
```

```
Leu Arg  His Trp Leu Leu Leu  Phe Ile Ser Val Val  Leu Ala Cys
    1025                1030                1035

Thr Phe  Leu Val Cys Ala Val  Phe Leu Leu Asn Pro  Trp Thr Ala
    1040                1045                1050

Gly Ile  Ile Val Met Val Leu  Ala Leu Met Thr Val  Glu Leu Phe
    1055                1060                1065

Gly Met  Met Gly Leu Ile Gly  Ile Lys Leu Ser Ala  Val Pro Val
    1070                1075                1080

Val Ile  Leu Ile Ala Ser Val  Gly Ile Gly Val Glu  Phe Thr Val
    1085                1090                1095

His Val  Ala Leu Ala Phe Leu  Thr Ala Ile Gly Asp  Lys Asn Arg
    1100                1105                1110

Arg Ala  Val Leu Ala Leu Glu  His Met Phe Ala Pro  Val Leu Asp
    1115                1120                1125

Gly Ala  Val Ser Thr Leu Leu  Gly Val Leu Met Leu  Ala Gly Ser
    1130                1135                1140

Glu Phe  Asp Phe Ile Val Arg  Tyr Phe Phe Ala Val  Leu Ala Ile
    1145                1150                1155

Leu Thr  Ile Leu Gly Val Leu  Asn Gly Leu Val Leu  Leu Pro Val
    1160                1165                1170

Leu Leu  Ser Phe Phe Gly Pro  Tyr Pro Glu Val Ser  Pro Ala Asn
    1175                1180                1185

Gly Leu  Asn Arg Leu Pro Thr  Pro Ser Pro Glu Pro  Pro Pro Ser
    1190                1195                1200

Val Val  Arg Phe Ala Met Pro  Pro Gly His Thr His  Ser Gly Ser
    1205                1210                1215

Asp Ser  Ser Asp Ser Glu Tyr  Ser Ser Gln Thr Thr  Val Ser Gly
    1220                1225                1230

Leu Ser  Glu Glu Leu Arg His  Tyr Glu Ala Gln Gln  Gly Ala Gly
    1235                1240                1245

Gly Pro  Ala His Gln Val Ile  Val Glu Ala Thr Glu  Asn Pro Val
    1250                1255                1260

Phe Ala  His Ser Thr Val Val  His Pro Glu Ser Arg  His His Pro
    1265                1270                1275
```

```
Pro Ser  Asn Pro Arg Gln Gln  Pro His Leu Asp Ser  Gly Ser Leu
    1280                1285                1290

Pro Pro  Gly Arg Gln Gly Gln  Gln Pro Arg Arg Asp  Pro Pro Arg
    1295                1300                1305

Glu Gly  Leu Trp Pro Pro Pro  Tyr Arg Pro Arg Arg  Asp Ala Phe
    1310                1315                1320

Glu Ile  Ser Thr Glu Gly His  Ser Gly Pro Ser Asn  Arg Ala Arg
    1325                1330                1335

Trp Gly  Pro Arg Gly Ala Arg  Ser His Asn Pro Arg  Asn Pro Ala
    1340                1345                1350

Ser Thr  Ala Met Gly Ser Ser  Val Pro Gly Tyr Cys  Gln Pro Ile
    1355                1360                1365

Thr Thr  Val Thr Ala Ser Ala  Ser Val Thr Val Ala  Val His Pro
    1370                1375                1380

Pro Pro  Val Pro Gly Pro Gly  Arg Asn Pro Arg Gly  Gly Leu Cys
    1385                1390                1395

Pro Gly  Tyr Pro Glu Thr Asp  His Gly Leu Phe Glu  Asp Pro His
    1400                1405                1410

Val Pro  Phe His Val Arg Cys  Glu Arg Arg Asp Ser  Lys Val Glu
    1415                1420                1425

Val Ile  Glu Leu Gln Asp Val  Glu Cys Glu Glu Arg  Pro Arg Gly
    1430                1435                1440

Ser Ser  Ser Asn
    1445


<210>  206
<211>  1203
<212>  PRT
<213>  Homo sapiens

<400>  206

Met Thr Arg Ser Pro Pro Leu Arg Glu Leu Pro Pro Ser Tyr Thr Pro
1               5                  10                  15

Pro Ala Arg Thr Ala Ala Pro Gln Ile Leu Ala Gly Ser Leu Lys Ala
            20                  25                  30

Pro Leu Trp Leu Arg Ala Tyr Phe Gln Gly Leu Leu Phe Ser Leu Gly
        35                  40                  45
```

```
Cys Gly Ile Gln Arg His Cys Gly Lys Val Leu Phe Leu Gly Leu Leu
    50                  55                  60

Ala Phe Gly Ala Leu Ala Leu Gly Leu Arg Met Ala Ile Ile Glu Thr
65                  70                  75                  80

Asn Leu Glu Gln Leu Trp Val Glu Val Gly Ser Arg Val Ser Gln Glu
                85                  90                  95

Leu His Tyr Thr Lys Glu Lys Leu Gly Glu Glu Ala Ala Tyr Thr Ser
            100                 105                 110

Gln Met Leu Ile Gln Thr Ala Arg Gln Glu Gly Glu Asn Ile Leu Thr
        115                 120                 125

Pro Glu Ala Leu Gly Leu His Leu Gln Ala Ala Leu Thr Ala Ser Lys
    130                 135                 140

Val Gln Val Ser Leu Tyr Gly Lys Ser Trp Asp Leu Asn Lys Ile Cys
145                 150                 155                 160

Tyr Lys Ser Gly Val Pro Leu Ile Glu Asn Gly Met Ile Glu Arg Met
                165                 170                 175

Ile Glu Lys Leu Phe Pro Cys Val Ile Leu Thr Pro Leu Asp Cys Phe
            180                 185                 190

Trp Glu Gly Ala Lys Leu Gln Gly Gly Ser Ala Tyr Leu Pro Gly Arg
        195                 200                 205

Pro Asp Ile Gln Trp Thr Asn Leu Asp Pro Glu Gln Leu Leu Glu Glu
    210                 215                 220

Leu Gly Pro Phe Ala Ser Leu Glu Gly Phe Arg Glu Leu Leu Asp Lys
225                 230                 235                 240

Ala Gln Val Gly Gln Ala Tyr Val Gly Arg Pro Cys Leu His Pro Asp
                245                 250                 255

Asp Leu His Cys Pro Pro Ser Ala Pro Asn His His Ser Arg Gln Ala
            260                 265                 270

Pro Asn Val Ala His Glu Leu Ser Gly Gly Cys His Gly Phe Ser His
        275                 280                 285

Lys Phe Met His Trp Gln Glu Glu Leu Leu Leu Gly Gly Met Ala Arg
    290                 295                 300

Asp Pro Gln Gly Glu Leu Leu Arg Ala Glu Ala Leu Gln Ser Thr Phe
305                 310                 315                 320
```

```
Leu Leu Met Ser Pro Arg Gln Leu Tyr Glu His Phe Arg Gly Asp Tyr
                325                 330                 335

Gln Thr His Asp Ile Gly Trp Ser Glu Glu Gln Ala Ser Thr Val Leu
            340                 345                 350

Gln Ala Trp Gln Arg Arg Phe Val Gln Leu Ala Gln Glu Ala Leu Pro
        355                 360                 365

Glu Asn Ala Ser Gln Gln Ile His Ala Phe Ser Ser Thr Thr Leu Asp
    370                 375                 380

Asp Ile Leu His Ala Phe Ser Glu Val Ser Ala Ala Arg Val Val Gly
385                 390                 395                 400

Gly Tyr Leu Leu Met Leu Ala Tyr Ala Cys Val Thr Met Leu Arg Trp
                405                 410                 415

Asp Cys Ala Gln Ser Gln Gly Ser Val Gly Leu Ala Gly Val Leu Leu
            420                 425                 430

Val Ala Leu Ala Val Ala Ser Gly Leu Gly Leu Cys Ala Leu Leu Gly
        435                 440                 445

Ile Thr Phe Asn Ala Ala Thr Thr Gln Val Leu Pro Phe Leu Ala Leu
    450                 455                 460

Gly Ile Gly Val Asp Asp Val Phe Leu Leu Ala His Ala Phe Thr Glu
465                 470                 475                 480

Ala Leu Pro Gly Thr Pro Leu Gln Glu Arg Met Gly Glu Cys Leu Gln
                485                 490                 495

Arg Thr Gly Thr Ser Val Val Leu Thr Ser Ile Asn Asn Met Ala Ala
            500                 505                 510

Phe Leu Met Ala Ala Leu Val Pro Ile Pro Ala Leu Arg Ala Phe Ser
        515                 520                 525

Leu Gln Ala Ala Ile Val Val Gly Cys Thr Phe Val Ala Val Met Leu
    530                 535                 540

Val Phe Pro Ala Ile Leu Ser Leu Asp Leu Arg Arg Arg His Cys Gln
545                 550                 555                 560

Arg Leu Asp Val Leu Cys Cys Phe Ser Ser Pro Cys Ser Ala Gln Val
                565                 570                 575

Ile Gln Ile Leu Pro Gln Glu Leu Gly Asp Gly Thr Val Pro Val Gly
            580                 585                 590
```

```
Ile Ala His Leu Thr Ala Thr Val Gln Ala Phe Thr His Cys Glu Ala
        595                 600                 605

Ser Ser Gln His Val Val Thr Ile Leu Pro Pro Gln Ala His Leu Val
    610                 615                 620

Pro Pro Pro Ser Asp Pro Leu Gly Ser Glu Leu Phe Ser Pro Gly Gly
625                 630                 635                 640

Ser Thr Arg Asp Leu Leu Gly Gln Glu Glu Glu Thr Arg Gln Lys Ala
                645                 650                 655

Ala Cys Lys Ser Leu Pro Cys Ala Arg Trp Asn Leu Ala His Phe Ala
            660                 665                 670

Arg Tyr Gln Phe Ala Pro Leu Leu Leu Gln Ser His Ala Lys Ala Ile
        675                 680                 685

Val Leu Val Leu Phe Gly Ala Leu Leu Gly Leu Ser Leu Tyr Gly Ala
    690                 695                 700

Thr Leu Val Gln Asp Gly Leu Ala Leu Thr Asp Val Val Pro Arg Gly
705                 710                 715                 720

Thr Lys Glu His Ala Phe Leu Ser Ala Gln Leu Arg Tyr Phe Ser Leu
                725                 730                 735

Tyr Glu Val Ala Leu Val Thr Gln Gly Gly Phe Asp Tyr Ala His Ser
            740                 745                 750

Gln Arg Ala Leu Phe Asp Leu His Gln Arg Phe Ser Ser Leu Lys Ala
        755                 760                 765

Val Leu Pro Pro Pro Ala Thr Gln Ala Pro Arg Thr Trp Leu His Tyr
    770                 775                 780

Tyr Arg Asn Trp Leu Gln Gly Ile Gln Ala Ala Phe Asp Gln Asp Trp
785                 790                 795                 800

Ala Ser Gly Arg Ile Thr Arg His Ser Tyr Arg Asn Gly Ser Glu Asp
                805                 810                 815

Gly Ala Leu Ala Tyr Lys Leu Leu Ile Gln Thr Gly Asp Ala Gln Glu
            820                 825                 830

Pro Leu Asp Phe Ser Gln Leu Thr Thr Arg Lys Leu Val Asp Arg Glu
        835                 840                 845

Gly Leu Ile Pro Pro Glu Leu Phe Tyr Met Gly Leu Thr Val Trp Val
    850                 855                 860
```

```
Ser Ser Asp Pro Leu Gly Leu Ala Ala Ser Gln Ala Asn Phe Tyr Pro
865                 870                 875                 880

Pro Pro Pro Glu Trp Leu His Asp Lys Tyr Asp Thr Thr Gly Glu Asn
                885                 890                 895

Leu Arg Ile Pro Pro Ala Gln Pro Leu Glu Phe Ala Gln Phe Pro Phe
            900                 905                 910

Leu Leu Arg Gly Leu Gln Lys Thr Ala Asp Phe Val Glu Ala Ile Glu
        915                 920                 925

Gly Ala Arg Ala Ala Cys Ala Glu Ala Gly Gln Ala Gly Val His Ala
    930                 935                 940

Tyr Pro Ser Gly Ser Pro Phe Leu Phe Trp Glu Gln Tyr Leu Gly Leu
945                 950                 955                 960

Arg Arg Cys Phe Leu Leu Ala Val Cys Ile Leu Leu Val Cys Thr Phe
                965                 970                 975

Leu Val Cys Ala Leu Leu Leu Leu Asn Pro Trp Thr Ala Gly Leu Ile
            980                 985                 990

Val Leu Val Leu Ala Met Met Thr  Val Glu Leu Phe Gly  Ile Met Gly
        995                 1000                1005

Phe Leu  Gly Ile Lys Leu Ser  Ala Ile Pro Val Val  Ile Leu Val
    1010                1015                1020

Ala Ser  Val Gly Ile Gly Val  Glu Phe Thr Val His  Val Ala Leu
    1025                1030                1035

Gly Phe  Leu Thr Thr Gln Gly  Ser Arg Asn Leu Arg  Ala Ala His
    1040                1045                1050

Ala Leu  Glu His Thr Phe Ala  Pro Val Thr Asp Gly  Ala Ile Ser
    1055                1060                1065

Thr Leu  Leu Gly Leu Leu Met  Leu Ala Gly Ser His  Phe Asp Phe
    1070                1075                1080

Ile Val  Arg Tyr Phe Phe Ala  Ala Leu Thr Val Leu  Thr Leu Leu
    1085                1090                1095

Gly Leu  Leu His Gly Leu Val  Leu Leu Pro Val Leu  Leu Ser Ile
    1100                1105                1110

Leu Gly  Pro Pro Pro Glu Val  Ile Gln Met Tyr Lys  Glu Ser Pro
    1115                1120                1125
```

Glu Ile Leu Ser Pro Pro Ala Pro Gln Gly Gly Gly Leu Arg Trp
1130 1135 1140

Gly Ala Ser Ser Ser Leu Pro Gln Ser Phe Ala Arg Val Thr Thr
1145 1150 1155

Ser Met Thr Val Ala Ile His Pro Pro Pro Leu Pro Gly Ala Tyr
1160 1165 1170

Ile His Pro Ala Pro Asp Glu Pro Pro Trp Ser Pro Ala Ala Thr
1175 1180 1185

Ser Ser Gly Asn Leu Ser Ser Arg Gly Pro Gly Pro Ala Thr Gly
1190 1195 1200

<210> 207
<211> 375
<212> PRT
<213> Homo sapiens

<400> 207

Met Asp Ala Leu Gln Leu Ala Asn Ser Ala Phe Ala Val Asp Leu Phe
1 5 10 15

Lys Gln Leu Cys Glu Lys Glu Pro Leu Gly Asn Val Leu Phe Ser Pro
20 25 30

Ile Cys Leu Ser Thr Ser Leu Ser Leu Ala Gln Val Gly Ala Lys Gly
35 40 45

Asp Thr Ala Asn Glu Ile Gly Gln Val Leu His Phe Glu Asn Val Lys
50 55 60

Asp Val Pro Phe Gly Phe Gln Thr Val Thr Ser Asp Val Asn Lys Leu
65 70 75 80

Ser Ser Phe Tyr Ser Leu Lys Leu Ile Lys Arg Leu Tyr Val Asp Lys
85 90 95

Ser Leu Asn Leu Ser Thr Glu Phe Ile Ser Ser Thr Lys Arg Pro Tyr
100 105 110

Ala Lys Glu Leu Glu Thr Val Asp Phe Lys Asp Lys Leu Glu Glu Thr
115 120 125

Lys Gly Gln Ile Asn Asn Ser Ile Lys Asp Leu Thr Asp Gly His Phe
130 135 140

Glu Asn Ile Leu Ala Asp Asn Ser Val Asn Asp Gln Thr Lys Ile Leu
145 150 155 160

Val Val Asn Ala Ala Tyr Phe Val Gly Lys Trp Met Lys Lys Phe Ser

165 170 175

Glu Ser Glu Thr Lys Glu Cys Pro Phe Arg Val Asn Lys Thr Asp Thr
180 185 190

Lys Pro Val Gln Met Met Asn Met Glu Ala Thr Phe Cys Met Gly Asn
195 200 205

Ile Asp Ser Ile Asn Cys Lys Ile Ile Glu Leu Pro Phe Gln Asn Lys
210 215 220

His Leu Ser Met Phe Ile Leu Leu Pro Lys Asp Val Glu Asp Glu Ser
225 230 235 240

Thr Gly Leu Glu Lys Ile Glu Lys Gln Leu Asn Ser Glu Ser Leu Ser
245 250 255

Gln Trp Thr Asn Pro Ser Thr Met Ala Asn Ala Lys Val Lys Leu Ser
260 265 270

Ile Pro Lys Phe Lys Val Glu Lys Met Ile Asp Pro Lys Ala Cys Leu
275 280 285

Glu Asn Leu Gly Leu Lys His Ile Phe Ser Glu Asp Thr Ser Asp Phe
290 295 300

Ser Gly Met Ser Glu Thr Lys Gly Val Ala Leu Ser Asn Val Ile His
305 310 315 320

Lys Val Cys Leu Glu Ile Thr Glu Asp Gly Gly Asp Ser Ile Glu Val
325 330 335

Pro Gly Ala Arg Ile Leu Gln His Lys Asp Glu Leu Asn Ala Asp His
340 345 350

Pro Phe Ile Tyr Ile Ile Arg His Asn Lys Thr Arg Asn Ile Ile Phe
355 360 365

Phe Gly Lys Phe Cys Ser Pro
370 375

<210> 208
<211> 1754
<212> PRT
<213> Homo sapiens

<400> 208

Met Ala Pro Tyr Pro Cys Gly Cys His Ile Leu Leu Leu Leu Phe Cys
1 5 10 15

Cys Leu Ala Ala Ala Arg Ala Asn Leu Leu Asn Leu Asn Trp Leu Trp
20 25 30

```
Phe Asn Asn Glu Asp Thr Ser His Ala Ala Thr Thr Ile Pro Glu Pro
        35                  40                  45

Gln Gly Pro Leu Pro Val Gln Pro Thr Ala Asp Thr Thr Thr His Val
    50                  55                  60

Thr Pro Arg Asn Gly Ser Thr Glu Pro Ala Thr Ala Pro Gly Ser Pro
65                  70                  75                  80

Glu Pro Pro Ser Glu Leu Leu Glu Asp Gly Gln Asp Thr Pro Thr Ser
                85                  90                  95

Ala Glu Ser Pro Asp Ala Pro Glu Glu Asn Ile Ala Gly Val Gly Ala
            100                 105                 110

Glu Ile Leu Asn Val Ala Lys Gly Ile Arg Ser Phe Val Gln Leu Trp
        115                 120                 125

Asn Asp Thr Val Pro Thr Glu Ser Leu Ala Arg Ala Glu Thr Leu Val
    130                 135                 140

Leu Glu Thr Pro Val Gly Pro Leu Ala Leu Ala Gly Pro Ser Ser Thr
145                 150                 155                 160

Pro Gln Glu Asn Gly Thr Thr Leu Trp Pro Ser Arg Gly Ile Pro Ser
                165                 170                 175

Ser Pro Gly Ala His Thr Thr Glu Ala Gly Thr Leu Pro Ala Pro Thr
            180                 185                 190

Pro Ser Pro Pro Ser Leu Gly Arg Pro Trp Ala Pro Leu Thr Gly Pro
        195                 200                 205

Ser Val Pro Pro Pro Ser Ser Gly Arg Ala Ser Leu Ser Ser Leu Leu
    210                 215                 220

Gly Gly Ala Pro Pro Trp Gly Ser Leu Gln Asp Pro Asp Ser Gln Gly
225                 230                 235                 240

Leu Ser Pro Ala Ala Ala Ala Pro Ser Gln Gln Leu Gln Arg Pro Asp
                245                 250                 255

Val Arg Leu Arg Thr Pro Leu Leu His Pro Leu Val Met Gly Ser Leu
            260                 265                 270

Gly Lys His Ala Ala Pro Ser Ala Phe Ser Ser Gly Leu Pro Gly Ala
        275                 280                 285

Leu Ser Gln Val Ala Val Thr Thr Leu Thr Arg Asp Ser Gly Ala Trp
    290                 295                 300
```

```
Val Ser His Val Ala Asn Ser Val Gly Pro Gly Leu Ala Asn Asn Ser
305                 310                 315                 320

Ala Leu Leu Gly Ala Asp Pro Glu Ala Pro Ala Gly Arg Cys Leu Pro
                325                 330                 335

Leu Pro Pro Ser Leu Pro Val Cys Gly His Leu Gly Ile Ser Arg Phe
            340                 345                 350

Trp Leu Pro Asn His Leu His His Glu Ser Gly Glu Gln Val Arg Ala
        355                 360                 365

Gly Ala Arg Ala Trp Gly Gly Leu Leu Gln Thr His Cys His Pro Phe
    370                 375                 380

Leu Ala Trp Phe Phe Cys Leu Leu Leu Val Pro Pro Cys Gly Ser Val
385                 390                 395                 400

Pro Pro Pro Ala Pro Pro Pro Cys Cys Gln Phe Cys Glu Ala Leu Gln
                405                 410                 415

Asp Ala Cys Trp Ser Arg Leu Gly Gly Gly Arg Leu Pro Val Ala Cys
            420                 425                 430

Ala Ser Leu Pro Thr Gln Glu Asp Gly Tyr Cys Val Leu Ile Gly Pro
        435                 440                 445

Ala Ala Glu Arg Ile Ser Glu Glu Val Gly Leu Leu Gln Leu Leu Gly
    450                 455                 460

Asp Pro Pro Pro Gln Gln Val Thr Gln Thr Asp Asp Pro Asp Val Gly
465                 470                 475                 480

Leu Ala Tyr Val Phe Gly Pro Asp Ala Asn Ser Gly Gln Val Ala Arg
                485                 490                 495

Tyr His Phe Pro Ser Leu Phe Phe Arg Asp Phe Ser Leu Leu Phe His
            500                 505                 510

Ile Arg Pro Ala Thr Glu Gly Pro Gly Val Leu Phe Ala Ile Thr Asp
        515                 520                 525

Ser Ala Gln Ala Met Val Leu Leu Gly Val Lys Leu Ser Gly Val Gln
    530                 535                 540

Asp Gly His Gln Asp Ile Ser Leu Leu Tyr Thr Glu Pro Gly Ala Gly
545                 550                 555                 560

Gln Thr His Thr Ala Ala Ser Phe Arg Leu Pro Ala Phe Val Gly Gln
                565                 570                 575
```

```
Trp Thr His Leu Ala Leu Ser Val Ala Gly Gly Phe Val Ala Leu Tyr
            580                 585                 590

Val Asp Cys Glu Glu Phe Gln Arg Met Pro Leu Ala Arg Ser Ser Arg
        595                 600                 605

Gly Leu Glu Leu Glu Pro Gly Ala Gly Leu Phe Val Ala Gln Ala Gly
    610                 615                 620

Gly Ala Asp Pro Asp Lys Phe Gln Gly Val Ile Ala Glu Leu Lys Val
625                 630                 635                 640

Arg Arg Asp Pro Gln Val Ser Pro Met His Cys Leu Asp Glu Glu Gly
                645                 650                 655

Asp Asp Ser Asp Gly Ala Ser Gly Asp Ser Gly Ser Gly Leu Gly Asp
            660                 665                 670

Ala Arg Glu Leu Leu Arg Glu Glu Thr Gly Ala Ala Leu Lys Pro Arg
        675                 680                 685

Leu Pro Ala Pro Pro Pro Val Thr Thr Pro Pro Leu Ala Gly Gly Ser
    690                 695                 700

Ser Thr Glu Asp Ser Arg Ser Glu Glu Val Glu Glu Gln Thr Thr Val
705                 710                 715                 720

Ala Ser Leu Gly Ala Gln Thr Leu Pro Gly Ser Asp Ser Val Ser Thr
                725                 730                 735

Trp Asp Gly Ser Val Arg Thr Pro Gly Gly Arg Val Lys Glu Gly Gly
            740                 745                 750

Leu Lys Gly Gln Lys Gly Glu Pro Gly Val Pro Gly Pro Pro Gly Arg
        755                 760                 765

Ala Gly Pro Pro Gly Ser Pro Cys Leu Pro Gly Pro Pro Gly Leu Pro
    770                 775                 780

Cys Pro Val Ser Pro Leu Gly Pro Ala Gly Pro Ala Leu Gln Thr Val
785                 790                 795                 800

Pro Gly Pro Gln Gly Pro Pro Gly Pro Pro Gly Arg Asp Gly Thr Pro
                805                 810                 815

Gly Arg Asp Gly Glu Pro Gly Asp Pro Gly Glu Asp Gly Lys Pro Gly
            820                 825                 830

Asp Thr Gly Pro Gln Gly Phe Pro Gly Thr Pro Gly Asp Val Gly Pro
        835                 840                 845
```

```
Lys Gly Asp Lys Gly Asp Pro Gly Val Gly Glu Arg Gly Pro Pro Gly
    850                 855                 860

Pro Gln Gly Pro Pro Gly Pro Pro Gly Pro Ser Phe Arg His Asp Lys
865                 870                 875                 880

Leu Thr Phe Ile Asp Met Glu Gly Ser Gly Phe Gly Gly Asp Leu Glu
                885                 890                 895

Ala Leu Arg Gly Pro Arg Gly Phe Pro Gly Pro Pro Gly Pro Pro Gly
            900                 905                 910

Val Pro Gly Leu Pro Gly Glu Pro Gly Arg Phe Gly Val Asn Ser Ser
        915                 920                 925

Asp Val Pro Gly Pro Ala Gly Leu Pro Gly Val Pro Gly Arg Glu Gly
    930                 935                 940

Pro Pro Gly Phe Pro Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Arg
945                 950                 955                 960

Glu Gly Pro Pro Gly Arg Thr Gly Gln Lys Gly Ser Leu Gly Glu Ala
                965                 970                 975

Gly Ala Pro Gly His Lys Gly Ser Lys Gly Ala Pro Gly Pro Ala Gly
            980                 985                 990

Ala Arg Gly Glu Ser Gly Leu Ala  Gly Ala Pro Gly Pro  Ala Gly Pro
        995                 1000                1005

Pro Gly  Pro Pro Gly Pro Pro  Gly Pro Pro Gly Pro  Gly Leu Pro
    1010                1015                1020

Ala Gly  Phe Asp Asp Met Glu  Gly Ser Gly Gly Pro  Phe Trp Ser
    1025                1030                1035

Thr Ala  Arg Ser Ala Asp Gly  Pro Gln Gly Pro Pro  Gly Leu Pro
    1040                1045                1050

Gly Leu  Lys Gly Asp Pro Gly  Val Pro Gly Leu Pro  Gly Ala Lys
    1055                1060                1065

Gly Glu  Val Gly Ala Asp Gly  Val Pro Gly Phe Pro  Gly Leu Pro
    1070                1075                1080

Gly Arg  Glu Gly Ile Ala Gly  Pro Gln Gly Pro Lys  Gly Asp Arg
    1085                1090                1095

Gly Ser  Arg Gly Glu Lys Gly  Asp Pro Gly Lys Asp  Gly Val Gly
    1100                1105                1110
```

```
Gln Pro  Gly Leu Pro Gly Pro  Pro Gly Pro Pro Gly  Pro Val Val
    1115                 1120                 1125

Tyr Val  Ser Glu Gln Asp Gly  Ser Val Leu Ser Val  Pro Gly Pro
    1130                 1135                 1140

Glu Gly  Arg Pro Gly Phe Ala  Gly Phe Pro Gly Pro  Ala Gly Pro
    1145                 1150                 1155

Lys Gly  Asn Leu Gly Ser Lys  Gly Glu Arg Gly Ser  Pro Gly Pro
    1160                 1165                 1170

Lys Gly  Glu Lys Gly Glu Pro  Gly Ser Ile Phe Ser  Pro Asp Gly
    1175                 1180                 1185

Gly Ala  Leu Gly Pro Ala Gln  Lys Gly Ala Lys Gly  Glu Pro Gly
    1190                 1195                 1200

Phe Arg  Gly Pro Pro Gly Pro  Tyr Gly Arg Pro Gly  Tyr Lys Gly
    1205                 1210                 1215

Glu Ile  Gly Phe Pro Gly Arg  Pro Gly Arg Pro Gly  Met Asn Gly
    1220                 1225                 1230

Leu Lys  Gly Glu Lys Gly Glu  Pro Gly Asp Ala Ser  Leu Gly Phe
    1235                 1240                 1245

Gly Met  Arg Gly Met Pro Gly  Pro Pro Gly Pro Pro  Gly Pro Pro
    1250                 1255                 1260

Gly Pro  Pro Gly Thr Pro Val  Tyr Asp Ser Asn Val  Phe Ala Glu
    1265                 1270                 1275

Ser Ser  Arg Pro Gly Pro Pro  Gly Leu Pro Gly Asn  Gln Gly Pro
    1280                 1285                 1290

Pro Gly  Pro Lys Gly Ala Lys  Gly Glu Val Gly Pro  Pro Gly Pro
    1295                 1300                 1305

Pro Gly  Gln Phe Pro Phe Asp  Phe Leu Gln Leu Glu  Ala Glu Met
    1310                 1315                 1320

Lys Gly  Glu Lys Gly Asp Arg  Gly Asp Ala Gly Gln  Lys Gly Glu
    1325                 1330                 1335

Arg Gly  Glu Pro Gly Gly Gly  Gly Phe Phe Gly Ser  Ser Leu Pro
    1340                 1345                 1350

Gly Pro  Pro Gly Pro Pro Gly  Pro Pro Gly Pro Arg  Gly Tyr Pro
    1355                 1360                 1365
```

```
Gly Ile  Pro Gly Pro Lys Gly  Glu Ser Ile Arg Gly  Gln Pro Gly
    1370                1375                1380

Pro Pro  Gly Pro Gln Gly Pro  Pro Gly Ile Gly Tyr  Glu Gly Arg
    1385                1390                1395

Gln Gly  Pro Pro Gly Pro Pro  Gly Pro Pro Gly Pro  Pro Ser Phe
    1400                1405                1410

Pro Gly  Pro His Arg Gln Thr  Ile Ser Val Pro Gly  Pro Pro Gly
    1415                1420                1425

Pro Pro  Gly Pro Pro Gly Pro  Pro Gly Thr Met Gly  Ala Ser Ser
    1430                1435                1440

Gly Val  Arg Leu Trp Ala Thr  Arg Gln Ala Met Leu  Gly Gln Val
    1445                1450                1455

His Glu  Val Pro Glu Gly Trp  Leu Ile Phe Val Ala  Glu Gln Glu
    1460                1465                1470

Glu Leu  Tyr Val Arg Val Gln  Asn Gly Phe Arg Lys  Val Gln Leu
    1475                1480                1485

Glu Ala  Arg Thr Pro Leu Pro  Arg Gly Thr Asp Asn  Glu Val Ala
    1490                1495                1500

Ala Leu  Gln Pro Pro Val Val  Gln Leu His Asp Ser  Asn Pro Tyr
    1505                1510                1515

Pro Arg  Arg Glu His Pro His  Pro Thr Ala Arg Pro  Trp Arg Ala
    1520                1525                1530

Asp Asp  Ile Leu Ala Ser Pro  Pro Arg Leu Pro Glu  Pro Gln Pro
    1535                1540                1545

Tyr Pro  Gly Ala Pro His His  Ser Ser Tyr Val His  Leu Arg Pro
    1550                1555                1560

Ala Arg  Pro Thr Ser Pro Pro  Ala His Ser His Arg  Asp Phe Gln
    1565                1570                1575

Pro Val  Leu His Leu Val Ala  Leu Asn Ser Pro Leu  Ser Gly Gly
    1580                1585                1590

Met Arg  Gly Ile Arg Gly Ala  Asp Phe Gln Cys Phe  Gln Gln Ala
    1595                1600                1605

Arg Ala  Val Gly Leu Ala Gly  Thr Phe Arg Ala Phe  Leu Ser Ser
    1610                1615                1620
```

```
Arg Leu  Gln Asp Leu Tyr Ser  Ile Val Arg Arg Ala  Asp Arg Ala
    1625                 1630                 1635


Ala Val  Pro Ile Val Asn Leu  Lys Asp Glu Leu Leu  Phe Pro Ser
    1640                 1645                 1650


Trp Glu  Ala Leu Phe Ser Gly  Ser Glu Gly Pro Leu  Lys Pro Gly
    1655                 1660                 1665


Ala Arg  Ile Phe Ser Phe Asp  Gly Lys Asp Val Leu  Arg His Pro
    1670                 1675                 1680


Thr Trp  Pro Gln Lys Ser Val  Trp His Gly Ser Asp  Pro Asn Gly
    1685                 1690                 1695


Arg Arg  Leu Thr Glu Ser Tyr  Cys Glu Thr Trp Arg  Thr Glu Ala
    1700                 1705                 1710


Pro Ser  Ala Thr Gly Gln Ala  Ser Ser Leu Leu Gly  Gly Arg Leu
    1715                 1720                 1725


Leu Gly  Gln Ser Ala Ala Ser  Cys His His Ala Tyr  Ile Val Leu
    1730                 1735                 1740


Cys Ile  Glu Asn Ser Phe Met  Thr Ala Ser Lys
    1745                 1750
```

<210> 209
<211> 155
<212> PRT
<213> Homo sapiens

<400> 209

```
Met Ala Glu Gly Glu Ile Thr Thr Phe Thr Ala Leu Thr Glu Lys Phe
1               5                  10                  15


Asn Leu Pro Pro Gly Asn Tyr Lys Lys Pro Lys Leu Leu Tyr Cys Ser
            20                  25                  30


Asn Gly Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly
        35                  40                  45


Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu
    50                  55                  60


Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu
65                  70                  75                  80


Ala Met Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu
                85                  90                  95
```

Glu Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr
100 105 110

Ile Ser Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys
115 120 125

Asn Gly Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala
130 135 140

Ile Leu Phe Leu Pro Leu Pro Val Ser Ser Asp
145 150 155

<210> 210
<211> 288
<212> PRT
<213> Homo sapiens

<400> 210

Met Val Gly Val Gly Gly Gly Asp Val Glu Asp Val Thr Pro Arg Pro
1 5 10 15

Gly Gly Cys Gln Ile Ser Gly Arg Gly Ala Arg Gly Cys Asn Gly Ile
20 25 30

Pro Gly Ala Ala Ala Trp Glu Ala Ala Leu Pro Arg Arg Arg Pro Arg
35 40 45

Arg His Pro Ser Val Asn Pro Arg Ser Arg Ala Ala Gly Ser Pro Arg
50 55 60

Thr Arg Gly Arg Arg Thr Glu Glu Arg Pro Ser Gly Ser Arg Leu Gly
65 70 75 80

Asp Arg Gly Arg Gly Arg Ala Leu Pro Gly Gly Arg Leu Gly Gly Arg
85 90 95

Gly Arg Gly Arg Ala Pro Glu Arg Val Gly Gly Arg Gly Arg Gly Arg
100 105 110

Gly Thr Ala Ala Pro Arg Ala Ala Pro Ala Ala Arg Gly Ser Arg Pro
115 120 125

Gly Pro Ala Gly Thr Met Ala Ala Gly Ser Ile Thr Thr Leu Pro Ala
130 135 140

Leu Pro Glu Asp Gly Gly Ser Gly Ala Phe Pro Pro Gly His Phe Lys
145 150 155 160

Asp Pro Lys Arg Leu Tyr Cys Lys Asn Gly Gly Phe Phe Leu Arg Ile
165 170 175

His Pro Asp Gly Arg Val Asp Gly Val Arg Glu Lys Ser Asp Pro His
180 185 190

Ile Lys Leu Gln Leu Gln Ala Glu Glu Arg Gly Val Val Ser Ile Lys
195 200 205

Gly Val Cys Ala Asn Arg Tyr Leu Ala Met Lys Glu Asp Gly Arg Leu
210 215 220

Leu Ala Ser Lys Cys Val Thr Asp Glu Cys Phe Phe Phe Glu Arg Leu
225 230 235 240

Glu Ser Asn Asn Tyr Asn Thr Tyr Arg Ser Arg Lys Tyr Thr Ser Trp
245 250 255

Tyr Val Ala Leu Lys Arg Thr Gly Gln Tyr Lys Leu Gly Ser Lys Thr
260 265 270

Gly Pro Gly Gln Lys Ala Ile Leu Phe Leu Pro Met Ser Ala Lys Ser
275 280 285

<210> 211
<211> 239
<212> PRT
<213> Homo sapiens

<400> 211

Met Gly Leu Ile Trp Leu Leu Leu Leu Ser Leu Leu Glu Pro Gly Trp
1 5 10 15

Pro Ala Ala Gly Pro Gly Ala Arg Leu Arg Arg Asp Ala Gly Gly Arg
20 25 30

Gly Gly Val Tyr Glu His Leu Gly Gly Ala Pro Arg Arg Arg Lys Leu
35 40 45

Tyr Cys Ala Thr Lys Tyr His Leu Gln Leu His Pro Ser Gly Arg Val
50 55 60

Asn Gly Ser Leu Glu Asn Ser Ala Tyr Ser Ile Leu Glu Ile Thr Ala
65 70 75 80

Val Glu Val Gly Ile Val Ala Ile Arg Gly Leu Phe Ser Gly Arg Tyr
85 90 95

Leu Ala Met Asn Lys Arg Gly Arg Leu Tyr Ala Ser Glu His Tyr Ser
100 105 110

Ala Glu Cys Glu Phe Val Glu Arg Ile His Glu Leu Gly Tyr Asn Thr
115 120 125

Tyr Ala Ser Arg Leu Tyr Arg Thr Val Ser Ser Thr Pro Gly Ala Arg

130 135 140

Arg Gln Pro Ser Ala Glu Arg Leu Trp Tyr Val Ser Val Asn Gly Lys
145 150 155 160

Gly Arg Pro Arg Arg Gly Phe Lys Thr Arg Arg Thr Gln Lys Ser Ser
165 170 175

Leu Phe Leu Pro Arg Val Leu Asp His Arg Asp His Glu Met Val Arg
180 185 190

Gln Leu Gln Ser Gly Leu Pro Arg Pro Pro Gly Lys Gly Val Gln Pro
195 200 205

Arg Arg Arg Arg Gln Lys Gln Ser Pro Asp Asn Leu Glu Pro Ser His
210 215 220

Val Gln Ala Ser Arg Leu Gly Ser Gln Leu Glu Ala Ser Ala His
225 230 235

<210> 212
<211> 206
<212> PRT
<213> Homo sapiens

<400> 212

Met Ser Gly Pro Gly Thr Ala Ala Val Ala Leu Leu Pro Ala Val Leu
1 5 10 15

Leu Ala Leu Leu Ala Pro Trp Ala Gly Arg Gly Gly Ala Ala Ala Pro
20 25 30

Thr Ala Pro Asn Gly Thr Leu Glu Ala Glu Leu Glu Arg Arg Trp Glu
35 40 45

Ser Leu Val Ala Leu Ser Leu Ala Arg Leu Pro Val Ala Ala Gln Pro
50 55 60

Lys Glu Ala Ala Val Gln Ser Gly Ala Gly Asp Tyr Leu Leu Gly Ile
65 70 75 80

Lys Arg Leu Arg Arg Leu Tyr Cys Asn Val Gly Ile Gly Phe His Leu
85 90 95

Gln Ala Leu Pro Asp Gly Arg Ile Gly Gly Ala His Ala Asp Thr Arg
100 105 110

Asp Ser Leu Leu Glu Leu Ser Pro Val Glu Arg Gly Val Val Ser Ile
115 120 125

Phe Gly Val Ala Ser Arg Phe Phe Val Ala Met Ser Ser Lys Gly Lys
130 135 140

```
Leu Tyr Gly Ser Pro Phe Phe Thr Asp Glu Cys Thr Phe Lys Glu Ile
145                 150                 155                 160


Leu Leu Pro Asn Asn Tyr Asn Ala Tyr Glu Ser Tyr Lys Tyr Pro Gly
                165                 170                 175


Met Phe Ile Ala Leu Ser Lys Asn Gly Lys Thr Lys Lys Gly Asn Arg
            180                 185                 190


Val Ser Pro Thr Met Lys Val Thr His Phe Leu Pro Arg Leu
        195                 200                 205


<210>  213
<211>  268
<212>  PRT
<213>  Homo sapiens

<400>  213

Met Ser Leu Ser Phe Leu Leu Leu Leu Phe Phe Ser His Leu Ile Leu
1               5                   10                  15


Ser Ala Trp Ala His Gly Glu Lys Arg Leu Ala Pro Lys Gly Gln Pro
            20                  25                  30


Gly Pro Ala Ala Thr Asp Arg Asn Pro Arg Gly Ser Ser Ser Arg Gln
        35                  40                  45


Ser Ser Ser Ser Ala Met Ser Ser Ser Ser Ala Ser Ser Ser Pro Ala
    50                  55                  60


Ala Ser Leu Gly Ser Gln Gly Ser Gly Leu Glu Gln Ser Ser Phe Gln
65                  70                  75                  80


Trp Ser Pro Ser Gly Arg Arg Thr Gly Ser Leu Tyr Cys Arg Val Gly
                85                  90                  95


Ile Gly Phe His Leu Gln Ile Tyr Pro Asp Gly Lys Val Asn Gly Ser
            100                 105                 110


His Glu Ala Asn Met Leu Ser Val Leu Glu Ile Phe Ala Val Ser Gln
        115                 120                 125


Gly Ile Val Gly Ile Arg Gly Val Phe Ser Asn Lys Phe Leu Ala Met
    130                 135                 140


Ser Lys Lys Gly Lys Leu His Ala Ser Ala Lys Phe Thr Asp Asp Cys
145                 150                 155                 160


Lys Phe Arg Glu Arg Phe Gln Glu Asn Ser Tyr Asn Thr Tyr Ala Ser
                165                 170                 175
```

```
Ala Ile His Arg Thr Glu Lys Thr Gly Arg Glu Trp Tyr Val Ala Leu
            180                 185                 190

Asn Lys Arg Gly Lys Ala Lys Arg Gly Cys Ser Pro Arg Val Lys Pro
        195                 200                 205

Gln His Ile Ser Thr His Phe Leu Pro Arg Phe Lys Gln Ser Glu Gln
    210                 215                 220

Pro Glu Leu Ser Phe Thr Val Thr Val Pro Glu Lys Lys Lys Pro Pro
225                 230                 235                 240

Ser Pro Ile Lys Pro Lys Ile Pro Leu Ser Ala Pro Arg Lys Asn Thr
                245                 250                 255

Asn Ser Val Lys Tyr Arg Leu Lys Phe Arg Phe Gly
            260                 265


<210>  214
<211>  208
<212>  PRT
<213>  Homo sapiens

<400>  214

Met Ala Leu Gly Gln Lys Leu Phe Ile Thr Met Ser Arg Gly Ala Gly
1               5                   10                  15

Arg Leu Gln Gly Thr Leu Trp Ala Leu Val Phe Leu Gly Ile Leu Val
            20                  25                  30

Gly Met Val Val Pro Ser Pro Ala Gly Thr Arg Ala Asn Asn Thr Leu
        35                  40                  45

Leu Asp Ser Arg Gly Trp Gly Thr Leu Leu Ser Arg Ser Arg Ala Gly
    50                  55                  60

Leu Ala Gly Glu Ile Ala Gly Val Asn Trp Glu Ser Gly Tyr Leu Val
65                  70                  75                  80

Gly Ile Lys Arg Gln Arg Arg Leu Tyr Cys Asn Val Gly Ile Gly Phe
                85                  90                  95

His Leu Gln Val Leu Pro Asp Gly Arg Ile Ser Gly Thr His Glu Glu
            100                 105                 110

Asn Pro Tyr Ser Leu Leu Glu Ile Ser Thr Val Glu Arg Gly Val Val
        115                 120                 125

Ser Leu Phe Gly Val Arg Ser Ala Leu Phe Val Ala Met Asn Ser Lys
    130                 135                 140
```

Gly Arg Leu Tyr Ala Thr Pro Ser Phe Gln Glu Glu Cys Lys Phe Arg
145 150 155 160

Glu Thr Leu Leu Pro Asn Asn Tyr Asn Ala Tyr Glu Ser Asp Leu Tyr
165 170 175

Gln Gly Thr Tyr Ile Ala Leu Ser Lys Tyr Gly Arg Val Lys Arg Gly
180 185 190

Ser Lys Val Ser Pro Ile Met Thr Val Thr His Phe Leu Pro Arg Ile
195 200 205

<210> 215
<211> 233
<212> PRT
<213> Homo sapiens

<400> 215

Met Gly Ser Pro Arg Ser Ala Leu Ser Cys Leu Leu Leu His Leu Leu
1 5 10 15

Val Leu Cys Leu Gln Ala Gln Glu Gly Pro Gly Arg Gly Pro Ala Leu
20 25 30

Gly Arg Glu Leu Ala Ser Leu Phe Arg Ala Gly Arg Glu Pro Gln Gly
35 40 45

Val Ser Gln Gln His Val Arg Glu Gln Ser Leu Val Thr Asp Gln Leu
50 55 60

Ser Arg Arg Leu Ile Arg Thr Tyr Gln Leu Tyr Ser Arg Thr Ser Gly
65 70 75 80

Lys His Val Gln Val Leu Ala Asn Lys Arg Ile Asn Ala Met Ala Glu
85 90 95

Asp Gly Asp Pro Phe Ala Lys Leu Ile Val Glu Thr Asp Thr Phe Gly
100 105 110

Ser Arg Val Arg Val Arg Gly Ala Glu Thr Gly Leu Tyr Ile Cys Met
115 120 125

Asn Lys Lys Gly Lys Leu Ile Ala Lys Ser Asn Gly Lys Gly Lys Asp
130 135 140

Cys Val Phe Thr Glu Ile Val Leu Glu Asn Asn Tyr Thr Ala Leu Gln
145 150 155 160

Asn Ala Lys Tyr Glu Gly Trp Tyr Met Ala Phe Thr Arg Lys Gly Arg
165 170 175

Pro Arg Lys Gly Ser Lys Thr Arg Gln His Gln Arg Glu Val His Phe

180 185 190

Met Lys Arg Leu Pro Arg Gly His His Thr Thr Glu Gln Ser Leu Arg
195 200 205

Phe Glu Phe Leu Asn Tyr Pro Pro Phe Thr Arg Ser Leu Arg Gly Ser
210 215 220

Gln Arg Thr Trp Ala Pro Glu Pro Arg
225 230

<210> 216
<211> 208
<212> PRT
<213> Homo sapiens

<400> 216

Met Ala Pro Leu Gly Glu Val Gly Asn Tyr Phe Gly Val Gln Asp Ala
1 5 10 15

Val Pro Phe Gly Asn Val Pro Val Leu Pro Val Asp Ser Pro Val Leu
20 25 30

Leu Ser Asp His Leu Gly Gln Ser Glu Ala Gly Gly Leu Pro Arg Gly
35 40 45

Pro Ala Val Thr Asp Leu Asp His Leu Lys Gly Ile Leu Arg Arg Arg
50 55 60

Gln Leu Tyr Cys Arg Thr Gly Phe His Leu Glu Ile Phe Pro Asn Gly
65 70 75 80

Thr Ile Gln Gly Thr Arg Lys Asp His Ser Arg Phe Gly Ile Leu Glu
85 90 95

Phe Ile Ser Ile Ala Val Gly Leu Val Ser Ile Arg Gly Val Asp Ser
100 105 110

Gly Leu Tyr Leu Gly Met Asn Glu Lys Gly Glu Leu Tyr Gly Ser Glu
115 120 125

Lys Leu Thr Gln Glu Cys Val Phe Arg Glu Gln Phe Glu Glu Asn Trp
130 135 140

Tyr Asn Thr Tyr Ser Ser Asn Leu Tyr Lys His Val Asp Thr Gly Arg
145 150 155 160

Arg Tyr Tyr Val Ala Leu Asn Lys Asp Gly Thr Pro Arg Glu Gly Thr
165 170 175

Arg Thr Lys Arg His Gln Lys Phe Thr His Phe Leu Pro Arg Pro Val
180 185 190

```
Asp Pro Asp Lys Val Pro Glu Leu Tyr Lys Asp Ile Leu Ser Gln Ser
        195                 200                 205


<210>  217
<211>  243
<212>  PRT
<213>  Homo sapiens

<400>  217

Met Ala Ala Ala Ile Ala Ser Ser Leu Ile Arg Gln Lys Arg Gln Ala
1               5                   10                  15


Arg Glu Ser Asn Ser Asp Arg Val Ser Ala Ser Lys Arg Arg Ser Ser
            20                  25                  30


Pro Ser Lys Asp Gly Arg Ser Leu Cys Glu Arg His Val Leu Gly Val
        35                  40                  45


Phe Ser Lys Val Arg Phe Cys Ser Gly Arg Lys Arg Pro Val Arg Arg
    50                  55                  60


Arg Pro Glu Pro Gln Leu Lys Gly Ile Val Thr Arg Leu Phe Ser Gln
65                  70                  75                  80


Gln Gly Tyr Phe Leu Gln Met His Pro Asp Gly Thr Ile Asp Gly Thr
                85                  90                  95


Lys Asp Glu Asn Ser Asp Tyr Thr Leu Phe Asn Leu Ile Pro Val Gly
            100                 105                 110


Leu Arg Val Val Ala Ile Gln Gly Val Lys Ala Ser Leu Tyr Val Ala
        115                 120                 125


Met Asn Gly Glu Gly Tyr Leu Tyr Ser Ser Asp Val Phe Thr Pro Glu
    130                 135                 140


Cys Lys Phe Lys Glu Ser Val Phe Glu Asn Tyr Tyr Val Ile Tyr Ser
145                 150                 155                 160


Ser Thr Leu Tyr Arg Gln Gln Glu Ser Gly Arg Ala Trp Phe Leu Gly
                165                 170                 175


Leu Asn Lys Glu Gly Gln Ile Met Lys Gly Asn Arg Val Lys Lys Thr
            180                 185                 190


Lys Pro Ser Ser His Phe Val Pro Lys Pro Ile Glu Val Cys Met Tyr
        195                 200                 205


Arg Glu Pro Ser Leu His Glu Ile Gly Glu Lys Gln Gly Arg Ser Arg
    210                 215                 220
```

```
Lys Ser Ser Gly Thr Pro Thr Met Asn Gly Gly Lys Val Val Asn Gln
225                 230                 235                 240


Asp Ser Thr



<210>  218
<211>  216
<212>  PRT
<213>  Homo sapiens

<400>  218

Met Arg Ser Gly Cys Val Val Val His Val Trp Ile Leu Ala Gly Leu
1               5                   10                  15


Trp Leu Ala Val Ala Gly Arg Pro Leu Ala Phe Ser Asp Ala Gly Pro
            20                  25                  30


His Val His Tyr Gly Trp Gly Asp Pro Ile Arg Leu Arg His Leu Tyr
        35                  40                  45


Thr Ser Gly Pro His Gly Leu Ser Ser Cys Phe Leu Arg Ile Arg Ala
    50                  55                  60


Asp Gly Val Val Asp Cys Ala Arg Gly Gln Ser Ala His Ser Leu Leu
65                  70                  75                  80


Glu Ile Lys Ala Val Ala Leu Arg Thr Val Ala Ile Lys Gly Val His
                85                  90                  95


Ser Val Arg Tyr Leu Cys Met Gly Ala Asp Gly Lys Met Gln Gly Leu
            100                 105                 110


Leu Gln Tyr Ser Glu Glu Asp Cys Ala Phe Glu Glu Glu Ile Arg Pro
        115                 120                 125


Asp Gly Tyr Asn Val Tyr Arg Ser Glu Lys His Arg Leu Pro Val Ser
    130                 135                 140


Leu Ser Ser Ala Lys Gln Arg Gln Leu Tyr Lys Asn Arg Gly Phe Leu
145                 150                 155                 160


Pro Leu Ser His Phe Leu Pro Met Leu Pro Met Val Pro Glu Glu Pro
                165                 170                 175


Glu Asp Leu Arg Gly His Leu Glu Ser Asp Met Phe Ser Ser Pro Leu
            180                 185                 190


Glu Thr Asp Ser Met Asp Pro Phe Gly Leu Val Thr Gly Leu Glu Ala
        195                 200                 205
```

Val Arg Ser Pro Ser Phe Glu Lys
210 215

<210> 219
<211> 207
<212> PRT
<213> Homo sapiens

<400> 219

Met Ala Glu Val Gly Gly Val Phe Ala Ser Leu Asp Trp Asp Leu His
1 5 10 15

Gly Phe Ser Ser Ser Leu Gly Asn Val Pro Leu Ala Asp Ser Pro Gly
20 25 30

Phe Leu Asn Glu Arg Leu Gly Gln Ile Glu Gly Lys Leu Gln Arg Gly
35 40 45

Ser Pro Thr Asp Phe Ala His Leu Lys Gly Ile Leu Arg Arg Arg Gln
50 55 60

Leu Tyr Cys Arg Thr Gly Phe His Leu Glu Ile Phe Pro Asn Gly Thr
65 70 75 80

Val His Gly Thr Arg His Asp His Ser Arg Phe Gly Ile Leu Glu Phe
85 90 95

Ile Ser Leu Ala Val Gly Leu Ile Ser Ile Arg Gly Val Asp Ser Gly
100 105 110

Leu Tyr Leu Gly Met Asn Glu Arg Gly Glu Leu Tyr Gly Ser Lys Lys
115 120 125

Leu Thr Arg Glu Cys Val Phe Arg Glu Gln Phe Glu Glu Asn Trp Tyr
130 135 140

Asn Thr Tyr Ala Ser Thr Leu Tyr Lys His Ser Asp Ser Glu Arg Gln
145 150 155 160

Tyr Tyr Val Ala Leu Asn Lys Asp Gly Ser Pro Arg Glu Gly Tyr Arg
165 170 175

Thr Lys Arg His Gln Lys Phe Thr His Phe Leu Pro Arg Pro Val Asp
180 185 190

Pro Ser Lys Leu Pro Ser Met Ser Arg Asp Leu Phe His Tyr Arg
195 200 205

<210> 220
<211> 207
<212> PRT
<213> Homo sapiens

<400> 220

Met Tyr Ser Ala Pro Ser Ala Cys Thr Cys Leu Cys Leu His Phe Leu
1 5 10 15

Leu Leu Cys Phe Gln Val Gln Val Leu Val Ala Glu Glu Asn Val Asp
20 25 30

Phe Arg Ile His Val Glu Asn Gln Thr Arg Ala Arg Asp Asp Val Ser
35 40 45

Arg Lys Gln Leu Arg Leu Tyr Gln Leu Tyr Ser Arg Thr Ser Gly Lys
50 55 60

His Ile Gln Val Leu Gly Arg Arg Ile Ser Ala Arg Gly Glu Asp Gly
65 70 75 80

Asp Lys Tyr Ala Gln Leu Leu Val Glu Thr Asp Thr Phe Gly Ser Gln
85 90 95

Val Arg Ile Lys Gly Lys Glu Thr Glu Phe Tyr Leu Cys Met Asn Arg
100 105 110

Lys Gly Lys Leu Val Gly Lys Pro Asp Gly Thr Ser Lys Glu Cys Val
115 120 125

Phe Ile Glu Lys Val Leu Glu Asn Asn Tyr Thr Ala Leu Met Ser Ala
130 135 140

Lys Tyr Ser Gly Trp Tyr Val Gly Phe Thr Lys Lys Gly Arg Pro Arg
145 150 155 160

Lys Gly Pro Lys Thr Arg Glu Asn Gln Gln Asp Val His Phe Met Lys
165 170 175

Arg Tyr Pro Lys Gly Gln Pro Glu Leu Gln Lys Pro Phe Lys Tyr Thr
180 185 190

Thr Val Thr Lys Arg Ser Arg Arg Ile Arg Pro Thr His Pro Ala
195 200 205

<210> 221
<211> 235
<212> PRT
<213> Homo sapiens

<400> 221

Met Thr Val Leu Ala Pro Ala Trp Ser Pro Thr Thr Tyr Leu Leu Leu
1 5 10 15

Leu Leu Leu Leu Ser Ser Gly Leu Ser Gly Thr Gln Asp Cys Ser Phe
20 25 30

```
Gln His Ser Pro Ile Ser Ser Asp Phe Ala Val Lys Ile Arg Glu Leu
        35                  40                  45

Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
    50                  55                  60

Gln Asp Glu Glu Leu Cys Gly Gly Leu Trp Arg Leu Val Leu Ala Gln
65                  70                  75                  80

Arg Trp Met Glu Arg Leu Lys Thr Val Ala Gly Ser Lys Met Gln Gly
                85                  90                  95

Leu Leu Glu Arg Val Asn Thr Glu Ile His Phe Val Thr Lys Cys Ala
            100                 105                 110

Phe Gln Pro Pro Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
        115                 120                 125

Arg Leu Leu Gln Glu Thr Ser Glu Gln Leu Val Ala Leu Lys Pro Trp
    130                 135                 140

Ile Thr Arg Gln Asn Phe Ser Arg Cys Leu Glu Leu Gln Cys Gln Pro
145                 150                 155                 160

Asp Ser Ser Thr Leu Pro Pro Pro Trp Ser Pro Arg Pro Leu Glu Ala
                165                 170                 175

Thr Ala Pro Thr Ala Pro Gln Pro Pro Leu Leu Leu Leu Leu Leu Leu
            180                 185                 190

Pro Val Gly Leu Leu Leu Leu Ala Ala Ala Trp Cys Leu His Trp Gln
        195                 200                 205

Arg Thr Arg Arg Arg Thr Pro Arg Pro Gly Glu Gln Val Pro Pro Val
    210                 215                 220

Pro Ser Pro Gln Asp Leu Leu Leu Val Glu His
225                 230                 235


<210>  222
<211>  110
<212>  PRT
<213>  Homo sapiens

<400>  222

Ala Pro Met Ala Glu Gly Gly Gly Gln Asn His His Glu Val Val Lys
1               5                   10                  15

Phe Met Asp Val Tyr Gln Arg Ser Tyr Cys His Pro Ile Glu Thr Leu
            20                  25                  30
```

```
Val Asp Ile Phe Gln Glu Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys
        35                  40                  45

Pro Ser Cys Val Pro Leu Met Arg Cys Gly Gly Cys Cys Asn Asp Glu
    50                  55                  60

Gly Leu Glu Cys Val Pro Thr Glu Glu Ser Asn Ile Thr Met Gln Ile
65                  70                  75                  80

Met Arg Ile Lys Pro His Gln Gly Gln His Ile Gly Glu Met Ser Phe
                85                  90                  95

Leu Gln His Asn Lys Cys Glu Cys Arg Pro Lys Lys Asp Arg
            100                 105                 110

<210>  223
<211>  147
<212>  PRT
<213>  Homo sapiens

<400>  223

Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1               5                   10                  15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
            20                  25                  30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
        35                  40                  45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
    50                  55                  60

Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65                  70                  75                  80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
                85                  90                  95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
            100                 105                 110

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
        115                 120                 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Cys Asp Lys
    130                 135                 140

Pro Arg Arg
145

<210>  224
```

<211> 145
<212> PRT
<213> Homo sapiens

<400> 224

Ala Pro Met Ala Glu Gly Gly Gly Gln Asn His His Glu Val Val Lys
1 5 10 15

Phe Met Asp Val Tyr Gln Arg Ser Tyr Cys His Pro Ile Glu Thr Leu
20 25 30

Val Asp Ile Phe Gln Glu Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys
35 40 45

Pro Ser Cys Val Pro Leu Met Arg Cys Gly Gly Cys Cys Asn Asp Glu
50 55 60

Gly Leu Glu Cys Val Pro Thr Glu Glu Ser Asn Ile Thr Met Gln Ile
65 70 75 80

Met Arg Ile Lys Pro His Gln Gly Gln His Ile Gly Glu Met Ser Phe
85 90 95

Leu Gln His Asn Lys Cys Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg
100 105 110

Gln Glu Lys Lys Ser Val Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys
115 120 125

Arg Lys Lys Ser Arg Tyr Lys Ser Trp Ser Val Cys Asp Lys Pro Arg
130 135 140

Arg
145

<210> 225
<211> 191
<212> PRT
<213> Homo sapiens

<400> 225

Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1 5 10 15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
20 25 30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
35 40 45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
50 55 60

```
Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65                  70                  75                  80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
                85                  90                  95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
            100                 105                 110

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
        115                 120                 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Asn Pro Cys Gly
    130                 135                 140

Pro Cys Ser Glu Arg Arg Lys His Leu Phe Val Gln Asp Pro Gln Thr
145                 150                 155                 160

Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg Gln
                165                 170                 175

Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg
            180                 185                 190
```

<210> 226
<211> 215
<212> PRT
<213> Homo sapiens

<400> 226

```
Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1               5                   10                  15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
            20                  25                  30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
        35                  40                  45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
    50                  55                  60

Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65                  70                  75                  80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
                85                  90                  95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
            100                 105                 110
```

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
115 120 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val
130 135 140

Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr
145 150 155 160

Lys Ser Trp Ser Val Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys His
165 170 175

Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn Thr
180 185 190

Asp Ser Arg Cys Lys Ala Arg Gln Leu Glu Leu Asn Glu Arg Thr Cys
195 200 205

Arg Cys Asp Lys Pro Arg Arg
210 215

<210> 227
<211> 232
<212> PRT
<213> Homo sapiens

<400> 227

Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1 5 10 15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
20 25 30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
35 40 45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
50 55 60

Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65 70 75 80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
85 90 95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
100 105 110

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
115 120 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val

130 135 140

Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr
145 150 155 160

Lys Ser Trp Ser Val Tyr Val Gly Ala Arg Cys Cys Leu Met Pro Trp
165 170 175

Ser Leu Pro Gly Pro His Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys
180 185 190

His Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn
195 200 205

Thr Asp Ser Arg Cys Lys Ala Arg Gln Leu Glu Leu Asn Glu Arg Thr
210 215 220

Cys Arg Cys Asp Lys Pro Arg Arg
225 230

<210> 228
<211> 345
<212> PRT
<213> Homo sapiens

<400> 228

Met Ser Leu Phe Gly Leu Leu Leu Leu Thr Ser Ala Leu Ala Gly Gln
1 5 10 15

Arg Gln Gly Thr Gln Ala Glu Ser Asn Leu Ser Ser Lys Phe Gln Phe
20 25 30

Ser Ser Asn Lys Glu Gln Asn Gly Val Gln Asp Pro Gln His Glu Arg
35 40 45

Ile Ile Thr Val Ser Thr Asn Gly Ser Ile His Ser Pro Arg Phe Pro
50 55 60

His Thr Tyr Pro Arg Asn Thr Val Leu Val Trp Arg Leu Val Ala Val
65 70 75 80

Glu Glu Asn Val Trp Ile Gln Leu Thr Phe Asp Glu Arg Phe Gly Leu
85 90 95

Glu Asp Pro Glu Asp Asp Ile Cys Lys Tyr Asp Phe Val Glu Val Glu
100 105 110

Glu Pro Ser Asp Gly Thr Ile Leu Gly Arg Trp Cys Gly Ser Gly Thr
115 120 125

Val Pro Gly Lys Gln Ile Ser Lys Gly Asn Gln Ile Arg Ile Arg Phe
130 135 140

```
Val Ser Asp Glu Tyr Phe Pro Ser Glu Pro Gly Phe Cys Ile His Tyr
145                 150                 155                 160

Asn Ile Val Met Pro Gln Phe Thr Glu Ala Val Ser Pro Ser Val Leu
                165                 170                 175

Pro Pro Ser Ala Leu Pro Leu Asp Leu Leu Asn Asn Ala Ile Thr Ala
            180                 185                 190

Phe Ser Thr Leu Glu Asp Leu Ile Arg Tyr Leu Glu Pro Glu Arg Trp
        195                 200                 205

Gln Leu Asp Leu Glu Asp Leu Tyr Arg Pro Thr Trp Gln Leu Leu Gly
    210                 215                 220

Lys Ala Phe Val Phe Gly Arg Lys Ser Arg Val Val Asp Leu Asn Leu
225                 230                 235                 240

Leu Thr Glu Glu Val Arg Leu Tyr Ser Cys Thr Pro Arg Asn Phe Ser
                245                 250                 255

Val Ser Ile Arg Glu Glu Leu Lys Arg Thr Asp Thr Ile Phe Trp Pro
            260                 265                 270

Gly Cys Leu Leu Val Lys Arg Cys Gly Gly Asn Cys Ala Cys Cys Leu
        275                 280                 285

His Asn Cys Asn Glu Cys Gln Cys Val Pro Ser Lys Val Thr Lys Lys
    290                 295                 300

Tyr His Glu Val Leu Gln Leu Arg Pro Lys Thr Gly Val Arg Gly Leu
305                 310                 315                 320

His Lys Ser Leu Thr Asp Val Ala Leu Glu His His Glu Glu Cys Asp
                325                 330                 335

Cys Val Cys Arg Gly Ser Thr Gly Gly
            340                 345


<210>  229
<211>  1356
<212>  PRT
<213>  Homo sapiens

<400>  229

Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
1               5                   10                  15

Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
            20                  25                  30
```

```
Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
        35                  40                  45

Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
    50                  55                  60

Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
65                  70                  75                  80

Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
                85                  90                  95

Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
            100                 105                 110

Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
        115                 120                 125

Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
    130                 135                 140

Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
145                 150                 155                 160

Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
                165                 170                 175

Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
            180                 185                 190

Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
        195                 200                 205

Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
    210                 215                 220

Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
225                 230                 235                 240

Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
                245                 250                 255

Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
            260                 265                 270

Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
        275                 280                 285

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
    290                 295                 300
```

```
Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305                 310                 315                 320

Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
                325                 330                 335

Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
            340                 345                 350

Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
        355                 360                 365

Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
    370                 375                 380

Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
385                 390                 395                 400

Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
                405                 410                 415

Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
            420                 425                 430

Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
        435                 440                 445

Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
    450                 455                 460

Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr
465                 470                 475                 480

Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
                485                 490                 495

Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
            500                 505                 510

Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
        515                 520                 525

Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
    530                 535                 540

Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
545                 550                 555                 560

Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
                565                 570                 575
```

```
Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
            580                 585                 590

Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
        595                 600                 605

Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
    610                 615                 620

Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
625                 630                 635                 640

Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
                645                 650                 655

Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
            660                 665                 670

Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
        675                 680                 685

Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
    690                 695                 700

Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705                 710                 715                 720

Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr
                725                 730                 735

Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe
            740                 745                 750

Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu
        755                 760                 765

Val Gly Thr Ala Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile
    770                 775                 780

Ile Leu Arg Thr Val Lys Arg Ala Asn Gly Gly Glu Leu Lys Thr Gly
785                 790                 795                 800

Tyr Leu Ser Ile Val Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His
                805                 810                 815

Cys Glu Arg Leu Pro Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp
            820                 825                 830

Arg Leu Lys Leu Gly Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val
        835                 840                 845
```

```
Ile Glu Ala Asp Ala Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr
    850                 855                 860

Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr His Ser Glu His Arg
865                 870                 875                 880

Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly His His Leu
                885                 890                 895

Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu
            900                 905                 910

Met Val Ile Val Glu Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu
        915                 920                 925

Arg Ser Lys Arg Asn Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg
    930                 935                 940

Phe Arg Gln Gly Lys Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys
945                 950                 955                 960

Arg Arg Leu Asp Ser Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly
                965                 970                 975

Phe Val Glu Glu Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro
            980                 985                 990

Glu Asp Leu Tyr Lys Asp Phe Leu  Thr Leu Glu His Leu  Ile Cys Tyr
        995                 1000                1005

Ser Phe  Gln Val Ala Lys Gly  Met Glu Phe Leu Ala  Ser Arg Lys
    1010                1015                1020

Cys Ile  His Arg Asp Leu Ala  Ala Arg Asn Ile Leu  Leu Ser Glu
    1025                1030                1035

Lys Asn  Val Val Lys Ile Cys  Asp Phe Gly Leu Ala  Arg Asp Ile
    1040                1045                1050

Tyr Lys  Asp Pro Asp Tyr Val  Arg Lys Gly Asp Ala  Arg Leu Pro
    1055                1060                1065

Leu Lys  Trp Met Ala Pro Glu  Thr Ile Phe Asp Arg  Val Tyr Thr
    1070                1075                1080

Ile Gln  Ser Asp Val Trp Ser  Phe Gly Val Leu Leu  Trp Glu Ile
    1085                1090                1095

Phe Ser  Leu Gly Ala Ser Pro  Tyr Pro Gly Val Lys  Ile Asp Glu
    1100                1105                1110
```

```
Glu Phe  Cys Arg Arg Leu Lys  Glu Gly Thr Arg Met  Arg Ala Pro
    1115                1120                1125

Asp Tyr  Thr Thr Pro Glu Met  Tyr Gln Thr Met Leu  Asp Cys Trp
    1130                1135                1140

His Gly  Glu Pro Ser Gln Arg  Pro Thr Phe Ser Glu  Leu Val Glu
    1145                1150                1155

His Leu  Gly Asn Leu Leu Gln  Ala Asn Ala Gln Gln  Asp Gly Lys
    1160                1165                1170

Asp Tyr  Ile Val Leu Pro Ile  Ser Glu Thr Leu Ser  Met Glu Glu
    1175                1180                1185

Asp Ser  Gly Leu Ser Leu Pro  Thr Ser Pro Val Ser  Cys Met Glu
    1190                1195                1200

Glu Glu  Glu Val Cys Asp Pro  Lys Phe His Tyr Asp  Asn Thr Ala
    1205                1210                1215

Gly Ile  Ser Gln Tyr Leu Gln  Asn Ser Lys Arg Lys  Ser Arg Pro
    1220                1225                1230

Val Ser  Val Lys Thr Phe Glu  Asp Ile Pro Leu Glu  Glu Pro Glu
    1235                1240                1245

Val Lys  Val Ile Pro Asp Asp  Asn Gln Thr Asp Ser  Gly Met Val
    1250                1255                1260

Leu Ala  Ser Glu Glu Leu Lys  Thr Leu Glu Asp Arg  Thr Lys Leu
    1265                1270                1275

Ser Pro  Ser Phe Gly Gly Met  Val Pro Ser Lys Ser  Arg Glu Ser
    1280                1285                1290

Val Ala  Ser Glu Gly Ser Asn  Gln Thr Ser Gly Tyr  Gln Ser Gly
    1295                1300                1305

Tyr His  Ser Asp Asp Thr Asp  Thr Thr Val Tyr Ser  Ser Glu Glu
    1310                1315                1320

Ala Glu  Leu Leu Lys Leu Ile  Glu Ile Gly Val Gln  Thr Gly Ser
    1325                1330                1335

Thr Ala  Gln Ile Leu Gln Pro  Asp Ser Gly Thr Thr  Leu Ser Ser
    1340                1345                1350

Pro Pro  Val
    1355
```

<210> 230
<211> 1338
<212> PRT
<213> Homo sapiens

<400> 230

```
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                  10                  15

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30

Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45

Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60

Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80

Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95

Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110

Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125

Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240
```

```
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255

Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270

Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285

Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300

Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320

Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335

Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350

Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365

Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380

Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385                 390                 395                 400

Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
                405                 410                 415

Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
            420                 425                 430

Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
        435                 440                 445

Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
    450                 455                 460

Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys
465                 470                 475                 480

Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser
                485                 490                 495

Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile
            500                 505                 510
```

```
Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp Ser Arg
        515                 520                 525

Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val
    530                 535                 540

Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly Phe His
545                 550                 555                 560

Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu Asp Leu Lys Leu Ser
                565                 570                 575

Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr Trp Ile Leu Leu
            580                 585                 590

Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys
        595                 600                 605

Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu Asn Leu Thr Ile Met
    610                 615                 620

Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr Ala Cys Arg Ala Arg Asn
625                 630                 635                 640

Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys Lys Glu Ile Thr Ile Arg
                645                 650                 655

Asp Gln Glu Ala Pro Tyr Leu Leu Arg Asn Leu Ser Asp His Thr Val
            660                 665                 670

Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro
        675                 680                 685

Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn His Lys Ile Gln Gln Glu
    690                 695                 700

Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser Thr Leu Phe Ile Glu Arg
705                 710                 715                 720

Val Thr Glu Glu Asp Glu Gly Val Tyr His Cys Lys Ala Thr Asn Gln
                725                 730                 735

Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu Thr Val Gln Gly Thr Ser
            740                 745                 750

Asp Lys Ser Asn Leu Glu Leu Ile Thr Leu Thr Cys Thr Cys Val Ala
        755                 760                 765

Ala Thr Leu Phe Trp Leu Leu Leu Thr Leu Phe Ile Arg Lys Met Lys
    770                 775                 780
```

```
Arg Ser Ser Ser Glu Ile Lys Thr Asp Tyr Leu Ser Ile Ile Met Asp
785                 790                 795                 800

Pro Asp Glu Val Pro Leu Asp Glu Gln Cys Glu Arg Leu Pro Tyr Asp
                805                 810                 815

Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg Leu Lys Leu Gly Lys Ser
            820                 825                 830

Leu Gly Arg Gly Ala Phe Gly Lys Val Val Gln Ala Ser Ala Phe Gly
        835                 840                 845

Ile Lys Lys Ser Pro Thr Cys Arg Thr Val Ala Val Lys Met Leu Lys
    850                 855                 860

Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala Leu Met Thr Glu Leu Lys
865                 870                 875                 880

Ile Leu Thr His Ile Gly His His Leu Asn Val Val Asn Leu Leu Gly
                885                 890                 895

Ala Cys Thr Lys Gln Gly Gly Pro Leu Met Val Ile Val Glu Tyr Cys
            900                 905                 910

Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys Ser Lys Arg Asp Leu Phe
        915                 920                 925

Phe Leu Asn Lys Asp Ala Ala Leu His Met Glu Pro Lys Lys Glu Lys
    930                 935                 940

Met Glu Pro Gly Leu Glu Gln Gly Lys Lys Pro Arg Leu Asp Ser Val
945                 950                 955                 960

Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly Phe Gln Glu Asp Lys Ser
                965                 970                 975

Leu Ser Asp Val Glu Glu Glu Glu Asp Ser Asp Gly Phe Tyr Lys Glu
            980                 985                 990

Pro Ile Thr Met Glu Asp Leu Ile  Ser Tyr Ser Phe Gln  Val Ala Arg
        995                 1000                1005

Gly Met  Glu Phe Leu Ser Ser  Arg Lys Cys Ile His  Arg Asp Leu
    1010                1015                1020

Ala Ala  Arg Asn Ile Leu Leu  Ser Glu Asn Asn Val  Val Lys Ile
    1025                1030                1035

Cys Asp  Phe Gly Leu Ala Arg  Asp Ile Tyr Lys Asn  Pro Asp Tyr
    1040                1045                1050
```

```
Val Arg  Lys Gly Asp Thr Arg  Leu Pro Leu Lys Trp  Met Ala Pro
    1055                1060                1065

Glu Ser  Ile Phe Asp Lys Ile  Tyr Ser Thr Lys Ser  Asp Val Trp
    1070                1075                1080

Ser Tyr  Gly Val Leu Leu Trp  Glu Ile Phe Ser Leu  Gly Gly Ser
    1085                1090                1095

Pro Tyr  Pro Gly Val Gln Met  Asp Glu Asp Phe Cys  Ser Arg Leu
    1100                1105                1110

Arg Glu  Gly Met Arg Met Arg  Ala Pro Glu Tyr Ser  Thr Pro Glu
    1115                1120                1125

Ile Tyr  Gln Ile Met Leu Asp  Cys Trp His Arg Asp  Pro Lys Glu
    1130                1135                1140

Arg Pro  Arg Phe Ala Glu Leu  Val Glu Lys Leu Gly  Asp Leu Leu
    1145                1150                1155

Gln Ala  Asn Val Gln Gln Asp  Gly Lys Asp Tyr Ile  Pro Ile Asn
    1160                1165                1170

Ala Ile  Leu Thr Gly Asn Ser  Gly Phe Thr Tyr Ser  Thr Pro Ala
    1175                1180                1185

Phe Ser  Glu Asp Phe Phe Lys  Glu Ser Ile Ser Ala  Pro Lys Phe
    1190                1195                1200

Asn Ser  Gly Ser Ser Asp Asp  Val Arg Tyr Val Asn  Ala Phe Lys
    1205                1210                1215

Phe Met  Ser Leu Glu Arg Ile  Lys Thr Phe Glu Glu  Leu Leu Pro
    1220                1225                1230

Asn Ala  Thr Ser Met Phe Asp  Asp Tyr Gln Gly Asp  Ser Ser Thr
    1235                1240                1245

Leu Leu  Ala Ser Pro Met Leu  Lys Arg Phe Thr Trp  Thr Asp Ser
    1250                1255                1260

Lys Pro  Lys Ala Ser Leu Lys  Ile Asp Leu Arg Val  Thr Ser Lys
    1265                1270                1275

Ser Lys  Glu Ser Gly Leu Ser  Asp Val Ser Arg Pro  Ser Phe Cys
    1280                1285                1290

His Ser  Ser Cys Gly His Val  Ser Glu Gly Lys Arg  Arg Phe Thr
    1295                1300                1305
```

Tyr Asp His Ala Glu Leu Glu Arg Lys Ile Ala Cys Cys Ser Pro
1310 1315 1320

Pro Pro Asp Tyr Asn Ser Val Val Leu Tyr Ser Thr Pro Pro Ile
1325 1330 1335

<210> 231
<211> 1363
<212> PRT
<213> Homo sapiens

<400> 231

Met Gln Arg Gly Ala Ala Leu Cys Leu Arg Leu Trp Leu Cys Leu Gly
1 5 10 15

Leu Leu Asp Gly Leu Val Ser Gly Tyr Ser Met Thr Pro Pro Thr Leu
20 25 30

Asn Ile Thr Glu Glu Ser His Val Ile Asp Thr Gly Asp Ser Leu Ser
35 40 45

Ile Ser Cys Arg Gly Gln His Pro Leu Glu Trp Ala Trp Pro Gly Ala
50 55 60

Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp Ser Glu Asp Thr Gly Val
65 70 75 80

Val Arg Asp Cys Glu Gly Thr Asp Ala Arg Pro Tyr Cys Lys Val Leu
85 90 95

Leu Leu His Glu Val His Ala Asn Asp Thr Gly Ser Tyr Val Cys Tyr
100 105 110

Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly Thr Thr Ala Ala Ser Ser
115 120 125

Tyr Val Phe Val Arg Asp Phe Glu Gln Pro Phe Ile Asn Lys Pro Asp
130 135 140

Thr Leu Leu Val Asn Arg Lys Asp Ala Met Trp Val Pro Cys Leu Val
145 150 155 160

Ser Ile Pro Gly Leu Asn Val Thr Leu Arg Ser Gln Ser Ser Val Leu
165 170 175

Trp Pro Asp Gly Gln Glu Val Val Trp Asp Asp Arg Arg Gly Met Leu
180 185 190

Val Ser Thr Pro Leu Leu His Asp Ala Leu Tyr Leu Gln Cys Glu Thr
195 200 205

Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn Pro Phe Leu Val His Ile

210 215 220

Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu
225 230 235 240

Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala
245 250 255

Glu Phe Asn Ser Gly Val Thr Phe Asp Trp Asp Tyr Pro Gly Lys Gln
260 265 270

Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His
275 280 285

Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp
290 295 300

Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg
305 310 315 320

Glu Ser Thr Glu Val Ile Val His Glu Asn Pro Phe Ile Ser Val Glu
325 330 335

Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr Ala Gly Asp Glu Leu Val
340 345 350

Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro Pro Pro Glu Phe Gln Trp
355 360 365

Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg His Ser Pro His Ala Leu
370 375 380

Val Leu Lys Glu Val Thr Glu Ala Ser Thr Gly Thr Tyr Thr Leu Ala
385 390 395 400

Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg Asn Ile Ser Leu Glu Leu
405 410 415

Val Val Asn Val Pro Pro Gln Ile His Glu Lys Glu Ala Ser Ser Pro
420 425 430

Ser Ile Tyr Ser Arg His Ser Arg Gln Ala Leu Thr Cys Thr Ala Tyr
435 440 445

Gly Val Pro Leu Pro Leu Ser Ile Gln Trp His Trp Arg Pro Trp Thr
450 455 460

Pro Cys Lys Met Phe Ala Gln Arg Ser Leu Arg Arg Arg Gln Gln Gln
465 470 475 480

Asp Leu Met Pro Gln Cys Arg Asp Trp Arg Ala Val Thr Thr Gln Asp

485 490 495

Ala Val Asn Pro Ile Glu Ser Leu Asp Thr Trp Thr Glu Phe Val Glu
500 505 510

Gly Lys Asn Lys Thr Val Ser Lys Leu Val Ile Gln Asn Ala Asn Val
515 520 525

Ser Ala Met Tyr Lys Cys Val Val Ser Asn Lys Val Gly Gln Asp Glu
530 535 540

Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile Pro Asp Gly Phe Thr Ile
545 550 555 560

Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu Gly Gln Pro Val Leu Leu
565 570 575

Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu His Leu Arg Trp Tyr Arg
580 585 590

Leu Asn Leu Ser Thr Leu His Asp Ala His Gly Asn Pro Leu Leu Leu
595 600 605

Asp Cys Lys Asn Val His Leu Phe Ala Thr Pro Leu Ala Ala Ser Leu
610 615 620

Glu Glu Val Ala Pro Gly Ala Arg His Ala Thr Leu Ser Leu Ser Ile
625 630 635 640

Pro Arg Val Ala Pro Glu His Glu Gly His Tyr Val Cys Glu Val Gln
645 650 655

Asp Arg Arg Ser His Asp Lys His Cys His Lys Lys Tyr Leu Ser Val
660 665 670

Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln Asn Leu Thr Asp Leu Leu
675 680 685

Val Asn Val Ser Asp Ser Leu Glu Met Gln Cys Leu Val Ala Gly Ala
690 695 700

His Ala Pro Ser Ile Val Trp Tyr Lys Asp Glu Arg Leu Leu Glu Glu
705 710 715 720

Lys Ser Gly Val Asp Leu Ala Asp Ser Asn Gln Lys Leu Ser Ile Gln
725 730 735

Arg Val Arg Glu Glu Asp Ala Gly Arg Tyr Leu Cys Ser Val Cys Asn
740 745 750

Ala Lys Gly Cys Val Asn Ser Ser Ala Ser Val Ala Val Glu Gly Ser

```
        755                 760                 765

Glu Asp Lys Gly Ser Met Glu Ile Val Ile Leu Val Gly Thr Gly Val
    770                 775                 780

Ile Ala Val Phe Phe Trp Val Leu Leu Leu Leu Ile Phe Cys Asn Met
785                 790                 795                 800

Arg Arg Pro Ala His Ala Asp Ile Lys Thr Gly Tyr Leu Ser Ile Ile
                805                 810                 815

Met Asp Pro Gly Glu Val Pro Leu Glu Glu Gln Cys Glu Tyr Leu Ser
            820                 825                 830

Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg Glu Arg Leu His Leu Gly
        835                 840                 845

Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys Val Val Glu Ala Ser Ala
    850                 855                 860

Phe Gly Ile His Lys Gly Ser Ser Cys Asp Thr Val Ala Val Lys Met
865                 870                 875                 880

Leu Lys Glu Gly Ala Thr Ala Ser Glu His Arg Ala Leu Met Ser Glu
                885                 890                 895

Leu Lys Ile Leu Ile His Ile Gly Asn His Leu Asn Val Val Asn Leu
            900                 905                 910

Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro Leu Met Val Ile Val Glu
        915                 920                 925

Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe Leu Arg Ala Lys Arg Asp
    930                 935                 940

Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro Glu Gln Arg Gly Arg Phe
945                 950                 955                 960

Arg Ala Met Val Glu Leu Ala Arg Leu Asp Arg Arg Arg Pro Gly Ser
                965                 970                 975

Ser Asp Arg Val Leu Phe Ala Arg Phe Ser Lys Thr Glu Gly Gly Ala
            980                 985                 990

Arg Arg Ala Ser Pro Asp Gln Glu  Ala Glu Asp Leu Trp  Leu Ser Pro
        995                 1000                1005

Leu Thr  Met Glu Asp Leu Val  Cys Tyr Ser Phe Gln  Val Ala Arg
    1010                1015                1020

Gly Met  Glu Phe Leu Ala Ser  Arg Lys Cys Ile His  Arg Asp Leu
```

1025 1030 1035

Ala Ala Arg Asn Ile Leu Leu Ser Glu Ser Asp Val Val Lys Ile
1040 1045 1050

Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr
1055 1060 1065

Val Arg Lys Gly Ser Ala Arg Leu Pro Leu Lys Trp Met Ala Pro
1070 1075 1080

Glu Ser Ile Phe Asp Lys Val Tyr Thr Thr Gln Ser Asp Val Trp
1085 1090 1095

Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser
1100 1105 1110

Pro Tyr Pro Gly Val Gln Ile Asn Glu Glu Phe Cys Gln Arg Leu
1115 1120 1125

Arg Asp Gly Thr Arg Met Arg Ala Pro Glu Leu Ala Thr Pro Ala
1130 1135 1140

Ile Arg Arg Ile Met Leu Asn Cys Trp Ser Gly Asp Pro Lys Ala
1145 1150 1155

Arg Pro Ala Phe Ser Glu Leu Val Glu Ile Leu Gly Asp Leu Leu
1160 1165 1170

Gln Gly Arg Gly Leu Gln Glu Glu Glu Glu Val Cys Met Ala Pro
1175 1180 1185

Arg Ser Ser Gln Ser Ser Glu Glu Gly Ser Phe Ser Gln Val Ser
1190 1195 1200

Thr Met Ala Leu His Ile Ala Gln Ala Asp Ala Glu Asp Ser Pro
1205 1210 1215

Pro Ser Leu Gln Arg His Ser Leu Ala Ala Arg Tyr Tyr Asn Trp
1220 1225 1230

Val Ser Phe Pro Gly Cys Leu Ala Arg Gly Ala Glu Thr Arg Gly
1235 1240 1245

Ser Ser Arg Met Lys Thr Phe Glu Glu Phe Pro Met Thr Pro Thr
1250 1255 1260

Thr Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp Ser Gly Met Val
1265 1270 1275

Leu Ala Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg His Arg Gln

1280 1285 1290

Glu Ser Gly Phe Ser Cys Lys Gly Pro Gly Gln Asn Val Ala Val
1295 1300 1305

Thr Arg Ala His Pro Asp Ser Gln Gly Arg Arg Arg Arg Pro Glu
1310 1315 1320

Arg Gly Ala Arg Gly Gly Gln Val Phe Tyr Asn Ser Glu Tyr Gly
1325 1330 1335

Glu Leu Ser Glu Pro Ser Glu Glu Asp His Cys Ser Pro Ser Ala
1340 1345 1350

Arg Val Thr Phe Phe Thr Asp Asn Ser Tyr
1355 1360

<210> 232
<211> 923
<212> PRT
<213> Homo sapiens

<400> 232

Met Glu Arg Gly Leu Pro Leu Leu Cys Ala Val Leu Ala Leu Val Leu
1 5 10 15

Ala Pro Ala Gly Ala Phe Arg Asn Asp Lys Cys Gly Asp Thr Ile Lys
20 25 30

Ile Glu Ser Pro Gly Tyr Leu Thr Ser Pro Gly Tyr Pro His Ser Tyr
35 40 45

His Pro Ser Glu Lys Cys Glu Trp Leu Ile Gln Ala Pro Asp Pro Tyr
50 55 60

Gln Arg Ile Met Ile Asn Phe Asn Pro His Phe Asp Leu Glu Asp Arg
65 70 75 80

Asp Cys Lys Tyr Asp Tyr Val Glu Val Phe Asp Gly Glu Asn Glu Asn
85 90 95

Gly His Phe Arg Gly Lys Phe Cys Gly Lys Ile Ala Pro Pro Pro Val
100 105 110

Val Ser Ser Gly Pro Phe Leu Phe Ile Lys Phe Val Ser Asp Tyr Glu
115 120 125

Thr His Gly Ala Gly Phe Ser Ile Arg Tyr Glu Ile Phe Lys Arg Gly
130 135 140

Pro Glu Cys Ser Gln Asn Tyr Thr Thr Pro Ser Gly Val Ile Lys Ser
145 150 155 160

```
Pro Gly Phe Pro Glu Lys Tyr Pro Asn Ser Leu Glu Cys Thr Tyr Ile
                165                 170                 175

Val Phe Val Pro Lys Met Ser Glu Ile Ile Leu Glu Phe Glu Ser Phe
            180                 185                 190

Asp Leu Glu Pro Asp Ser Asn Pro Pro Gly Gly Met Phe Cys Arg Tyr
        195                 200                 205

Asp Arg Leu Glu Ile Trp Asp Gly Phe Pro Asp Val Gly Pro His Ile
    210                 215                 220

Gly Arg Tyr Cys Gly Gln Lys Thr Pro Gly Arg Ile Arg Ser Ser Ser
225                 230                 235                 240

Gly Ile Leu Ser Met Val Phe Tyr Thr Asp Ser Ala Ile Ala Lys Glu
                245                 250                 255

Gly Phe Ser Ala Asn Tyr Ser Val Leu Gln Ser Ser Val Ser Glu Asp
            260                 265                 270

Phe Lys Cys Met Glu Ala Leu Gly Met Glu Ser Gly Glu Ile His Ser
        275                 280                 285

Asp Gln Ile Thr Ala Ser Ser Gln Tyr Ser Thr Asn Trp Ser Ala Glu
    290                 295                 300

Arg Ser Arg Leu Asn Tyr Pro Glu Asn Gly Trp Thr Pro Gly Glu Asp
305                 310                 315                 320

Ser Tyr Arg Glu Trp Ile Gln Val Asp Leu Gly Leu Leu Arg Phe Val
                325                 330                 335

Thr Ala Val Gly Thr Gln Gly Ala Ile Ser Lys Glu Thr Lys Lys Lys
            340                 345                 350

Tyr Tyr Val Lys Thr Tyr Lys Ile Asp Val Ser Ser Asn Gly Glu Asp
        355                 360                 365

Trp Ile Thr Ile Lys Glu Gly Asn Lys Pro Val Leu Phe Gln Gly Asn
    370                 375                 380

Thr Asn Pro Thr Asp Val Val Val Ala Val Phe Pro Lys Pro Leu Ile
385                 390                 395                 400

Thr Arg Phe Val Arg Ile Lys Pro Ala Thr Trp Glu Thr Gly Ile Ser
                405                 410                 415

Met Arg Phe Glu Val Tyr Gly Cys Lys Ile Thr Asp Tyr Pro Cys Ser
            420                 425                 430
```

```
Gly Met Leu Gly Met Val Ser Gly Leu Ile Ser Asp Ser Gln Ile Thr
        435                 440                 445

Ser Ser Asn Gln Gly Asp Arg Asn Trp Met Pro Glu Asn Ile Arg Leu
    450                 455                 460

Val Thr Ser Arg Ser Gly Trp Ala Leu Pro Pro Ala Pro His Ser Tyr
465                 470                 475                 480

Ile Asn Glu Trp Leu Gln Ile Asp Leu Gly Glu Glu Lys Ile Val Arg
                485                 490                 495

Gly Ile Ile Ile Gln Gly Gly Lys His Arg Glu Asn Lys Val Phe Met
            500                 505                 510

Arg Lys Phe Lys Ile Gly Tyr Ser Asn Asn Gly Ser Asp Trp Lys Met
        515                 520                 525

Ile Met Asp Asp Ser Lys Arg Lys Ala Lys Ser Phe Glu Gly Asn Asn
    530                 535                 540

Asn Tyr Asp Thr Pro Glu Leu Arg Thr Phe Pro Ala Leu Ser Thr Arg
545                 550                 555                 560

Phe Ile Arg Ile Tyr Pro Glu Arg Ala Thr His Gly Gly Leu Gly Leu
                565                 570                 575

Arg Met Glu Leu Leu Gly Cys Glu Val Glu Ala Pro Thr Ala Gly Pro
            580                 585                 590

Thr Thr Pro Asn Gly Asn Leu Val Asp Glu Cys Asp Asp Asp Gln Ala
        595                 600                 605

Asn Cys His Ser Gly Thr Gly Asp Asp Phe Gln Leu Thr Gly Gly Thr
    610                 615                 620

Thr Val Leu Ala Thr Glu Lys Pro Thr Val Ile Asp Ser Thr Ile Gln
625                 630                 635                 640

Ser Glu Phe Pro Thr Tyr Gly Phe Asn Cys Glu Phe Gly Trp Gly Ser
                645                 650                 655

His Lys Thr Phe Cys His Trp Glu His Asp Asn His Val Gln Leu Lys
            660                 665                 670

Trp Ser Val Leu Thr Ser Lys Thr Gly Pro Ile Gln Asp His Thr Gly
        675                 680                 685

Asp Gly Asn Phe Ile Tyr Ser Gln Ala Asp Glu Asn Gln Lys Gly Lys
    690                 695                 700
```

```
Val Ala Arg Leu Val Ser Pro Val Val Tyr Ser Gln Asn Ser Ala His
705                 710                 715                 720

Cys Met Thr Phe Trp Tyr His Met Ser Gly Ser His Val Gly Thr Leu
                725                 730                 735

Arg Val Lys Leu Arg Tyr Gln Lys Pro Glu Glu Tyr Asp Gln Leu Val
            740                 745                 750

Trp Met Ala Ile Gly His Gln Gly Asp His Trp Lys Glu Gly Arg Val
        755                 760                 765

Leu Leu His Lys Ser Leu Lys Leu Tyr Gln Val Ile Phe Glu Gly Glu
    770                 775                 780

Ile Gly Lys Gly Asn Leu Gly Gly Ile Ala Val Asp Asp Ile Ser Ile
785                 790                 795                 800

Asn Asn His Ile Ser Gln Glu Asp Cys Ala Lys Pro Ala Asp Leu Asp
                805                 810                 815

Lys Lys Asn Pro Glu Ile Lys Ile Asp Glu Thr Gly Ser Thr Pro Gly
            820                 825                 830

Tyr Glu Gly Glu Gly Glu Gly Asp Lys Asn Ile Ser Arg Lys Pro Gly
        835                 840                 845

Asn Val Leu Lys Thr Leu Asp Pro Ile Leu Ile Thr Ile Ile Ala Met
    850                 855                 860

Ser Ala Leu Gly Val Leu Leu Gly Ala Val Cys Gly Val Val Leu Tyr
865                 870                 875                 880

Cys Ala Cys Trp His Asn Gly Met Ser Glu Arg Asn Leu Ser Ala Leu
                885                 890                 895

Glu Asn Tyr Asn Phe Glu Leu Val Asp Gly Val Lys Leu Lys Lys Asp
            900                 905                 910

Lys Leu Asn Thr Gln Ser Thr Tyr Ser Glu Ala
        915                 920
```

<210> 233
<211> 931
<212> PRT
<213> Homo sapiens

<400> 233

```
Met Asp Met Phe Pro Leu Thr Trp Val Phe Leu Ala Leu Tyr Phe Ser
1               5                   10                  15
```

```
Arg His Gln Val Arg Gly Gln Pro Asp Pro Pro Cys Gly Gly Arg Leu
            20                  25                  30

Asn Ser Lys Asp Ala Gly Tyr Ile Thr Ser Pro Gly Tyr Pro Gln Asp
        35                  40                  45

Tyr Pro Ser His Gln Asn Cys Glu Trp Ile Val Tyr Ala Pro Glu Pro
    50                  55                  60

Asn Gln Lys Ile Val Leu Asn Phe Asn Pro His Phe Glu Ile Glu Lys
65                  70                  75                  80

His Asp Cys Lys Tyr Asp Phe Ile Glu Ile Arg Asp Gly Asp Ser Glu
                85                  90                  95

Ser Ala Asp Leu Leu Gly Lys His Cys Gly Asn Ile Ala Pro Pro Thr
            100                 105                 110

Ile Ile Ser Ser Gly Ser Met Leu Tyr Ile Arg Phe Thr Ser Asp Tyr
        115                 120                 125

Ala Arg Gln Gly Ala Gly Phe Ser Leu Arg Tyr Glu Ile Phe Lys Thr
    130                 135                 140

Gly Ser Glu Asp Cys Ser Lys Asn Phe Thr Ser Pro Asn Gly Thr Ile
145                 150                 155                 160

Glu Ser Pro Gly Phe Pro Glu Lys Tyr Pro His Asn Leu Asp Cys Thr
                165                 170                 175

Phe Thr Ile Leu Ala Lys Pro Lys Met Glu Ile Ile Leu Gln Phe Leu
            180                 185                 190

Ile Phe Asp Leu Glu His Asp Pro Leu Gln Val Gly Glu Gly Asp Cys
        195                 200                 205

Lys Tyr Asp Trp Leu Asp Ile Trp Asp Gly Ile Pro His Val Gly Pro
    210                 215                 220

Leu Ile Gly Lys Tyr Cys Gly Thr Lys Thr Pro Ser Glu Leu Arg Ser
225                 230                 235                 240

Ser Thr Gly Ile Leu Ser Leu Thr Phe His Thr Asp Met Ala Val Ala
                245                 250                 255

Lys Asp Gly Phe Ser Ala Arg Tyr Tyr Leu Val His Gln Glu Pro Leu
            260                 265                 270

Glu Asn Phe Gln Cys Asn Val Pro Leu Gly Met Glu Ser Gly Arg Ile
        275                 280                 285
```

```
Ala Asn Glu Gln Ile Ser Ala Ser Ser Thr Tyr Ser Asp Gly Arg Trp
    290                 295                 300

Thr Pro Gln Gln Ser Arg Leu His Gly Asp Asp Asn Gly Trp Thr Pro
305                 310                 315                 320

Asn Leu Asp Ser Asn Lys Glu Tyr Leu Gln Val Asp Leu Arg Phe Leu
                325                 330                 335

Thr Met Leu Thr Ala Ile Ala Thr Gln Gly Ala Ile Ser Arg Glu Thr
            340                 345                 350

Gln Asn Gly Tyr Tyr Val Lys Ser Tyr Lys Leu Glu Val Ser Thr Asn
        355                 360                 365

Gly Glu Asp Trp Met Val Tyr Arg His Gly Lys Asn His Lys Val Phe
    370                 375                 380

Gln Ala Asn Asn Asp Ala Thr Glu Val Val Leu Asn Lys Leu His Ala
385                 390                 395                 400

Pro Leu Leu Thr Arg Phe Val Arg Ile Arg Pro Gln Thr Trp His Ser
                405                 410                 415

Gly Ile Ala Leu Arg Leu Glu Leu Phe Gly Cys Arg Val Thr Asp Ala
            420                 425                 430

Pro Cys Ser Asn Met Leu Gly Met Leu Ser Gly Leu Ile Ala Asp Ser
        435                 440                 445

Gln Ile Ser Ala Ser Ser Thr Gln Glu Tyr Leu Trp Ser Pro Ser Ala
    450                 455                 460

Ala Arg Leu Val Ser Ser Arg Ser Gly Trp Phe Pro Arg Ile Pro Gln
465                 470                 475                 480

Ala Gln Pro Gly Glu Glu Trp Leu Gln Val Asp Leu Gly Thr Pro Lys
                485                 490                 495

Thr Val Lys Gly Val Ile Ile Gln Gly Ala Arg Gly Gly Asp Ser Ile
            500                 505                 510

Thr Ala Val Glu Ala Arg Ala Phe Val Arg Lys Phe Lys Val Ser Tyr
        515                 520                 525

Ser Leu Asn Gly Lys Asp Trp Glu Tyr Ile Gln Asp Pro Arg Thr Gln
    530                 535                 540

Gln Pro Lys Leu Phe Glu Gly Asn Met His Tyr Asp Thr Pro Asp Ile
545                 550                 555                 560
```

```
Arg Arg Phe Asp Pro Ile Pro Ala Gln Tyr Val Arg Val Tyr Pro Glu
                565                 570                 575

Arg Trp Ser Pro Ala Gly Ile Gly Met Arg Leu Glu Val Leu Gly Cys
            580                 585                 590

Asp Trp Thr Asp Ser Lys Pro Thr Val Glu Thr Leu Gly Pro Thr Val
        595                 600                 605

Lys Ser Glu Glu Thr Thr Thr Pro Tyr Pro Thr Glu Glu Glu Ala Thr
    610                 615                 620

Glu Cys Gly Glu Asn Cys Ser Phe Glu Asp Asp Lys Asp Leu Gln Leu
625                 630                 635                 640

Pro Ser Gly Phe Asn Cys Asn Phe Asp Phe Leu Glu Glu Pro Cys Gly
                645                 650                 655

Trp Met Tyr Asp His Ala Lys Trp Leu Arg Thr Thr Trp Ala Ser Ser
            660                 665                 670

Ser Ser Pro Asn Asp Arg Thr Phe Pro Asp Asp Arg Asn Phe Leu Arg
        675                 680                 685

Leu Gln Ser Asp Ser Gln Arg Glu Gly Gln Tyr Ala Arg Leu Ile Ser
    690                 695                 700

Pro Pro Val His Leu Pro Arg Ser Pro Val Cys Met Glu Phe Gln Tyr
705                 710                 715                 720

Gln Ala Thr Gly Gly Arg Gly Val Ala Leu Gln Val Val Arg Glu Ala
                725                 730                 735

Ser Gln Glu Ser Lys Leu Leu Trp Val Ile Arg Glu Asp Gln Gly Gly
            740                 745                 750

Glu Trp Lys His Gly Arg Ile Ile Leu Pro Ser Tyr Asp Met Glu Tyr
        755                 760                 765

Gln Ile Val Phe Glu Gly Val Ile Gly Lys Gly Arg Ser Gly Glu Ile
    770                 775                 780

Ala Ile Asp Asp Ile Arg Ile Ser Thr Asp Val Pro Leu Glu Asn Cys
785                 790                 795                 800

Met Glu Pro Ile Ser Ala Phe Ala Gly Glu Asn Phe Lys Val Asp Ile
                805                 810                 815

Pro Glu Ile His Glu Arg Glu Gly Tyr Glu Asp Glu Ile Asp Asp Glu
            820                 825                 830
```

```
Tyr Glu Val Asp Trp Ser Asn Ser Ser Ser Ala Thr Ser Gly Ser Gly
        835                 840                 845

Ala Pro Ser Thr Asp Lys Glu Lys Ser Trp Leu Tyr Thr Leu Asp Pro
    850                 855                 860

Ile Leu Ile Thr Ile Ile Ala Met Ser Ser Leu Gly Val Leu Leu Gly
865                 870                 875                 880

Ala Thr Cys Ala Gly Leu Leu Leu Tyr Cys Thr Cys Ser Tyr Ser Gly
                885                 890                 895

Leu Ser Ser Arg Ser Cys Thr Thr Leu Glu Asn Tyr Asn Phe Glu Leu
            900                 905                 910

Tyr Asp Gly Leu Lys His Lys Val Lys Met Asn His Gln Lys Cys Cys
        915                 920                 925

Ser Glu Ala
    930


<210>  234
<211>  160
<212>  PRT
<213>  Homo sapiens

<400>  234

Met Thr Asp Gln Gln Ala Glu Ala Arg Ser Tyr Leu Ser Glu Glu Met
1               5                   10                  15

Ile Ala Glu Phe Lys Ala Ala Phe Asp Met Phe Asp Ala Asp Gly Gly
            20                  25                  30

Gly Asp Ile Ser Val Lys Glu Leu Gly Thr Val Met Arg Met Leu Gly
        35                  40                  45

Gln Thr Pro Thr Lys Glu Glu Leu Asp Ala Ile Ile Glu Glu Val Asp
    50                  55                  60

Glu Asp Gly Ser Gly Thr Ile Asp Phe Glu Glu Phe Leu Val Met Met
65                  70                  75                  80

Val Arg Gln Met Lys Glu Asp Ala Lys Gly Lys Ser Glu Glu Glu Leu
                85                  90                  95

Ala Glu Cys Phe Arg Ile Phe Asp Arg Asn Ala Asp Gly Tyr Ile Asp
            100                 105                 110

Pro Glu Glu Leu Ala Glu Ile Phe Arg Ala Ser Gly Glu His Val Thr
        115                 120                 125
```

```
Asp Glu Glu Ile Glu Ser Leu Met Lys Asp Gly Asp Lys Asn Asn Asp
    130                 135                 140

Gly Arg Ile Asp Phe Asp Glu Phe Leu Lys Met Met Glu Gly Val Gln
145                 150                 155                 160

<210>  235
<211>  182
<212>  PRT
<213>  Homo sapiens

<400>  235

Met Gly Asp Glu Glu Lys Arg Asn Arg Ala Ile Thr Ala Arg Arg Gln
1               5                   10                  15

His Leu Lys Ser Val Met Leu Gln Ile Ala Ala Thr Glu Leu Glu Lys
            20                  25                  30

Glu Glu Ser Arg Arg Glu Ala Glu Lys Gln Asn Tyr Leu Ala Glu His
        35                  40                  45

Cys Pro Pro Leu His Ile Pro Gly Ser Met Ser Glu Val Gln Glu Leu
    50                  55                  60

Cys Lys Gln Leu His Ala Lys Ile Asp Ala Ala Glu Glu Glu Lys Tyr
65                  70                  75                  80

Asp Met Glu Val Arg Val Gln Lys Thr Ser Lys Glu Leu Glu Asp Met
                85                  90                  95

Asn Gln Lys Leu Phe Asp Leu Arg Gly Lys Phe Lys Arg Pro Pro Leu
            100                 105                 110

Arg Arg Val Arg Met Ser Ala Asp Ala Met Leu Lys Ala Leu Leu Gly
        115                 120                 125

Ser Lys His Lys Val Cys Met Asp Leu Arg Ala Asn Leu Lys Gln Val
    130                 135                 140

Lys Lys Glu Asp Thr Glu Lys Glu Arg Asp Leu Arg Asp Val Gly Asp
145                 150                 155                 160

Trp Arg Lys Asn Ile Glu Glu Lys Ser Gly Met Glu Gly Arg Lys Lys
                165                 170                 175

Met Phe Glu Ser Glu Ser
            180

<210>  236
<211>  258
<212>  PRT
<213>  Homo sapiens
```

<400> 236

Met Ser Asp Glu Glu Val Glu Gln Val Glu Glu Gln Tyr Glu Glu Glu
1 5 10 15

Glu Glu Ala Gln Glu Glu Glu Glu Val Gln Glu Asp Thr Ala Glu Glu
20 25 30

Asp Ala Glu Glu Glu Lys Pro Arg Pro Lys Leu Thr Ala Pro Lys Ile
35 40 45

Pro Glu Gly Glu Lys Val Asp Phe Asp Asp Ile Gln Lys Lys Arg Gln
50 55 60

Asn Lys Asp Leu Met Glu Leu Gln Ala Leu Ile Asp Ser His Phe Glu
65 70 75 80

Ala Arg Lys Lys Glu Glu Glu Glu Leu Val Ala Leu Lys Glu Arg Ile
85 90 95

Glu Lys Arg Arg Ala Glu Arg Ala Glu Gln Gln Arg Ile Arg Ala Glu
100 105 110

Lys Glu Arg Glu Arg Gln Asn Arg Leu Ala Glu Glu Lys Ala Arg Arg
115 120 125

Glu Glu Glu Asp Ala Lys Arg Arg Ala Glu Asp Asp Leu Lys Lys Lys
130 135 140

Lys Ala Leu Ser Ser Met Gly Ala Asn Tyr Ser Ser Tyr Leu Ala Lys
145 150 155 160

Ala Asp Gln Lys Arg Gly Lys Lys Gln Thr Ala Arg Glu Met Lys Lys
165 170 175

Lys Ile Leu Ala Glu Arg Arg Lys Pro Leu Asn Ile Asp His Leu Gly
180 185 190

Glu Asp Lys Leu Arg Asp Lys Ala Lys Glu Leu Trp Glu Thr Leu His
195 200 205

Gln Leu Glu Ile Asp Lys Phe Glu Phe Gly Glu Lys Leu Lys Arg Gln
210 215 220

Lys Tyr Asp Ile Thr Thr Leu Arg Ser Arg Ile Asp Gln Ala Gln Lys
225 230 235 240

His Ser Lys Lys Ala Gly Thr Pro Ala Lys Gly Lys Val Gly Gly Arg
245 250 255

Trp Lys

<210> 237
<211> 153
<212> PRT
<213> Homo sapiens

<220>
<221> MISC_FEATURE
<222> (79)..(79)
<223> S-carboxyamidomethylcysteine

<220>
<221> MISC_FEATURE
<222> (96)..(96)
<223> S-carboxyamidomethylcysteine

<400> 237

```
Ala Asp Gly Ser Ser Asp Ala Ala Arg Glu Pro Arg Pro Ala Pro Ala
1               5                   10                  15

Pro Ile Arg Arg Arg Ser Ser Asn Tyr Arg Ala Tyr Ala Thr Glu Pro
            20                  25                  30

His Ala Lys Lys Lys Ser Lys Ile Ser Ala Ser Arg Lys Leu Gln Leu
        35                  40                  45

Lys Thr Leu Leu Leu Gln Ile Ala Lys Gln Glu Leu Glu Arg Glu Ala
    50                  55                  60

Glu Glu Arg Arg Gly Glu Lys Gly Arg Ala Leu Ser Thr Arg Cys Gln
65                  70                  75                  80

Pro Leu Glu Leu Thr Gly Leu Gly Phe Ala Glu Leu Gln Asp Leu Cys
                85                  90                  95

Arg Gln Leu His Ala Arg Val Asp Lys Val Asp Glu Glu Arg Tyr Asp
            100                 105                 110

Ile Glu Ala Lys Val Thr Lys Asn Ile Thr Glu Ile Ala Asp Leu Thr
        115                 120                 125

Gln Lys Ile Phe Asp Leu Arg Gly Lys Phe Lys Arg Pro Thr Leu Arg
    130                 135                 140

Arg Val Arg Ile Ser Ala Asp Ala Met
145                 150
```

<210> 238
<211> 402
<212> PRT
<213> Homo sapiens

<400> 238

```
Met Gln Met Ser Pro Ala Leu Thr Cys Leu Val Leu Gly Leu Ala Leu
```

1 5 10 15

Val Phe Gly Glu Gly Ser Ala Val His His Pro Pro Ser Tyr Val Ala
20 25 30

His Leu Ala Ser Asp Phe Gly Val Arg Val Phe Gln Gln Val Ala Gln
35 40 45

Ala Ser Lys Asp Arg Asn Val Val Phe Ser Pro Tyr Gly Val Ala Ser
50 55 60

Val Leu Ala Met Leu Gln Leu Thr Thr Gly Gly Glu Thr Gln Gln Gln
65 70 75 80

Ile Gln Ala Ala Met Gly Phe Lys Ile Asp Asp Lys Gly Met Ala Pro
85 90 95

Ala Leu Arg His Leu Tyr Lys Glu Leu Met Gly Pro Trp Asn Lys Asp
100 105 110

Glu Ile Ser Thr Thr Asp Ala Ile Phe Val Gln Arg Asp Leu Lys Leu
115 120 125

Val Gln Gly Phe Met Pro His Phe Phe Arg Leu Phe Arg Ser Thr Val
130 135 140

Lys Gln Val Asp Phe Ser Glu Val Glu Arg Ala Arg Phe Ile Ile Asn
145 150 155 160

Asp Trp Val Lys Thr His Thr Lys Gly Met Ile Ser Asn Leu Leu Gly
165 170 175

Lys Gly Ala Val Asp Gln Leu Thr Arg Leu Val Leu Val Asn Ala Leu
180 185 190

Tyr Phe Asn Gly Gln Trp Lys Thr Pro Phe Pro Asp Ser Ser Thr His
195 200 205

Arg Arg Leu Phe His Lys Ser Asp Gly Ser Thr Val Ser Val Pro Met
210 215 220

Met Ala Gln Thr Asn Lys Phe Asn Tyr Thr Glu Phe Thr Thr Pro Asp
225 230 235 240

Gly His Tyr Tyr Asp Ile Leu Glu Leu Pro Tyr His Gly Asp Thr Leu
245 250 255

Ser Met Phe Ile Ala Ala Pro Tyr Glu Lys Glu Val Pro Leu Ser Ala
260 265 270

Leu Thr Asn Ile Leu Ser Ala Gln Leu Ile Ser His Trp Lys Gly Asn

275 280 285

Met Thr Arg Leu Pro Arg Leu Leu Val Leu Pro Lys Phe Ser Leu Glu
290 295 300

Thr Glu Val Asp Leu Arg Lys Pro Leu Glu Asn Leu Gly Met Thr Asp
305 310 315 320

Met Phe Arg Gln Phe Gln Ala Asp Phe Thr Ser Leu Ser Asp Gln Glu
325 330 335

Pro Leu His Val Ala Gln Ala Leu Gln Lys Val Lys Ile Glu Val Asn
340 345 350

Glu Ser Gly Thr Val Ala Ser Ser Ser Thr Ala Val Ile Val Ser Ala
355 360 365

Arg Met Ala Pro Glu Glu Ile Ile Met Asp Arg Pro Phe Leu Phe Val
370 375 380

Val Arg His Asn Pro Thr Gly Thr Val Leu Phe Met Gly Gln Val Met
385 390 395 400

Glu Pro

<210> 239
<211> 415
<212> PRT
<213> Homo sapiens

<400> 239

Met Glu Asp Leu Cys Val Ala Asn Thr Leu Phe Ala Leu Asn Leu Phe
1 5 10 15

Lys His Leu Ala Lys Ala Ser Pro Thr Gln Asn Leu Phe Leu Ser Pro
20 25 30

Trp Ser Ile Ser Ser Thr Met Ala Met Val Tyr Met Gly Ser Arg Gly
35 40 45

Ser Thr Glu Asp Gln Met Ala Lys Val Leu Gln Phe Asn Glu Val Gly
50 55 60

Ala Asn Ala Val Thr Pro Met Thr Pro Glu Asn Phe Thr Ser Cys Gly
65 70 75 80

Phe Met Gln Gln Ile Gln Lys Gly Ser Tyr Pro Asp Ala Ile Leu Gln
85 90 95

Ala Gln Ala Ala Asp Lys Ile His Ser Ser Phe Arg Ser Leu Ser Ser
100 105 110

```
Ala Ile Asn Ala Ser Thr Gly Asn Tyr Leu Leu Glu Ser Val Asn Lys
        115                 120                 125

Leu Phe Gly Glu Lys Ser Ala Ser Phe Arg Glu Glu Tyr Ile Arg Leu
    130                 135                 140

Cys Gln Lys Tyr Tyr Ser Ser Glu Pro Gln Ala Val Asp Phe Leu Glu
145                 150                 155                 160

Cys Ala Glu Glu Ala Arg Lys Lys Ile Asn Ser Trp Val Lys Thr Gln
                165                 170                 175

Thr Lys Gly Lys Ile Pro Asn Leu Leu Pro Glu Gly Ser Val Asp Gly
            180                 185                 190

Asp Thr Arg Met Val Leu Val Asn Ala Val Tyr Phe Lys Gly Lys Trp
        195                 200                 205

Lys Thr Pro Phe Glu Lys Lys Leu Asn Gly Leu Tyr Pro Phe Arg Val
    210                 215                 220

Asn Ser Ala Gln Arg Thr Pro Val Gln Met Met Tyr Leu Arg Glu Lys
225                 230                 235                 240

Leu Asn Ile Gly Tyr Ile Glu Asp Leu Lys Ala Gln Ile Leu Glu Leu
                245                 250                 255

Pro Tyr Ala Gly Asp Val Ser Met Phe Leu Leu Leu Pro Asp Glu Ile
            260                 265                 270

Ala Asp Val Ser Thr Gly Leu Glu Leu Leu Glu Ser Glu Ile Thr Tyr
        275                 280                 285

Asp Lys Leu Asn Lys Trp Thr Ser Lys Asp Lys Met Ala Glu Asp Glu
    290                 295                 300

Val Glu Val Tyr Ile Pro Gln Phe Lys Leu Glu Glu His Tyr Glu Leu
305                 310                 315                 320

Arg Ser Ile Leu Arg Ser Met Gly Met Glu Asp Ala Phe Asn Lys Gly
                325                 330                 335

Arg Ala Asn Phe Ser Gly Met Ser Glu Arg Asn Asp Leu Phe Leu Ser
            340                 345                 350

Glu Val Phe His Gln Ala Met Val Asp Val Asn Glu Glu Gly Thr Glu
        355                 360                 365

Ala Ala Ala Gly Thr Gly Gly Val Met Thr Gly Arg Thr Gly His Gly
    370                 375                 380
```

```
Gly Pro Gln Phe Val Ala Asp His Pro Phe Leu Phe Leu Ile Met His
385                 390                 395                 400


Lys Ile Thr Asn Cys Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro
                405                 410                 415


<210>  240
<211>  368
<212>  PRT
<213>  Homo sapiens

<400>  240

Met Val Leu Glu Val Ser Asp His Gln Val Leu Asn Asp Ala Glu Val
1               5                   10                  15


Ala Ala Leu Leu Glu Asn Phe Ser Ser Ser Tyr Asp Tyr Gly Glu Asn
            20                  25                  30


Glu Ser Asp Ser Cys Cys Thr Ser Pro Pro Cys Pro Gln Asp Phe Ser
        35                  40                  45


Leu Asn Phe Asp Arg Ala Phe Leu Pro Ala Leu Tyr Ser Leu Leu Phe
    50                  55                  60


Leu Leu Gly Leu Leu Gly Asn Gly Ala Val Ala Ala Val Leu Leu Ser
65                  70                  75                  80


Arg Arg Thr Ala Leu Ser Ser Thr Asp Thr Phe Leu Leu His Leu Ala
                85                  90                  95


Val Ala Asp Thr Leu Leu Val Leu Thr Leu Pro Leu Trp Ala Val Asp
            100                 105                 110


Ala Ala Val Gln Trp Val Phe Gly Ser Gly Leu Cys Lys Val Ala Gly
        115                 120                 125


Ala Leu Phe Asn Ile Asn Phe Tyr Ala Gly Ala Leu Leu Leu Ala Cys
    130                 135                 140


Ile Ser Phe Asp Arg Tyr Leu Asn Ile Val His Ala Thr Gln Leu Tyr
145                 150                 155                 160


Arg Arg Gly Pro Pro Ala Arg Val Thr Leu Thr Cys Leu Ala Val Trp
                165                 170                 175


Gly Leu Cys Leu Leu Phe Ala Leu Pro Asp Phe Ile Phe Leu Ser Ala
            180                 185                 190


His His Asp Glu Arg Leu Asn Ala Thr His Cys Gln Tyr Asn Phe Pro
        195                 200                 205
```

```
Gln Val Gly Arg Thr Ala Leu Arg Val Leu Gln Leu Val Ala Gly Phe
    210                 215                 220

Leu Leu Pro Leu Leu Val Met Ala Tyr Cys Tyr Ala His Ile Leu Ala
225                 230                 235                 240

Val Leu Leu Val Ser Arg Gly Gln Arg Arg Leu Arg Ala Met Arg Leu
                245                 250                 255

Val Val Val Val Val Val Ala Phe Ala Leu Cys Trp Thr Pro Tyr His
            260                 265                 270

Leu Val Val Leu Val Asp Ile Leu Met Asp Leu Gly Ala Leu Ala Arg
        275                 280                 285

Asn Cys Gly Arg Glu Ser Arg Val Asp Val Ala Lys Ser Val Thr Ser
    290                 295                 300

Gly Leu Gly Tyr Met His Cys Cys Leu Asn Pro Leu Leu Tyr Ala Phe
305                 310                 315                 320

Val Gly Val Lys Phe Arg Glu Arg Met Trp Met Leu Leu Leu Arg Leu
                325                 330                 335

Gly Cys Pro Asn Gln Arg Gly Leu Gln Arg Gln Pro Ser Ser Ser Arg
            340                 345                 350

Arg Asp Ser Ser Trp Ser Glu Thr Ser Glu Ala Ser Tyr Ser Gly Leu
        355                 360                 365


<210>  241
<211>  91
<212>  PRT
<213>  Homo sapiens

<400>  241

Met Lys Val Ser Ala Ala Ala Leu Ala Val Ile Leu Ile Ala Thr Ala
1               5                   10                  15

Leu Cys Ala Pro Ala Ser Ala Ser Pro Tyr Ser Ser Asp Thr Thr Pro
            20                  25                  30

Cys Cys Phe Ala Tyr Ile Ala Arg Pro Leu Pro Arg Ala His Ile Lys
        35                  40                  45

Glu Tyr Phe Tyr Thr Ser Gly Lys Cys Ser Asn Pro Ala Val Val Phe
    50                  55                  60

Val Thr Arg Lys Asn Arg Gln Val Cys Ala Asn Pro Glu Lys Lys Trp
65                  70                  75                  80
```

Val Arg Glu Tyr Ile Asn Ser Leu Glu Met Ser
85 90

<210> 242
<211> 98
<212> PRT
<213> Homo sapiens

<400> 242

Met Asn Gln Thr Ala Ile Leu Ile Cys Cys Leu Ile Phe Leu Thr Leu
1 5 10 15

Ser Gly Ile Gln Gly Val Pro Leu Ser Arg Thr Val Arg Cys Thr Cys
20 25 30

Ile Ser Ile Ser Asn Gln Pro Val Asn Pro Arg Ser Leu Glu Lys Leu
35 40 45

Glu Ile Ile Pro Ala Ser Gln Phe Cys Pro Arg Val Glu Ile Ile Ala
50 55 60

Thr Met Lys Lys Lys Gly Glu Lys Arg Cys Leu Asn Pro Glu Ser Lys
65 70 75 80

Ala Ile Lys Asn Leu Leu Lys Ala Val Ser Lys Glu Arg Ser Lys Arg
85 90 95

Ser Pro

<210> 243
<211> 378
<212> PRT
<213> Homo sapiens

<400> 243

Met Asp Leu Gly Lys Pro Met Lys Ser Val Leu Val Val Ala Leu Leu
1 5 10 15

Val Ile Phe Gln Val Cys Leu Cys Gln Asp Glu Val Thr Asp Asp Tyr
20 25 30

Ile Gly Asp Asn Thr Thr Val Asp Tyr Thr Leu Phe Glu Ser Leu Cys
35 40 45

Ser Lys Lys Asp Val Arg Asn Phe Lys Ala Trp Phe Leu Pro Ile Met
50 55 60

Tyr Ser Ile Ile Cys Phe Val Gly Leu Leu Gly Asn Gly Leu Val Val
65 70 75 80

Leu Thr Tyr Ile Tyr Phe Lys Arg Leu Lys Thr Met Thr Asp Thr Tyr
85 90 95

```
Leu Leu Asn Leu Ala Val Ala Asp Ile Leu Phe Leu Leu Thr Leu Pro
            100                 105                 110

Phe Trp Ala Tyr Ser Ala Ala Lys Ser Trp Val Phe Gly Val His Phe
        115                 120                 125

Cys Lys Leu Ile Phe Ala Ile Tyr Lys Met Ser Phe Phe Ser Gly Met
    130                 135                 140

Leu Leu Leu Leu Cys Ile Ser Ile Asp Arg Tyr Val Ala Ile Val Gln
145                 150                 155                 160

Ala Val Ser Ala His Arg His Arg Ala Arg Val Leu Leu Ile Ser Lys
                165                 170                 175

Leu Ser Cys Val Gly Ile Trp Ile Leu Ala Thr Val Leu Ser Ile Pro
            180                 185                 190

Glu Leu Leu Tyr Ser Asp Leu Gln Arg Ser Ser Ser Glu Gln Ala Met
        195                 200                 205

Arg Cys Ser Leu Ile Thr Glu His Val Glu Ala Phe Ile Thr Ile Gln
    210                 215                 220

Val Ala Gln Met Val Ile Gly Phe Leu Val Pro Leu Leu Ala Met Ser
225                 230                 235                 240

Phe Cys Tyr Leu Val Ile Ile Arg Thr Leu Leu Gln Ala Arg Asn Phe
                245                 250                 255

Glu Arg Asn Lys Ala Ile Lys Val Ile Ile Ala Val Val Val Val Phe
            260                 265                 270

Ile Val Phe Gln Leu Pro Tyr Asn Gly Val Val Leu Ala Gln Thr Val
        275                 280                 285

Ala Asn Phe Asn Ile Thr Ser Ser Thr Cys Glu Leu Ser Lys Gln Leu
    290                 295                 300

Asn Ile Ala Tyr Asp Val Thr Tyr Ser Leu Ala Cys Val Arg Cys Cys
305                 310                 315                 320

Val Asn Pro Phe Leu Tyr Ala Phe Ile Gly Val Lys Phe Arg Asn Asp
                325                 330                 335

Leu Phe Lys Leu Phe Lys Asp Leu Gly Cys Leu Ser Gln Glu Gln Leu
            340                 345                 350

Arg Gln Trp Ser Ser Cys Arg His Ile Arg Arg Ser Ser Met Ser Val
        355                 360                 365
```

```
Glu Ala Glu Thr Thr Thr Thr Phe Ser Pro
    370                 375


<210>  244
<211>  397
<212>  PRT
<213>  Homo sapiens

<400>  244

Met Ala Pro Ile Ser Leu Ser Trp Leu Leu Arg Leu Ala Thr Phe Cys
1               5                   10                  15


His Leu Thr Val Leu Leu Ala Gly Gln His His Gly Val Thr Lys Cys
            20                  25                  30


Asn Ile Thr Cys Ser Lys Met Thr Ser Lys Ile Pro Val Ala Leu Leu
        35                  40                  45


Ile His Tyr Gln Gln Asn Gln Ala Ser Cys Gly Lys Arg Ala Ile Ile
    50                  55                  60


Leu Glu Thr Arg Gln His Arg Leu Phe Cys Ala Asp Pro Lys Glu Gln
65                  70                  75                  80


Trp Val Lys Asp Ala Met Gln His Leu Asp Arg Gln Ala Ala Ala Leu
                85                  90                  95


Thr Arg Asn Gly Gly Thr Phe Glu Lys Gln Ile Gly Glu Val Lys Pro
            100                 105                 110


Arg Thr Thr Pro Ala Ala Gly Gly Met Asp Glu Ser Val Val Leu Glu
        115                 120                 125


Pro Glu Ala Thr Gly Glu Ser Ser Ser Leu Glu Pro Thr Pro Ser Ser
    130                 135                 140


Gln Glu Ala Gln Arg Ala Leu Gly Thr Ser Pro Glu Leu Pro Thr Gly
145                 150                 155                 160


Val Thr Gly Ser Ser Gly Thr Arg Leu Pro Pro Thr Pro Lys Ala Gln
                165                 170                 175


Asp Gly Gly Pro Val Gly Thr Glu Leu Phe Arg Val Pro Pro Val Ser
            180                 185                 190


Thr Ala Ala Thr Trp Gln Ser Ser Ala Pro His Gln Pro Gly Pro Ser
        195                 200                 205


Leu Trp Ala Glu Ala Lys Thr Ser Glu Ala Pro Ser Thr Gln Asp Pro
    210                 215                 220
```

```
Ser Thr Gln Ala Ser Thr Ala Ser Ser Pro Ala Pro Glu Glu Asn Ala
225                 230                 235                 240

Pro Ser Glu Gly Gln Arg Val Trp Gly Gln Gly Gln Ser Pro Arg Pro
                245                 250                 255

Glu Asn Ser Leu Glu Arg Glu Glu Met Gly Pro Val Pro Ala His Thr
            260                 265                 270

Asp Ala Phe Gln Asp Trp Gly Pro Gly Ser Met Ala His Val Ser Val
        275                 280                 285

Val Pro Val Ser Ser Glu Gly Thr Pro Ser Arg Glu Pro Val Ala Ser
    290                 295                 300

Gly Ser Trp Thr Pro Lys Ala Glu Glu Pro Ile His Ala Thr Met Asp
305                 310                 315                 320

Pro Gln Arg Leu Gly Val Leu Ile Thr Pro Val Pro Asp Ala Gln Ala
                325                 330                 335

Ala Thr Arg Arg Gln Ala Val Gly Leu Leu Ala Phe Leu Gly Leu Leu
            340                 345                 350

Phe Cys Leu Gly Val Ala Met Phe Thr Tyr Gln Ser Leu Gln Gly Cys
        355                 360                 365

Pro Arg Lys Met Ala Gly Glu Met Ala Glu Gly Leu Arg Tyr Ile Pro
    370                 375                 380

Arg Ser Cys Gly Ser Asn Ser Tyr Val Leu Val Pro Val
385                 390                 395


<210>  245
<211>  97
<212>  PRT
<213>  Homo sapiens

<400>  245

Met Lys Val Ser Ala Ala Leu Leu Trp Leu Leu Leu Ile Ala Ala Ala
1               5                   10                  15

Phe Ser Pro Gln Gly Leu Ala Gly Pro Ala Ser Val Pro Thr Thr Cys
            20                  25                  30

Cys Phe Asn Leu Ala Asn Arg Lys Ile Pro Leu Gln Arg Leu Glu Ser
        35                  40                  45

Tyr Arg Arg Ile Thr Ser Gly Lys Cys Pro Gln Lys Ala Val Ile Phe
    50                  55                  60
```

Lys Thr Lys Leu Ala Lys Asp Ile Cys Ala Asp Pro Lys Lys Lys Trp
65 70 75 80

Val Gln Asp Ser Met Lys Tyr Leu Asp Gln Lys Ser Pro Thr Pro Lys
85 90 95

Pro

<210> 246
<211> 134
<212> PRT
<213> Homo sapiens

<400> 246

Met Ala Gln Ser Leu Ala Leu Ser Leu Leu Ile Leu Val Leu Ala Phe
1 5 10 15

Gly Ile Pro Arg Thr Gln Gly Ser Asp Gly Gly Ala Gln Asp Cys Cys
20 25 30

Leu Lys Tyr Ser Gln Arg Lys Ile Pro Ala Lys Val Val Arg Ser Tyr
35 40 45

Arg Lys Gln Glu Pro Ser Leu Gly Cys Ser Ile Pro Ala Ile Leu Phe
50 55 60

Leu Pro Arg Lys Arg Ser Gln Ala Glu Leu Cys Ala Asp Pro Lys Glu
65 70 75 80

Leu Trp Val Gln Gln Leu Met Gln His Leu Asp Lys Thr Pro Ser Pro
85 90 95

Gln Lys Pro Ala Gln Gly Cys Arg Lys Asp Arg Gly Ala Ser Lys Thr
100 105 110

Gly Lys Lys Gly Lys Gly Ser Lys Gly Cys Lys Arg Thr Glu Arg Ser
115 120 125

Gln Thr Pro Lys Gly Pro
130

<210> 247
<211> 114
<212> PRT
<213> Homo sapiens

<400> 247

Met Arg Leu Leu Ile Leu Ala Leu Leu Gly Ile Cys Ser Leu Thr Ala
1 5 10 15

Tyr Ile Val Glu Gly Val Gly Ser Glu Val Ser Asp Lys Arg Thr Cys
20 25 30

```
Val Ser Leu Thr Thr Gln Arg Leu Pro Val Ser Arg Ile Lys Thr Tyr
        35                  40                  45

Thr Ile Thr Glu Gly Ser Leu Arg Ala Val Ile Phe Ile Thr Lys Arg
    50                  55                  60

Gly Leu Lys Val Cys Ala Asp Pro Gln Ala Thr Trp Val Arg Asp Val
65                  70                  75                  80

Val Arg Ser Met Asp Arg Lys Ser Asn Thr Arg Asn Asn Met Ile Gln
                85                  90                  95

Thr Lys Pro Thr Gly Thr Gln Gln Ser Thr Asn Thr Ala Val Thr Leu
            100                 105                 110

Thr Gly


<210>  248
<211>  96
<212>  PRT
<213>  Homo sapiens

<400>  248

Met Cys Cys Thr Lys Ser Leu Leu Leu Ala Ala Leu Met Ser Val Leu
1               5                   10                  15

Leu Leu His Leu Cys Gly Glu Ser Glu Ala Ala Ser Asn Phe Asp Cys
            20                  25                  30

Cys Leu Gly Tyr Thr Asp Arg Ile Leu His Pro Lys Phe Ile Val Gly
        35                  40                  45

Phe Thr Arg Gln Leu Ala Asn Glu Gly Cys Asp Ile Asn Ala Ile Ile
    50                  55                  60

Phe His Thr Lys Lys Lys Leu Ser Val Cys Ala Asn Pro Lys Gln Thr
65                  70                  75                  80

Trp Val Lys Tyr Ile Val Arg Leu Leu Ser Lys Lys Val Lys Asn Met
                85                  90                  95

<210>  249
<211>  98
<212>  PRT
<213>  Homo sapiens

<400>  249

Met Ala Leu Leu Leu Ala Leu Ser Leu Leu Val Leu Trp Thr Ser Pro
1               5                   10                  15
```

Ala Pro Thr Leu Ser Gly Thr Asn Asp Ala Glu Asp Cys Cys Leu Ser
            20   25   30

Val Thr Gln Lys Pro Ile Pro Gly Tyr Ile Val Arg Asn Phe His Tyr
        35   40   45

Leu Leu Ile Lys Asp Gly Cys Arg Val Pro Ala Val Val Phe Thr Thr
    50   55   60

Leu Arg Gly Arg Gln Leu Cys Ala Pro Pro Asp Gln Pro Trp Val Glu
65   70   75   80

Arg Ile Ile Gln Arg Leu Gln Arg Thr Ser Ala Lys Met Lys Arg Arg
                85   90   95

Ser Ser

<210> 250
<211> 353
<212> PRT
<213> Homo sapiens

<400> 250

Met Glu Leu Thr Glu Leu Leu Leu Val Val Met Leu Leu Leu Thr Ala
1   5   10   15

Arg Leu Thr Leu Ser Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val
            20   25   30

Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser
        35   40   45

Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala
    50   55   60

Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys
65   70   75   80

Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met
                85   90   95

Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly
            100   105   110

Gln Leu Ser Gly Gln Val Arg Leu Leu Leu Gly Ala Leu Gln Ser Leu
        115   120   125

Leu Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp
    130   135   140

Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val

145 150 155 160

Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Arg Ala
165 170 175

Pro Pro Thr Thr Ala Val Pro Ser Arg Thr Ser Leu Val Leu Thr Leu
180 185 190

Asn Glu Leu Pro Asn Arg Thr Ser Gly Leu Leu Glu Thr Asn Phe Thr
195 200 205

Ala Ser Ala Arg Thr Thr Gly Ser Gly Leu Leu Lys Trp Gln Gln Gly
210 215 220

Phe Arg Ala Lys Ile Pro Gly Leu Leu Asn Gln Thr Ser Arg Ser Leu
225 230 235 240

Asp Gln Ile Pro Gly Tyr Leu Asn Arg Ile His Glu Leu Leu Asn Gly
245 250 255

Thr Arg Gly Leu Phe Pro Gly Pro Ser Arg Arg Thr Leu Gly Ala Pro
260 265 270

Asp Ile Ser Ser Gly Thr Ser Asp Thr Gly Ser Leu Pro Pro Asn Leu
275 280 285

Gln Pro Gly Tyr Ser Pro Ser Pro Thr His Pro Pro Thr Gly Gln Tyr
290 295 300

Thr Leu Phe Pro Leu Pro Pro Thr Leu Pro Thr Pro Val Val Gln Leu
305 310 315 320

His Pro Leu Leu Pro Asp Pro Ser Ala Pro Thr Pro Thr Pro Thr Ser
325 330 335

Pro Leu Leu Asn Thr Ser Tyr Thr His Ser Gln Asn Leu Ser Gln Glu
340 345 350

Gly

<210> 251
<211> 273
<212> PRT
<213> Homo sapiens

<400> 251

Met Lys Lys Thr Gln Thr Trp Ile Leu Thr Cys Ile Tyr Leu Gln Leu
1 5 10 15

Leu Leu Phe Asn Pro Leu Val Lys Thr Glu Gly Ile Cys Arg Asn Arg
20 25 30

```
Val Thr Asn Asn Val Lys Asp Val Thr Lys Leu Val Ala Asn Leu Pro
        35                  40                  45

Lys Asp Tyr Met Ile Thr Leu Lys Tyr Val Pro Gly Met Asp Val Leu
    50                  55                  60

Pro Ser His Cys Trp Ile Ser Glu Met Val Val Gln Leu Ser Asp Ser
65                  70                  75                  80

Leu Thr Asp Leu Leu Asp Lys Phe Ser Asn Ile Ser Glu Gly Leu Ser
                85                  90                  95

Asn Tyr Ser Ile Ile Asp Lys Leu Val Asn Ile Val Asp Asp Leu Val
            100                 105                 110

Glu Cys Val Lys Glu Asn Ser Ser Lys Asp Leu Lys Lys Ser Phe Lys
        115                 120                 125

Ser Pro Glu Pro Arg Leu Phe Thr Pro Glu Glu Phe Phe Arg Ile Phe
    130                 135                 140

Asn Arg Ser Ile Asp Ala Phe Lys Asp Phe Val Val Ala Ser Glu Thr
145                 150                 155                 160

Ser Asp Cys Val Val Ser Ser Thr Leu Ser Pro Glu Lys Asp Ser Arg
                165                 170                 175

Val Ser Val Thr Lys Pro Phe Met Leu Pro Pro Val Ala Ala Ser Ser
            180                 185                 190

Leu Arg Asn Asp Ser Ser Ser Ser Asn Arg Lys Ala Lys Asn Pro Pro
        195                 200                 205

Gly Asp Ser Ser Leu His Trp Ala Ala Met Ala Leu Pro Ala Leu Phe
    210                 215                 220

Ser Leu Ile Ile Gly Phe Ala Phe Gly Ala Leu Tyr Trp Lys Lys Arg
225                 230                 235                 240

Gln Pro Ser Leu Thr Arg Ala Val Glu Asn Ile Gln Ile Asn Glu Glu
                245                 250                 255

Asp Asn Glu Ile Ser Met Leu Gln Glu Lys Glu Arg Glu Phe Gln Glu
            260                 265                 270

Val
```

<210> 252
<211> 149

<212> PRT
<213> Homo sapiens

<400> 252

Met Pro Val Met Arg Leu Phe Pro Cys Phe Leu Gln Leu Leu Ala Gly
1 5 10 15

Leu Ala Leu Pro Ala Val Pro Pro Gln Gln Trp Ala Leu Ser Ala Gly
20 25 30

Asn Gly Ser Ser Glu Val Glu Val Val Pro Phe Gln Glu Val Trp Gly
35 40 45

Arg Ser Tyr Cys Arg Ala Leu Glu Arg Leu Val Asp Val Val Ser Glu
50 55 60

Tyr Pro Ser Glu Val Glu His Met Phe Ser Pro Ser Cys Val Ser Leu
65 70 75 80

Leu Arg Cys Thr Gly Cys Cys Gly Asp Glu Asn Leu His Cys Val Pro
85 90 95

Val Glu Thr Ala Asn Val Thr Met Gln Leu Leu Lys Ile Arg Ser Gly
100 105 110

Asp Arg Pro Ser Tyr Val Glu Leu Thr Phe Ser Gln His Val Arg Cys
115 120 125

Glu Cys Arg Pro Leu Arg Glu Lys Met Lys Pro Glu Arg Cys Gly Asp
130 135 140

Ala Val Pro Arg Arg
145

<210> 253
<211> 170
<212> PRT
<213> Homo sapiens

<400> 253

Met Pro Val Met Arg Leu Phe Pro Cys Phe Leu Gln Leu Leu Ala Gly
1 5 10 15

Leu Ala Leu Pro Ala Val Pro Pro Gln Gln Trp Ala Leu Ser Ala Gly
20 25 30

Asn Gly Ser Ser Glu Val Glu Val Val Pro Phe Gln Glu Val Trp Gly
35 40 45

Arg Ser Tyr Cys Arg Ala Leu Glu Arg Leu Val Asp Val Val Ser Glu
50 55 60

```
Tyr Pro Ser Glu Val Glu His Met Phe Ser Pro Ser Cys Val Ser Leu
65                  70                  75                  80

Leu Arg Cys Thr Gly Cys Cys Gly Asp Glu Asn Leu His Cys Val Pro
                85                  90                  95

Val Glu Thr Ala Asn Val Thr Met Gln Leu Leu Lys Ile Arg Ser Gly
            100                 105                 110

Asp Arg Pro Ser Tyr Val Glu Leu Thr Phe Ser Gln His Val Arg Cys
        115                 120                 125

Glu Cys Arg Pro Leu Arg Glu Lys Met Lys Pro Glu Arg Arg Arg Pro
    130                 135                 140

Lys Gly Arg Gly Lys Arg Arg Arg Glu Lys Gln Arg Pro Thr Asp Cys
145                 150                 155                 160

His Leu Cys Gly Asp Ala Val Pro Arg Arg
                165                 170


<210>  254
<211>  241
<212>  PRT
<213>  Homo sapiens

<400>  254

Met Ser Met Leu Phe Tyr Thr Leu Ile Thr Ala Phe Leu Ile Gly Ile
1               5                   10                  15

Gln Ala Glu Pro His Ser Glu Ser Asn Val Pro Ala Gly His Thr Ile
            20                  25                  30

Pro Gln Ala His Trp Thr Lys Leu Gln His Ser Leu Asp Thr Ala Leu
        35                  40                  45

Arg Arg Ala Arg Ser Ala Pro Ala Ala Ala Ile Ala Ala Arg Val Ala
    50                  55                  60

Gly Gln Thr Arg Asn Ile Thr Val Asp Pro Arg Leu Phe Lys Lys Arg
65                  70                  75                  80

Arg Leu Arg Ser Pro Arg Val Leu Phe Ser Thr Gln Pro Pro Arg Glu
                85                  90                  95

Ala Ala Asp Thr Gln Asp Leu Asp Phe Glu Val Gly Gly Ala Ala Pro
            100                 105                 110

Phe Asn Arg Thr His Arg Ser Lys Arg Ser Ser Ser His Pro Ile Phe
        115                 120                 125

His Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly
```

130 135 140

Asp Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu
145 150 155 160

Gly Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu
165 170 175

Thr Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile
180 185 190

Asp Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val
195 200 205

Lys Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg
210 215 220

Ile Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg
225 230 235 240

Ala

<210> 255
<211> 257
<212> PRT
<213> Homo sapiens

<400> 255

Met Ser Ile Leu Phe Tyr Val Ile Phe Leu Ala Tyr Leu Arg Gly Ile
1 5 10 15

Gln Gly Asn Asn Met Asp Gln Arg Ser Leu Pro Glu Asp Ser Leu Asn
20 25 30

Ser Leu Ile Ile Lys Leu Ile Gln Ala Asp Ile Leu Lys Asn Lys Leu
35 40 45

Ser Lys Gln Met Val Asp Val Lys Glu Asn Tyr Gln Ser Thr Leu Pro
50 55 60

Lys Ala Glu Ala Pro Arg Glu Pro Glu Arg Gly Gly Pro Ala Lys Ser
65 70 75 80

Ala Phe Gln Pro Val Ile Ala Met Asp Thr Glu Leu Leu Arg Gln Gln
85 90 95

Arg Arg Tyr Asn Ser Pro Arg Val Leu Leu Ser Asp Ser Thr Pro Leu
100 105 110

Glu Pro Pro Pro Leu Tyr Leu Met Glu Asp Tyr Val Gly Ser Pro Val
115 120 125

```
Val Ala Asn Arg Thr Ser Arg Arg Lys Arg Tyr Ala Glu His Lys Ser
    130                 135                 140

His Arg Gly Glu Tyr Ser Val Cys Asp Ser Glu Ser Leu Trp Val Thr
145                 150                 155                 160

Asp Lys Ser Ser Ala Ile Asp Ile Arg Gly His Gln Val Thr Val Leu
                165                 170                 175

Gly Glu Ile Lys Thr Gly Asn Ser Pro Val Lys Gln Tyr Phe Tyr Glu
            180                 185                 190

Thr Arg Cys Lys Glu Ala Arg Pro Val Lys Asn Gly Cys Arg Gly Ile
        195                 200                 205

Asp Asp Lys His Trp Asn Ser Gln Cys Lys Thr Ser Gln Thr Tyr Val
    210                 215                 220

Arg Ala Leu Thr Ser Glu Asn Asn Lys Leu Val Gly Trp Arg Trp Ile
225                 230                 235                 240

Arg Ile Asp Thr Ser Cys Val Cys Ala Leu Ser Arg Lys Ile Gly Arg
                245                 250                 255

Thr
```

<210> 256
<211> 210
<212> PRT
<213> Homo sapiens

<400> 256

```
Met Leu Pro Leu Pro Ser Cys Ser Leu Pro Ile Leu Leu Leu Phe Leu
1               5                   10                  15

Leu Pro Ser Val Pro Ile Glu Ser Gln Pro Pro Pro Ser Thr Leu Pro
            20                  25                  30

Pro Phe Leu Ala Pro Glu Trp Asp Leu Leu Ser Pro Arg Val Val Leu
        35                  40                  45

Ser Arg Gly Ala Pro Ala Gly Pro Pro Leu Leu Phe Leu Leu Glu Ala
    50                  55                  60

Gly Ala Phe Arg Glu Ser Ala Gly Ala Pro Ala Asn Arg Ser Arg Arg
65                  70                  75                  80

Gly Val Ser Glu Thr Ala Pro Ala Ser Arg Arg Gly Glu Leu Ala Val
                85                  90                  95
```

```
Cys Asp Ala Val Ser Gly Trp Val Thr Asp Arg Arg Thr Ala Val Asp
            100                 105                 110

Leu Arg Gly Arg Glu Val Glu Val Leu Gly Glu Val Pro Ala Ala Gly
        115                 120                 125

Gly Ser Pro Leu Arg Gln Tyr Phe Phe Glu Thr Arg Cys Lys Ala Asp
    130                 135                 140

Asn Ala Glu Glu Gly Gly Pro Gly Ala Gly Gly Gly Gly Cys Arg Gly
145                 150                 155                 160

Val Asp Arg Arg His Trp Val Ser Glu Cys Lys Ala Lys Gln Ser Tyr
                165                 170                 175

Val Arg Ala Leu Thr Ala Asp Ala Gln Gly Arg Val Gly Trp Arg Trp
            180                 185                 190

Ile Arg Ile Asp Thr Ala Cys Val Cys Thr Leu Leu Ser Arg Thr Gly
        195                 200                 205

Arg Ala
    210
```

<210> 257
<211> 211
<212> PRT
<213> Homo sapiens

<400> 257

```
Met Arg Thr Leu Ala Cys Leu Leu Leu Leu Gly Cys Gly Tyr Leu Ala
1               5                   10                  15

His Val Leu Ala Glu Glu Ala Glu Ile Pro Arg Glu Val Ile Glu Arg
            20                  25                  30

Leu Ala Arg Ser Gln Ile His Ser Ile Arg Asp Leu Gln Arg Leu Leu
        35                  40                  45

Glu Ile Asp Ser Val Gly Ser Glu Asp Ser Leu Asp Thr Ser Leu Arg
    50                  55                  60

Ala His Gly Val His Ala Thr Lys His Val Pro Glu Lys Arg Pro Leu
65                  70                  75                  80

Pro Ile Arg Arg Lys Arg Ser Ile Glu Glu Ala Val Pro Ala Val Cys
                85                  90                  95

Lys Thr Arg Thr Val Ile Tyr Glu Ile Pro Arg Ser Gln Val Asp Pro
            100                 105                 110
```

```
Thr Ser Ala Asn Phe Leu Ile Trp Pro Pro Cys Val Glu Val Lys Arg
        115                 120                 125

Cys Thr Gly Cys Cys Asn Thr Ser Ser Val Lys Cys Gln Pro Ser Arg
    130                 135                 140

Val His His Arg Ser Val Lys Val Ala Lys Val Glu Tyr Val Arg Lys
145                 150                 155                 160

Lys Pro Lys Leu Lys Glu Val Gln Val Arg Leu Glu Glu His Leu Glu
                165                 170                 175

Cys Ala Cys Ala Thr Thr Ser Leu Asn Pro Asp Tyr Arg Glu Glu Asp
            180                 185                 190

Thr Gly Arg Pro Arg Glu Ser Gly Lys Lys Arg Lys Arg Lys Arg Leu
        195                 200                 205

Lys Pro Thr
    210
```

<210> 258
<211> 241
<212> PRT
<213> Homo sapiens

<400> 258

```
Met Asn Arg Cys Trp Ala Leu Phe Leu Ser Leu Cys Cys Tyr Leu Arg
1               5                   10                  15

Leu Val Ser Ala Glu Gly Asp Pro Ile Pro Glu Glu Leu Tyr Glu Met
            20                  25                  30

Leu Ser Asp His Ser Ile Arg Ser Phe Asp Asp Leu Gln Arg Leu Leu
        35                  40                  45

His Gly Asp Pro Gly Glu Glu Asp Gly Ala Glu Leu Asp Leu Asn Met
    50                  55                  60

Thr Arg Ser His Ser Gly Gly Glu Leu Glu Ser Leu Ala Arg Gly Arg
65                  70                  75                  80

Arg Ser Leu Gly Ser Leu Thr Ile Ala Glu Pro Ala Met Ile Ala Glu
                85                  90                  95

Cys Lys Thr Arg Thr Glu Val Phe Glu Ile Ser Arg Arg Leu Ile Asp
            100                 105                 110

Arg Thr Asn Ala Asn Phe Leu Val Trp Pro Pro Cys Val Glu Val Gln
        115                 120                 125

Arg Cys Ser Gly Cys Cys Asn Asn Arg Asn Val Gln Cys Arg Pro Thr
```

130 135 140

Gln Val Gln Leu Arg Pro Val Gln Val Arg Lys Ile Glu Ile Val Arg
145 150 155 160

Lys Lys Pro Ile Phe Lys Lys Ala Thr Val Thr Leu Glu Asp His Leu
165 170 175

Ala Cys Lys Cys Glu Thr Val Ala Ala Ala Arg Pro Val Thr Arg Ser
180 185 190

Pro Gly Gly Ser Gln Glu Gln Arg Ala Lys Thr Pro Gln Thr Arg Val
195 200 205

Thr Ile Arg Thr Val Arg Val Arg Arg Pro Pro Lys Gly Lys His Arg
210 215 220

Lys Phe Lys His Thr His Asp Lys Thr Ala Leu Lys Glu Thr Leu Gly
225 230 235 240

Ala

<210> 259
<211> 89
<212> PRT
<213> Homo sapiens

<400> 259

Met Asn Ala Lys Val Val Val Val Leu Val Leu Val Leu Thr Ala Leu
1 5 10 15

Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys
20 25 30

Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys
35 40 45

Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys
50 55 60

Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln
65 70 75 80

Glu Tyr Leu Glu Lys Ala Leu Asn Lys
85

<210> 260
<211> 93
<212> PRT
<213> Homo sapiens

<400> 260

```
Met Asn Ala Lys Val Val Val Val Leu Val Leu Val Leu Thr Ala Leu
1               5                   10                  15


Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys
            20                  25                  30


Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys
        35                  40                  45


Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys
    50                  55                  60


Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln
65                  70                  75                  80


Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met
                85                  90


<210>  261
<211>  94
<212>  PRT
<213>  Homo sapiens

<400>  261

Met Ala Pro Leu Lys Met Leu Ala Leu Val Thr Leu Leu Leu Gly Ala
1               5                   10                  15


Ser Leu Gln His Ile His Ala Ala Arg Gly Thr Asn Val Gly Arg Glu
            20                  25                  30


Cys Cys Leu Glu Tyr Phe Lys Gly Ala Ile Pro Leu Arg Lys Leu Lys
        35                  40                  45


Thr Trp Tyr Gln Thr Ser Glu Asp Cys Ser Arg Asp Ala Ile Val Phe
    50                  55                  60


Val Thr Val Gln Gly Arg Ala Ile Cys Ser Asp Pro Asn Asn Lys Arg
65                  70                  75                  80


Val Lys Asn Ala Val Lys Tyr Leu Gln Ser Leu Glu Arg Ser
                85                  90


<210>  262
<211>  227
<212>  PRT
<213>  Homo sapiens

<400>  262

Met Asn Ile Lys Gly Ser Pro Trp Lys Gly Ser Leu Leu Leu Leu Leu
1               5                   10                  15


Val Ser Asn Leu Leu Leu Cys Gln Ser Val Ala Pro Leu Pro Ile Cys
```

20 25 30

Pro Gly Gly Ala Ala Arg Cys Gln Val Thr Leu Arg Asp Leu Phe Asp
35 40 45

Arg Ala Val Val Leu Ser His Tyr Ile His Asn Leu Ser Ser Glu Met
50 55 60

Phe Ser Glu Phe Asp Lys Arg Tyr Thr His Gly Arg Gly Phe Ile Thr
65 70 75 80

Lys Ala Ile Asn Ser Cys His Thr Ser Ser Leu Ala Thr Pro Glu Asp
85 90 95

Lys Glu Gln Ala Gln Gln Met Asn Gln Lys Asp Phe Leu Ser Leu Ile
100 105 110

Val Ser Ile Leu Arg Ser Trp Asn Glu Pro Leu Tyr His Leu Val Thr
115 120 125

Glu Val Arg Gly Met Gln Glu Ala Pro Glu Ala Ile Leu Ser Lys Ala
130 135 140

Val Glu Ile Glu Glu Gln Thr Lys Arg Leu Leu Glu Gly Met Glu Leu
145 150 155 160

Ile Val Ser Gln Val His Pro Glu Thr Lys Glu Asn Glu Ile Tyr Pro
165 170 175

Val Trp Ser Gly Leu Pro Ser Leu Gln Met Ala Asp Glu Glu Ser Arg
180 185 190

Leu Ser Ala Tyr Tyr Asn Leu Leu His Cys Leu Arg Arg Asp Ser His
195 200 205

Lys Ile Asp Asn Tyr Leu Lys Leu Leu Lys Cys Arg Ile Ile His Asn
210 215 220

Asn Asn Cys
225

<210> 263
<211> 116
<212> PRT
<213> Homo sapiens

<400> 263

Met Asp Tyr Tyr Arg Lys Tyr Ala Ala Ile Phe Leu Val Thr Leu Ser
1 5 10 15

Val Phe Leu His Val Leu His Ser Ala Pro Asp Val Gln Asp Cys Pro
20 25 30

```
Glu Cys Thr Leu Gln Glu Asn Pro Phe Phe Ser Gln Pro Gly Ala Pro
        35                  40                  45

Ile Leu Gln Cys Met Gly Cys Cys Phe Ser Arg Ala Tyr Pro Thr Pro
    50                  55                  60

Leu Arg Ser Lys Lys Thr Met Leu Val Gln Lys Asn Val Thr Ser Glu
65                  70                  75                  80

Ser Thr Cys Cys Val Ala Lys Ser Tyr Asn Arg Val Thr Val Met Gly
                85                  90                  95

Gly Phe Lys Val Glu Asn His Thr Ala Cys His Cys Ser Thr Cys Tyr
            100                 105                 110

Tyr His Lys Ser
        115


<210>  264
<211>  129
<212>  PRT
<213>  Homo sapiens

<400>  264

Met Lys Thr Leu Gln Phe Phe Phe Leu Phe Cys Cys Trp Lys Ala Ile
1               5                   10                  15

Cys Cys Asn Ser Cys Glu Leu Thr Asn Ile Thr Ile Ala Ile Glu Lys
            20                  25                  30

Glu Glu Cys Arg Phe Cys Ile Ser Ile Asn Thr Thr Trp Cys Ala Gly
        35                  40                  45

Tyr Cys Tyr Thr Arg Asp Leu Val Tyr Lys Asp Pro Ala Arg Pro Lys
    50                  55                  60

Ile Gln Lys Thr Cys Thr Phe Lys Glu Leu Val Tyr Glu Thr Val Arg
65                  70                  75                  80

Val Pro Gly Cys Ala His His Ala Asp Ser Leu Tyr Thr Tyr Pro Val
                85                  90                  95

Ala Thr Gln Cys His Cys Gly Lys Cys Asp Ser Asp Ser Thr Asp Cys
            100                 105                 110

Thr Val Arg Gly Leu Gly Pro Ser Tyr Cys Ser Phe Gly Glu Met Lys
        115                 120                 125

Glu
```

<210> 265
<211> 125
<212> PRT
<213> Homo sapiens

<400> 265

Met Ala Gly Pro Ser Leu Ala Cys Cys Leu Leu Gly Leu Leu Ala Leu
1 5 10 15

Thr Ser Ala Cys Tyr Ile Gln Asn Cys Pro Leu Gly Gly Lys Arg Ala
20 25 30

Ala Pro Asp Leu Asp Val Arg Lys Cys Leu Pro Cys Gly Pro Gly Gly
35 40 45

Lys Gly Arg Cys Phe Gly Pro Asn Ile Cys Cys Ala Glu Glu Leu Gly
50 55 60

Cys Phe Val Gly Thr Ala Glu Ala Leu Arg Cys Gln Glu Glu Asn Tyr
65 70 75 80

Leu Pro Ser Pro Cys Gln Ser Gly Gln Lys Ala Cys Gly Ser Gly Gly
85 90 95

Arg Cys Ala Val Leu Gly Leu Cys Cys Ser Pro Asp Gly Cys His Ala
100 105 110

Asp Pro Ala Cys Asp Ala Glu Ala Thr Phe Ser Gln Arg
115 120 125

<210> 266
<211> 164
<212> PRT
<213> Homo sapiens

<400> 266

Met Pro Asp Thr Met Leu Pro Ala Cys Phe Leu Gly Leu Leu Ala Phe
1 5 10 15

Ser Ser Ala Cys Tyr Phe Gln Asn Cys Pro Arg Gly Gly Lys Arg Ala
20 25 30

Met Ser Asp Leu Glu Leu Arg Gln Cys Leu Pro Cys Gly Pro Gly Gly
35 40 45

Lys Gly Arg Cys Phe Gly Pro Ser Ile Cys Cys Ala Asp Glu Leu Gly
50 55 60

Cys Phe Val Gly Thr Ala Glu Ala Leu Arg Cys Gln Glu Glu Asn Tyr
65 70 75 80

Leu Pro Ser Pro Cys Gln Ser Gly Gln Lys Ala Cys Gly Ser Gly Gly

85 90 95

Arg Cys Ala Ala Phe Gly Val Cys Cys Asn Asp Glu Ser Cys Val Thr
100 105 110

Glu Pro Glu Cys Arg Glu Gly Phe His Arg Arg Ala Arg Ala Ser Asp
115 120 125

Arg Ser Asn Ala Thr Gln Leu Asp Gly Pro Ala Gly Ala Leu Leu Leu
130 135 140

Arg Leu Val Gln Leu Ala Gly Ala Pro Glu Pro Phe Glu Pro Ala Gln
145 150 155 160

Pro Asp Ala Tyr

<210> 267
<211> 269
<212> PRT
<213> Homo sapiens

<400> 267

Met Ala Glu Val Pro Glu Leu Ala Ser Glu Met Met Ala Tyr Tyr Ser
1 5 10 15

Gly Asn Glu Asp Asp Leu Phe Phe Glu Ala Asp Gly Pro Lys Gln Met
20 25 30

Lys Cys Ser Phe Gln Asp Leu Asp Leu Cys Pro Leu Asp Gly Gly Ile
35 40 45

Gln Leu Arg Ile Ser Asp His His Tyr Ser Lys Gly Phe Arg Gln Ala
50 55 60

Ala Ser Val Val Val Ala Met Asp Lys Leu Arg Lys Met Leu Val Pro
65 70 75 80

Cys Pro Gln Thr Phe Gln Glu Asn Asp Leu Ser Thr Phe Phe Pro Phe
85 90 95

Ile Phe Glu Glu Glu Pro Ile Phe Phe Asp Thr Trp Asp Asn Glu Ala
100 105 110

Tyr Val His Asp Ala Pro Val Arg Ser Leu Asn Cys Thr Leu Arg Asp
115 120 125

Ser Gln Gln Lys Ser Leu Val Met Ser Gly Pro Tyr Glu Leu Lys Ala
130 135 140

Leu His Leu Gln Gly Gln Asp Met Glu Gln Gln Val Val Phe Ser Met
145 150 155 160

```
Ser Phe Val Gln Gly Glu Glu Ser Asn Asp Lys Ile Pro Val Ala Leu
                165                 170                 175

Gly Leu Lys Glu Lys Asn Leu Tyr Leu Ser Cys Val Leu Lys Asp Asp
            180                 185                 190

Lys Pro Thr Leu Gln Leu Glu Ser Val Asp Pro Lys Asn Tyr Pro Lys
        195                 200                 205

Lys Lys Met Glu Lys Arg Phe Val Phe Asn Lys Ile Glu Ile Asn Asn
    210                 215                 220

Lys Leu Glu Phe Glu Ser Ala Gln Phe Pro Asn Trp Tyr Ile Ser Thr
225                 230                 235                 240

Ser Gln Ala Glu Asn Met Pro Val Phe Leu Gly Gly Thr Lys Gly Gly
                245                 250                 255

Gln Asp Ile Thr Asp Phe Thr Met Gln Phe Val Ser Ser
            260                 265


<210>  268
<211>  153
<212>  PRT
<213>  Homo sapiens

<400>  268

Met Gly Leu Thr Ser Gln Leu Leu Pro Pro Leu Phe Phe Leu Leu Ala
1               5                   10                  15

Cys Ala Gly Asn Phe Val His Gly His Lys Cys Asp Ile Thr Leu Gln
            20                  25                  30

Glu Ile Ile Lys Thr Leu Asn Ser Leu Thr Glu Gln Lys Thr Leu Cys
        35                  40                  45

Thr Glu Leu Thr Val Thr Asp Ile Phe Ala Ala Ser Lys Asn Thr Thr
    50                  55                  60

Glu Lys Glu Thr Phe Cys Arg Ala Ala Thr Val Leu Arg Gln Phe Tyr
65                  70                  75                  80

Ser His His Glu Lys Asp Thr Arg Cys Leu Gly Ala Thr Ala Gln Gln
                85                  90                  95

Phe His Arg His Lys Gln Leu Ile Arg Phe Leu Lys Arg Leu Asp Arg
            100                 105                 110

Asn Leu Trp Gly Leu Ala Gly Leu Asn Ser Cys Pro Val Lys Glu Ala
        115                 120                 125
```

```
Asn Gln Ser Thr Leu Glu Asn Phe Leu Glu Arg Leu Lys Thr Ile Met
    130                 135                 140

Arg Glu Lys Tyr Ser Lys Cys Ser Ser
145                 150
```

<210> 269
<211> 271
<212> PRT
<213> Homo sapiens

<400> 269

```
Met Ala Lys Val Pro Asp Met Phe Glu Asp Leu Lys Asn Cys Tyr Ser
1               5                   10                  15

Glu Asn Glu Glu Asp Ser Ser Ser Ile Asp His Leu Ser Leu Asn Gln
            20                  25                  30

Lys Ser Phe Tyr His Val Ser Tyr Gly Pro Leu His Glu Gly Cys Met
        35                  40                  45

Asp Gln Ser Val Ser Leu Ser Ile Ser Glu Thr Ser Lys Thr Ser Lys
    50                  55                  60

Leu Thr Phe Lys Glu Ser Met Val Val Val Ala Thr Asn Gly Lys Val
65                  70                  75                  80

Leu Lys Lys Arg Arg Leu Ser Leu Ser Gln Ser Ile Thr Asp Asp Asp
                85                  90                  95

Leu Glu Ala Ile Ala Asn Asp Ser Glu Glu Glu Ile Ile Lys Pro Arg
            100                 105                 110

Ser Ala Pro Phe Ser Phe Leu Ser Asn Val Lys Tyr Asn Phe Met Arg
        115                 120                 125

Ile Ile Lys Tyr Glu Phe Ile Leu Asn Asp Ala Leu Asn Gln Ser Ile
    130                 135                 140

Ile Arg Ala Asn Asp Gln Tyr Leu Thr Ala Ala Ala Leu His Asn Leu
145                 150                 155                 160

Asp Glu Ala Val Lys Phe Asp Met Gly Ala Tyr Lys Ser Ser Lys Asp
                165                 170                 175

Asp Ala Lys Ile Thr Val Ile Leu Arg Ile Ser Lys Thr Gln Leu Tyr
            180                 185                 190

Val Thr Ala Gln Asp Glu Asp Gln Pro Val Leu Leu Lys Glu Met Pro
        195                 200                 205
```

```
Glu Ile Pro Lys Thr Ile Thr Gly Ser Glu Thr Asn Leu Leu Phe Phe
    210                 215                 220


Trp Glu Thr His Gly Thr Lys Asn Tyr Phe Thr Ser Val Ala His Pro
225                 230                 235                 240


Asn Leu Phe Ile Ala Thr Lys Gln Asp Tyr Trp Val Cys Leu Ala Gly
                245                 250                 255


Gly Pro Pro Ser Ile Thr Asp Phe Gln Ile Leu Glu Asn Gln Ala
            260                 265                 270


<210>  270
<211>  212
<212>  PRT
<213>  Homo sapiens

<400>  270

Met Asn Ser Phe Ser Thr Ser Ala Phe Gly Pro Val Ala Phe Ser Leu
1               5                   10                  15


Gly Leu Leu Leu Val Leu Pro Ala Ala Phe Pro Ala Pro Val Pro Pro
            20                  25                  30


Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr
        35                  40                  45


Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile
    50                  55                  60


Ser Ala Leu Arg Lys Glu Thr Cys Asn Lys Ser Asn Met Cys Glu Ser
65                  70                  75                  80


Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala
                85                  90                  95


Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu
            100                 105                 110


Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr
        115                 120                 125


Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln
    130                 135                 140


Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn
145                 150                 155                 160


Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu
                165                 170                 175


Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His
```

180 185 190

Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala
195 200 205

Leu Arg Gln Met
210

<210> 271
<211> 146
<212> PRT
<213> Homo sapiens

<400> 271

Met His Pro Leu Leu Asn Pro Leu Leu Leu Ala Leu Gly Leu Met Ala
1 5 10 15

Leu Leu Leu Thr Thr Val Ile Ala Leu Thr Cys Leu Gly Gly Phe Ala
20 25 30

Ser Pro Gly Pro Val Pro Pro Ser Thr Ala Leu Arg Glu Leu Ile Glu
35 40 45

Glu Leu Val Asn Ile Thr Gln Asn Gln Lys Ala Pro Leu Cys Asn Gly
50 55 60

Ser Met Val Trp Ser Ile Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala
65 70 75 80

Leu Glu Ser Leu Ile Asn Val Ser Gly Cys Ser Ala Ile Glu Lys Thr
85 90 95

Gln Arg Met Leu Ser Gly Phe Cys Pro His Lys Val Ser Ala Gly Gln
100 105 110

Phe Ser Ser Leu His Val Arg Asp Thr Lys Ile Glu Val Ala Gln Phe
115 120 125

Val Lys Asp Leu Leu Leu His Leu Lys Lys Leu Phe Arg Glu Gly Arg
130 135 140

Phe Asn
145

<210> 272
<211> 178
<212> PRT
<213> Homo sapiens

<400> 272

Met His Ser Ser Ala Leu Leu Cys Cys Leu Val Leu Leu Thr Gly Val
1 5 10 15

```
Arg Ala Ser Pro Gly Gln Gly Thr Gln Ser Glu Asn Ser Cys Thr His
            20                  25                  30

Phe Pro Gly Asn Leu Pro Asn Met Leu Arg Asp Leu Arg Asp Ala Phe
        35                  40                  45

Ser Arg Val Lys Thr Phe Phe Gln Met Lys Asp Gln Leu Asp Asn Leu
    50                  55                  60

Leu Leu Lys Glu Ser Leu Leu Glu Asp Phe Lys Gly Tyr Leu Gly Cys
65                  70                  75                  80

Gln Ala Leu Ser Glu Met Ile Gln Phe Tyr Leu Glu Glu Val Met Pro
                85                  90                  95

Gln Ala Glu Asn Gln Asp Pro Asp Ile Lys Ala His Val Asn Ser Leu
            100                 105                 110

Gly Glu Asn Leu Lys Thr Leu Arg Leu Arg Leu Arg Arg Cys His Arg
        115                 120                 125

Phe Leu Pro Cys Glu Asn Lys Ser Lys Ala Val Glu Gln Val Lys Asn
    130                 135                 140

Ala Phe Asn Lys Leu Gln Glu Lys Gly Ile Tyr Lys Ala Met Ser Glu
145                 150                 155                 160

Phe Asp Ile Phe Ile Asn Tyr Ile Glu Ala Tyr Met Thr Met Lys Ile
                165                 170                 175

Arg Asn
```

<210> 273
<211> 160
<212> PRT
<213> Homo sapiens

<400> 273

```
Ser Pro Gly Gln Gly Thr Gln Ser Glu Asn Ser Cys Thr His Phe Pro
1               5                   10                  15

Gly Asn Leu Pro Asn Met Leu Arg Asp Leu Arg Asp Ala Phe Ser Arg
            20                  25                  30

Val Lys Thr Phe Phe Gln Met Lys Asp Gln Leu Asp Asn Leu Leu Leu
        35                  40                  45

Lys Glu Ser Leu Leu Glu Asp Phe Lys Gly Tyr Leu Gly Cys Gln Ala
    50                  55                  60
```

Leu Ser Glu Met Ile Gln Phe Tyr Leu Glu Glu Val Met Pro Gln Ala
65 70 75 80

Glu Asn Gln Asp Pro Asp Ile Lys Ala His Val Asn Ser Leu Gly Glu
85 90 95

Asn Leu Lys Thr Leu Arg Leu Arg Leu Arg Arg Cys His Arg Phe Leu
100 105 110

Pro Cys Glu Asn Lys Ser Lys Ala Val Glu Gln Val Lys Asn Ala Phe
115 120 125

Asn Lys Leu Gln Glu Lys Gly Ile Tyr Lys Ala Met Ser Glu Phe Asp
130 135 140

Ile Phe Ile Asn Tyr Ile Glu Ala Tyr Met Thr Met Lys Ile Arg Asn
145 150 155 160

<210> 274
<211> 269
<212> PRT
<213> Homo sapiens

<400> 274

Met Ala Glu Val Pro Glu Leu Ala Ser Glu Met Met Ala Tyr Tyr Ser
1 5 10 15

Gly Asn Glu Asp Asp Leu Phe Phe Glu Ala Asp Gly Pro Lys Gln Met
20 25 30

Lys Cys Ser Phe Gln Asp Leu Asp Leu Cys Pro Leu Asp Gly Gly Ile
35 40 45

Gln Leu Arg Ile Ser Asp His His Tyr Ser Lys Gly Phe Arg Gln Ala
50 55 60

Ala Ser Val Val Val Ala Met Asp Lys Leu Arg Lys Met Leu Val Pro
65 70 75 80

Cys Pro Gln Thr Phe Gln Glu Asn Asp Leu Ser Thr Phe Phe Pro Phe
85 90 95

Ile Phe Glu Glu Glu Pro Ile Phe Phe Asp Thr Trp Asp Asn Glu Ala
100 105 110

Tyr Val His Asp Ala Pro Val Arg Ser Leu Asn Cys Thr Leu Arg Asp
115 120 125

Ser Gln Gln Lys Ser Leu Val Met Ser Gly Pro Tyr Glu Leu Lys Ala
130 135 140

Leu His Leu Gln Gly Gln Asp Met Glu Gln Gln Val Val Phe Ser Met

145 150 155 160

Ser Phe Val Gln Gly Glu Glu Ser Asn Asp Lys Ile Pro Val Ala Leu
165 170 175

Gly Leu Lys Glu Lys Asn Leu Tyr Leu Ser Cys Val Leu Lys Asp Asp
180 185 190

Lys Pro Thr Leu Gln Leu Glu Ser Val Asp Pro Lys Asn Tyr Pro Lys
195 200 205

Lys Lys Met Glu Lys Arg Phe Val Phe Asn Lys Ile Glu Ile Asn Asn
210 215 220

Lys Leu Glu Phe Glu Ser Ala Gln Phe Pro Asn Trp Tyr Ile Ser Thr
225 230 235 240

Ser Gln Ala Glu Asn Met Pro Val Phe Leu Gly Gly Thr Lys Gly Gly
245 250 255

Gln Asp Ile Thr Asp Phe Thr Met Gln Phe Val Ser Ser
260 265

<210> 275
<211> 350
<212> PRT
<213> Homo sapiens

<400> 275

Met Ser Asn Ile Thr Asp Pro Gln Met Trp Asp Phe Asp Asp Leu Asn
1 5 10 15

Phe Thr Gly Met Pro Pro Ala Asp Glu Asp Tyr Ser Pro Cys Met Leu
20 25 30

Glu Thr Glu Thr Leu Asn Lys Tyr Val Val Ile Ile Ala Tyr Ala Leu
35 40 45

Val Phe Leu Leu Ser Leu Leu Gly Asn Ser Leu Val Met Leu Val Ile
50 55 60

Leu Tyr Ser Arg Val Gly Arg Ser Val Thr Asp Val Tyr Leu Leu Asn
65 70 75 80

Leu Ala Leu Ala Asp Leu Leu Phe Ala Leu Thr Leu Pro Ile Trp Ala
85 90 95

Ala Ser Lys Val Asn Gly Trp Ile Phe Gly Thr Phe Leu Cys Lys Val
100 105 110

Val Ser Leu Leu Lys Glu Val Asn Phe Tyr Ser Gly Ile Leu Leu Leu
115 120 125

```
Ala Cys Ile Ser Val Asp Arg Tyr Leu Ala Ile Val His Ala Thr Arg
    130                 135                 140

Thr Leu Thr Gln Lys Arg His Leu Val Lys Phe Val Cys Leu Gly Cys
145                 150                 155                 160

Trp Gly Leu Ser Met Asn Leu Ser Leu Pro Phe Phe Leu Phe Arg Gln
                165                 170                 175

Ala Tyr His Pro Asn Asn Ser Ser Pro Val Cys Tyr Glu Val Leu Gly
            180                 185                 190

Asn Asp Thr Ala Lys Trp Arg Met Val Leu Arg Ile Leu Pro His Thr
        195                 200                 205

Phe Gly Phe Ile Val Pro Leu Phe Val Met Leu Phe Cys Tyr Gly Phe
    210                 215                 220

Thr Leu Arg Thr Leu Phe Lys Ala His Met Gly Gln Lys His Arg Ala
225                 230                 235                 240

Met Arg Val Ile Phe Ala Val Val Leu Ile Phe Leu Leu Cys Trp Leu
                245                 250                 255

Pro Tyr Asn Leu Val Leu Leu Ala Asp Thr Leu Met Arg Thr Gln Val
            260                 265                 270

Ile Gln Glu Thr Cys Glu Arg Arg Asn Asn Ile Gly Arg Ala Leu Asp
        275                 280                 285

Ala Thr Glu Ile Leu Gly Phe Leu His Ser Cys Leu Asn Pro Ile Ile
    290                 295                 300

Tyr Ala Phe Ile Gly Gln Asn Phe Arg His Gly Phe Leu Lys Ile Leu
305                 310                 315                 320

Ala Met His Gly Leu Val Ser Lys Glu Phe Leu Ala Arg His Arg Val
                325                 330                 335

Thr Ser Tyr Thr Ser Ser Ser Val Asn Val Ser Ser Asn Leu
            340                 345                 350


<210>  276
<211>  177
<212>  PRT
<213>  Homo sapiens

<400>  276

Met Phe His Val Ser Phe Arg Tyr Ile Phe Gly Leu Pro Pro Leu Ile
1               5                   10                  15
```

```
Leu Val Leu Leu Pro Val Ala Ser Ser Asp Cys Asp Ile Glu Gly Lys
            20                  25                  30

Asp Gly Lys Gln Tyr Glu Ser Val Leu Met Val Ser Ile Asp Gln Leu
        35                  40                  45

Leu Asp Ser Met Lys Glu Ile Gly Ser Asn Cys Leu Asn Asn Glu Phe
    50                  55                  60

Asn Phe Phe Lys Arg His Ile Cys Asp Ala Asn Lys Glu Gly Met Phe
65                  70                  75                  80

Leu Phe Arg Ala Ala Arg Lys Leu Arg Gln Phe Leu Lys Met Asn Ser
                85                  90                  95

Thr Gly Asp Phe Asp Leu His Leu Leu Lys Val Ser Glu Gly Thr Thr
            100                 105                 110

Ile Leu Leu Asn Cys Thr Gly Gln Val Lys Gly Arg Lys Pro Ala Ala
        115                 120                 125

Leu Gly Glu Ala Gln Pro Thr Lys Ser Leu Glu Glu Asn Lys Ser Leu
    130                 135                 140

Lys Glu Gln Lys Lys Leu Asn Asp Leu Cys Phe Leu Lys Arg Leu Leu
145                 150                 155                 160

Gln Glu Ile Lys Thr Cys Trp Asn Lys Ile Leu Met Gly Thr Lys Glu
                165                 170                 175

His
```

<210> 277
<211> 328
<212> PRT
<213> Homo sapiens

<400> 277

```
Met Cys His Gln Gln Leu Val Ile Ser Trp Phe Ser Leu Val Phe Leu
1               5                   10                  15

Ala Ser Pro Leu Val Ala Ile Trp Glu Leu Lys Lys Asp Val Tyr Val
            20                  25                  30

Val Glu Leu Asp Trp Tyr Pro Asp Ala Pro Gly Glu Met Val Val Leu
        35                  40                  45

Thr Cys Asp Thr Pro Glu Glu Asp Gly Ile Thr Trp Thr Leu Asp Gln
    50                  55                  60
```

```
Ser Ser Glu Val Leu Gly Ser Gly Lys Thr Leu Thr Ile Gln Val Lys
65                  70                  75                  80

Glu Phe Gly Asp Ala Gly Gln Tyr Thr Cys His Lys Gly Gly Glu Val
                85                  90                  95

Leu Ser His Ser Leu Leu Leu Leu His Lys Lys Glu Asp Gly Ile Trp
            100                 105                 110

Ser Thr Asp Ile Leu Lys Asp Gln Lys Glu Pro Lys Asn Lys Thr Phe
        115                 120                 125

Leu Arg Cys Glu Ala Lys Asn Tyr Ser Gly Arg Phe Thr Cys Trp Trp
    130                 135                 140

Leu Thr Thr Ile Ser Thr Asp Leu Thr Phe Ser Val Lys Ser Ser Arg
145                 150                 155                 160

Gly Ser Ser Asp Pro Gln Gly Val Thr Cys Gly Ala Ala Thr Leu Ser
                165                 170                 175

Ala Glu Arg Val Arg Gly Asp Asn Lys Glu Tyr Glu Tyr Ser Val Glu
            180                 185                 190

Cys Gln Glu Asp Ser Ala Cys Pro Ala Ala Glu Glu Ser Leu Pro Ile
        195                 200                 205

Glu Val Met Val Asp Ala Val His Lys Leu Lys Tyr Glu Asn Tyr Thr
    210                 215                 220

Ser Ser Phe Phe Ile Arg Asp Ile Ile Lys Pro Asp Pro Pro Lys Asn
225                 230                 235                 240

Leu Gln Leu Lys Pro Leu Lys Asn Ser Arg Gln Val Glu Val Ser Trp
                245                 250                 255

Glu Tyr Pro Asp Thr Trp Ser Thr Pro His Ser Tyr Phe Ser Leu Thr
            260                 265                 270

Phe Cys Val Gln Val Gln Gly Lys Ser Lys Arg Glu Lys Lys Asp Arg
        275                 280                 285

Val Phe Thr Asp Lys Thr Ser Ala Thr Val Ile Cys Arg Lys Asn Ala
    290                 295                 300

Ser Ile Ser Val Arg Ala Gln Asp Arg Tyr Tyr Ser Ser Ser Trp Ser
305                 310                 315                 320

Glu Trp Ala Ser Val Pro Cys Ser
                325
```

<210> 278
<211> 470
<212> PRT
<213> Homo sapiens

<400> 278

```
Met Gly Lys Pro Trp Leu Arg Ala Leu Gln Leu Leu Leu Leu Leu Gly
1               5                  10                  15

Ala Ser Trp Ala Arg Ala Gly Ala Pro Arg Cys Thr Tyr Thr Phe Val
            20                  25                  30

Leu Pro Pro Gln Lys Phe Thr Gly Ala Val Cys Trp Ser Gly Pro Ala
        35                  40                  45

Ser Thr Arg Ala Thr Pro Glu Ala Ala Asn Ala Ser Glu Leu Ala Ala
    50                  55                  60

Leu Arg Met Arg Val Gly Arg His Glu Glu Leu Leu Arg Glu Leu Gln
65                  70                  75                  80

Arg Leu Ala Ala Ala Asp Gly Ala Val Ala Gly Glu Val Arg Ala Leu
                85                  90                  95

Arg Lys Glu Ser Arg Gly Leu Ser Ala Arg Leu Gly Gln Leu Arg Ala
            100                 105                 110

Gln Leu Gln His Glu Ala Gly Pro Gly Ala Gly Pro Gly Ala Asp Leu
        115                 120                 125

Gly Ala Glu Pro Ala Ala Ala Leu Ala Leu Leu Gly Glu Arg Val Leu
    130                 135                 140

Asn Ala Ser Ala Glu Ala Gln Arg Ala Ala Ala Arg Phe His Gln Leu
145                 150                 155                 160

Asp Val Lys Phe Arg Glu Leu Ala Gln Leu Val Thr Gln Gln Ser Ser
                165                 170                 175

Leu Ile Ala Arg Leu Glu Arg Leu Cys Pro Gly Gly Ala Gly Gly Gln
            180                 185                 190

Gln Gln Val Leu Pro Pro Pro Pro Leu Val Pro Val Val Pro Val Arg
        195                 200                 205

Leu Val Gly Ser Thr Ser Asp Thr Ser Arg Met Leu Asp Pro Ala Pro
    210                 215                 220

Glu Pro Gln Arg Asp Gln Thr Gln Arg Gln Gln Glu Pro Met Ala Ser
225                 230                 235                 240

Pro Met Pro Ala Gly His Pro Ala Val Pro Thr Lys Pro Val Gly Pro
```

245 250 255

Trp Gln Asp Cys Ala Glu Ala Arg Gln Ala Gly His Glu Gln Ser Gly
260 265 270

Val Tyr Glu Leu Arg Val Gly Arg His Val Val Ser Val Trp Cys Glu
275 280 285

Gln Gln Leu Glu Gly Gly Gly Trp Thr Val Ile Gln Arg Arg Gln Asp
290 295 300

Gly Ser Val Asn Phe Phe Thr Thr Trp Gln His Tyr Lys Ala Gly Phe
305 310 315 320

Gly Arg Pro Asp Gly Glu Tyr Trp Leu Gly Leu Glu Pro Val Tyr Gln
325 330 335

Leu Thr Ser Arg Gly Asp His Glu Leu Leu Val Leu Leu Glu Asp Trp
340 345 350

Gly Gly Arg Gly Ala Arg Ala His Tyr Asp Gly Phe Ser Leu Glu Pro
355 360 365

Glu Ser Asp His Tyr Arg Leu Arg Leu Gly Gln Tyr His Gly Asp Ala
370 375 380

Gly Asp Ser Leu Ser Trp His Asn Asp Lys Pro Phe Ser Thr Val Asp
385 390 395 400

Arg Asp Arg Asp Ser Tyr Ser Gly Asn Cys Ala Leu Tyr Gln Arg Gly
405 410 415

Gly Trp Trp Tyr His Ala Cys Ala His Ser Asn Leu Asn Gly Val Trp
420 425 430

His His Gly Gly His Tyr Arg Ser Arg Tyr Gln Asp Gly Val Tyr Trp
435 440 445

Ala Glu Phe Arg Gly Gly Ala Tyr Ser Leu Arg Lys Ala Ala Met Leu
450 455 460

Ile Arg Pro Leu Lys Leu
465 470

<210> 279
<211> 144
<212> PRT
<213> Homo sapiens

<400> 279

Met Leu Leu Ala Met Val Leu Thr Ser Ala Leu Leu Leu Cys Ser Val
1 5 10 15

```
Ala Gly Gln Gly Cys Pro Thr Leu Ala Gly Ile Leu Asp Ile Asn Phe
            20                  25                  30

Leu Ile Asn Lys Met Gln Glu Asp Pro Ala Ser Lys Cys His Cys Ser
        35                  40                  45

Ala Asn Val Thr Ser Cys Leu Cys Leu Gly Ile Pro Ser Asp Asn Cys
    50                  55                  60

Thr Arg Pro Cys Phe Ser Glu Arg Leu Ser Gln Met Thr Asn Thr Thr
65                  70                  75                  80

Met Gln Thr Arg Tyr Pro Leu Ile Phe Ser Arg Val Lys Lys Ser Val
                85                  90                  95

Glu Val Leu Lys Asn Asn Lys Cys Pro Tyr Phe Ser Cys Glu Gln Pro
            100                 105                 110

Cys Asn Gln Thr Thr Ala Gly Asn Ala Leu Thr Phe Leu Lys Ser Leu
        115                 120                 125

Leu Glu Ile Phe Gln Lys Glu Lys Met Arg Gly Met Arg Gly Lys Ile
    130                 135                 140


<210>  280
<211>  152
<212>  PRT
<213>  Homo sapiens

<400>  280

Met Ser Arg Leu Pro Val Leu Leu Leu Leu Gln Leu Leu Val Arg Pro
1               5                   10                  15

Gly Leu Gln Ala Pro Met Thr Gln Thr Thr Pro Leu Lys Thr Ser Trp
            20                  25                  30

Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
        35                  40                  45

Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln
    50                  55                  60

Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe
65                  70                  75                  80

Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile
                85                  90                  95

Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr
            100                 105                 110
```

Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg
        115   120   125

Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
    130   135   140

Thr Thr Leu Ser Leu Ala Ile Phe
145   150

<210> 281
<211> 134
<212> PRT
<213> Homo sapiens

<400> 281

Met Arg Met Leu Leu His Leu Ser Leu Leu Ala Leu Gly Ala Ala Tyr
1   5   10   15

Val Tyr Ala Ile Pro Thr Glu Ile Pro Thr Ser Ala Leu Val Lys Glu
            20   25   30

Thr Leu Ala Leu Leu Ser Thr His Arg Thr Leu Leu Ile Ala Asn Glu
        35   40   45

Thr Leu Arg Ile Pro Val Pro Val His Lys Asn His Gln Leu Cys Thr
    50   55   60

Glu Glu Ile Phe Gln Gly Ile Gly Thr Leu Glu Ser Gln Thr Val Gln
65   70   75   80

Gly Gly Thr Val Glu Arg Leu Phe Lys Asn Leu Ser Leu Ile Lys Lys
                85   90   95

Tyr Ile Asp Gly Gln Lys Lys Lys Cys Gly Glu Glu Arg Arg Arg Val
            100   105   110

Asn Gln Phe Leu Asp Tyr Leu Gln Glu Phe Leu Gly Val Met Asn Thr
        115   120   125

Glu Trp Ile Ile Glu Ser
    130

<210> 282
<211> 1332
<212> PRT
<213> Homo sapiens

<400> 282

Met Glu Ser His Ser Arg Ala Gly Lys Ser Arg Lys Ser Ala Lys Phe
1   5   10   15

Arg Ser Ile Ser Arg Ser Leu Met Leu Cys Asn Ala Lys Thr Ser Asp

```
            20                  25                  30

Asp Gly Ser Ser Pro Asp Glu Lys Tyr Pro Asp Pro Phe Glu Ile Ser
        35                  40                  45

Leu Ala Gln Gly Lys Glu Gly Ile Phe His Ser Ser Val Gln Leu Ala
    50                  55                  60

Asp Thr Ser Glu Ala Gly Pro Ser Ser Val Pro Asp Leu Ala Leu Ala
65                  70                  75                  80

Ser Glu Ala Ala Gln Leu Gln Ala Ala Gly Asn Asp Arg Gly Lys Thr
                85                  90                  95

Cys Arg Arg Ile Phe Phe Met Lys Glu Ser Ser Thr Ala Ser Ser Arg
            100                 105                 110

Glu Lys Pro Gly Lys Leu Glu Ala Gln Ser Ser Asn Phe Leu Phe Pro
        115                 120                 125

Lys Ala Cys His Gln Arg Ala Arg Ser Asn Ser Thr Ser Val Asn Pro
    130                 135                 140

Tyr Cys Thr Arg Glu Ile Asp Phe Pro Met Thr Lys Lys Ser Ala Ala
145                 150                 155                 160

Pro Thr Asp Arg Gln Pro Tyr Ser Leu Cys Ser Asn Arg Lys Ser Leu
                165                 170                 175

Ser Gln Gln Leu Asp Cys Pro Ala Gly Lys Ala Ala Gly Thr Ser Arg
            180                 185                 190

Pro Thr Arg Ser Leu Ser Thr Ala Gln Leu Val Gln Pro Ser Gly Gly
        195                 200                 205

Leu Gln Ala Ser Val Ile Ser Asn Ile Val Leu Met Lys Gly Gln Ala
    210                 215                 220

Lys Gly Leu Gly Phe Ser Ile Val Gly Gly Lys Asp Ser Ile Tyr Gly
225                 230                 235                 240

Pro Ile Gly Ile Tyr Val Lys Thr Ile Phe Ala Gly Gly Ala Ala Ala
                245                 250                 255

Ala Asp Gly Arg Leu Gln Glu Gly Asp Glu Ile Leu Glu Leu Asn Gly
            260                 265                 270

Glu Ser Met Ala Gly Leu Thr His Gln Asp Ala Leu Gln Lys Phe Lys
        275                 280                 285

Gln Ala Lys Lys Gly Leu Leu Thr Leu Thr Val Arg Thr Arg Leu Thr
```

290 295 300

Ala Pro Pro Ser Leu Cys Ser His Leu Ser Pro Pro Leu Cys Arg Ser
305 310 315 320

Leu Ser Ser Ser Thr Cys Ile Thr Lys Asp Ser Ser Ser Phe Ala Leu
325 330 335

Glu Ser Pro Ser Ala Pro Ile Ser Thr Ala Lys Pro Asn Tyr Arg Ile
340 345 350

Met Val Glu Val Ser Leu Gln Lys Glu Ala Gly Val Gly Leu Gly Ile
355 360 365

Gly Leu Cys Ser Val Pro Tyr Phe Gln Cys Ile Ser Gly Ile Phe Val
370 375 380

His Thr Leu Ser Pro Gly Ser Val Ala His Leu Asp Gly Arg Leu Arg
385 390 395 400

Cys Gly Asp Glu Ile Val Glu Ile Ser Asp Ser Pro Val His Cys Leu
405 410 415

Thr Leu Asn Glu Val Tyr Thr Ile Leu Ser His Cys Asp Pro Gly Pro
420 425 430

Val Pro Ile Ile Val Ser Arg His Pro Asp Pro Gln Val Ser Glu Gln
435 440 445

Gln Leu Lys Glu Ala Val Ala Gln Ala Val Glu Asn Thr Lys Phe Gly
450 455 460

Lys Glu Arg His Gln Trp Ser Leu Glu Gly Val Lys Arg Leu Glu Ser
465 470 475 480

Ser Trp His Gly Arg Pro Thr Leu Glu Lys Glu Arg Glu Lys Asn Ser
485 490 495

Ala Pro Pro His Arg Arg Ala Gln Lys Val Met Ile Arg Ser Ser Ser
500 505 510

Asp Ser Ser Tyr Met Ser Gly Ser Pro Gly Gly Ser Pro Gly Ser Gly
515 520 525

Ser Ala Glu Lys Pro Ser Ser Asp Val Asp Ile Ser Thr His Ser Pro
530 535 540

Ser Leu Pro Leu Ala Arg Glu Pro Val Val Leu Ser Ile Ala Ser Ser
545 550 555 560

Arg Leu Pro Gln Glu Ser Pro Pro Leu Pro Glu Ser Arg Asp Ser His

565 570 575

Pro Pro Leu Arg Leu Lys Lys Ser Phe Glu Ile Leu Val Arg Lys Pro
580 585 590

Met Ser Ser Lys Pro Lys Pro Pro Pro Arg Lys Tyr Phe Lys Ser Asp
595 600 605

Ser Asp Pro Gln Lys Ser Leu Glu Glu Arg Glu Asn Ser Ser Cys Ser
610 615 620

Ser Gly His Thr Pro Pro Thr Cys Gly Gln Glu Ala Arg Glu Leu Leu
625 630 635 640

Pro Leu Leu Leu Pro Gln Glu Asp Thr Ala Gly Arg Ser Pro Ser Ala
645 650 655

Ser Ala Gly Cys Pro Gly Pro Gly Ile Gly Pro Gln Thr Lys Ser Ser
660 665 670

Thr Glu Gly Glu Pro Gly Trp Arg Arg Ala Ser Pro Val Thr Gln Thr
675 680 685

Ser Pro Ile Lys His Pro Leu Leu Lys Arg Gln Ala Arg Met Asp Tyr
690 695 700

Ser Phe Asp Thr Thr Ala Glu Asp Pro Trp Val Arg Ile Ser Asp Cys
705 710 715 720

Ile Lys Asn Leu Phe Ser Pro Ile Met Ser Glu Asn His Gly His Met
725 730 735

Pro Leu Gln Pro Asn Ala Ser Leu Asn Glu Glu Glu Gly Thr Gln Gly
740 745 750

His Pro Asp Gly Thr Pro Pro Lys Leu Asp Thr Ala Asn Gly Thr Pro
755 760 765

Lys Val Tyr Lys Ser Ala Asp Ser Ser Thr Val Lys Lys Gly Pro Pro
770 775 780

Val Ala Pro Lys Pro Ala Trp Phe Arg Gln Ser Leu Lys Gly Leu Arg
785 790 795 800

Asn Arg Ala Ser Asp Pro Arg Gly Leu Pro Asp Pro Ala Leu Ser Thr
805 810 815

Gln Pro Ala Pro Ala Ser Arg Glu His Leu Gly Ser His Ile Arg Ala
820 825 830

Ser Ser Ser Ser Ser Ser Ile Arg Gln Arg Ile Ser Ser Phe Glu Thr

```
        835                 840                 845

Phe Gly Ser Ser Gln Leu Pro Asp Lys Gly Ala Gln Arg Leu Ser Leu
    850                 855                 860

Gln Pro Ser Ser Gly Glu Ala Ala Lys Pro Leu Gly Lys His Glu Glu
865                 870                 875                 880

Gly Arg Phe Ser Gly Leu Leu Gly Arg Gly Ala Ala Pro Thr Leu Val
                885                 890                 895

Pro Gln Gln Pro Glu Gln Val Leu Ser Ser Gly Ser Pro Ala Ala Ser
            900                 905                 910

Glu Ala Arg Asp Pro Gly Val Ser Glu Ser Pro Pro Pro Gly Arg Gln
        915                 920                 925

Pro Asn Gln Lys Thr Leu Pro Pro Gly Pro Asp Pro Leu Leu Arg Leu
    930                 935                 940

Leu Ser Thr Gln Ala Glu Glu Ser Gln Gly Pro Val Leu Lys Met Pro
945                 950                 955                 960

Ser Gln Arg Ala Arg Ser Phe Pro Leu Thr Arg Ser Gln Ser Cys Glu
                965                 970                 975

Thr Lys Leu Leu Asp Glu Lys Thr Ser Lys Leu Tyr Ser Ile Ser Ser
            980                 985                 990

Gln Val Ser Ser Ala Val Met Lys  Ser Leu Leu Cys Leu  Pro Ser Ser
        995                 1000                1005

Ile Ser  Cys Ala Gln Thr Pro  Cys Ile Pro Lys Glu  Gly Ala Ser
    1010                1015                1020

Pro Thr  Ser Ser Ser Asn Glu  Asp Ser Ala Ala Asn  Gly Ser Ala
    1025                1030                1035

Glu Thr  Ser Ala Leu Asp Thr  Gly Phe Ser Leu Asn  Leu Ser Glu
    1040                1045                1050

Leu Arg  Glu Tyr Thr Glu Gly  Leu Thr Glu Ala Lys  Glu Asp Asp
    1055                1060                1065

Asp Gly  Asp His Ser Ser Leu  Gln Ser Gly Gln Ser  Val Ile Ser
    1070                1075                1080

Leu Leu  Ser Ser Glu Glu Leu  Lys Lys Leu Ile Glu  Glu Val Lys
    1085                1090                1095

Val Leu  Asp Glu Ala Thr Leu  Lys Gln Leu Asp Gly  Ile His Val
```

1100 1105 1110

Thr Ile Leu His Lys Glu Glu Gly Ala Gly Leu Gly Phe Ser Leu
1115 1120 1125

Ala Gly Gly Ala Asp Leu Glu Asn Lys Val Ile Thr Val His Arg
1130 1135 1140

Val Phe Pro Asn Gly Leu Ala Ser Gln Glu Gly Thr Ile Gln Lys
1145 1150 1155

Gly Asn Glu Val Leu Ser Ile Asn Gly Lys Ser Leu Lys Gly Thr
1160 1165 1170

Thr His His Asp Ala Leu Ala Ile Leu Arg Gln Ala Arg Glu Pro
1175 1180 1185

Arg Gln Ala Val Ile Val Thr Arg Lys Leu Thr Pro Glu Ala Met
1190 1195 1200

Pro Asp Leu Asn Ser Ser Thr Asp Ser Ala Ala Ser Ala Ser Ala
1205 1210 1215

Ala Ser Asp Val Ser Val Glu Ser Thr Ala Glu Ala Thr Val Cys
1220 1225 1230

Thr Val Thr Leu Glu Lys Met Ser Ala Gly Leu Gly Phe Ser Leu
1235 1240 1245

Glu Gly Gly Lys Gly Ser Leu His Gly Asp Lys Pro Leu Thr Ile
1250 1255 1260

Asn Arg Ile Phe Lys Gly Ala Ala Ser Glu Gln Ser Glu Thr Val
1265 1270 1275

Gln Pro Gly Asp Glu Ile Leu Gln Leu Gly Gly Thr Ala Met Gln
1280 1285 1290

Gly Leu Thr Arg Phe Glu Ala Trp Asn Ile Ile Lys Ala Leu Pro
1295 1300 1305

Asp Gly Pro Val Thr Ile Val Ile Arg Arg Lys Ser Leu Gln Ser
1310 1315 1320

Lys Glu Thr Thr Ala Ala Gly Asp Ser
1325 1330

<210> 283
<211> 193
<212> PRT
<213> Homo sapiens

<400> 283

Met Ala Ala Glu Pro Val Glu Asp Asn Cys Ile Asn Phe Val Ala Met
1 5 10 15

Lys Phe Ile Asp Asn Thr Leu Tyr Phe Ile Ala Glu Asp Asp Glu Asn
20 25 30

Leu Glu Ser Asp Tyr Phe Gly Lys Leu Glu Ser Lys Leu Ser Val Ile
35 40 45

Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln Gly Asn Arg Pro
50 55 60

Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp Asn Ala Pro Arg
65 70 75 80

Thr Ile Phe Ile Ile Ser Met Tyr Lys Asp Ser Gln Pro Arg Gly Met
85 90 95

Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser Thr Leu Ser Cys
100 105 110

Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro Pro Asp Asn Ile
115 120 125

Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg Ser Val Pro Gly
130 135 140

His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr Glu Gly Tyr Phe
145 150 155 160

Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu Ile Leu Lys Lys
165 170 175

Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr Val Gln Asn Glu
180 185 190

Asp

<210> 284
<211> 219
<212> PRT
<213> Homo sapiens

<400> 284

Met Cys Pro Ala Arg Ser Leu Leu Leu Val Ala Thr Leu Val Leu Leu
1 5 10 15

Asp His Leu Ser Leu Ala Arg Asn Leu Pro Val Ala Thr Pro Asp Pro
20 25 30

```
Gly Met Phe Pro Cys Leu His His Ser Gln Asn Leu Leu Arg Ala Val
        35                  40                  45

Ser Asn Met Leu Gln Lys Ala Arg Gln Thr Leu Glu Phe Tyr Pro Cys
    50                  55                  60

Thr Ser Glu Glu Ile Asp His Glu Asp Ile Thr Lys Asp Lys Thr Ser
65                  70                  75                  80

Thr Val Glu Ala Cys Leu Pro Leu Glu Leu Thr Lys Asn Glu Ser Cys
                85                  90                  95

Leu Asn Ser Arg Glu Thr Ser Phe Ile Thr Asn Gly Ser Cys Leu Ala
            100                 105                 110

Ser Arg Lys Thr Ser Phe Met Met Ala Leu Cys Leu Ser Ser Ile Tyr
        115                 120                 125

Glu Asp Leu Lys Met Tyr Gln Val Glu Phe Lys Thr Met Asn Ala Lys
    130                 135                 140

Leu Leu Met Asp Pro Lys Arg Gln Ile Phe Leu Asp Gln Asn Met Leu
145                 150                 155                 160

Ala Val Ile Asp Glu Leu Met Gln Ala Leu Asn Phe Asn Ser Glu Thr
                165                 170                 175

Val Pro Gln Lys Ser Ser Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys
            180                 185                 190

Ile Lys Leu Cys Ile Leu Leu His Ala Phe Arg Ile Arg Ala Val Thr
        195                 200                 205

Ile Asp Arg Val Met Ser Tyr Leu Asn Ala Ser
    210                 215


<210>  285
<211>  162
<212>  PRT
<213>  Homo sapiens

<400>  285

Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser Ile Gln Cys Tyr
1               5                   10                  15

Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu Ala Gly Ile His
            20                  25                  30

Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala
        35                  40                  45
```

```
Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
    50                  55                  60

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
65                  70                  75                  80

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
                85                  90                  95

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
            100                 105                 110

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
        115                 120                 125

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
    130                 135                 140

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
145                 150                 155                 160

Thr Ser
```

<210> 286
<211> 153
<212> PRT
<213> Homo sapiens

<400> 286

```
Met Gly Leu Thr Ser Gln Leu Leu Pro Pro Leu Phe Phe Leu Leu Ala
1               5                   10                  15

Cys Ala Gly Asn Phe Val His Gly His Lys Cys Asp Ile Thr Leu Gln
            20                  25                  30

Glu Ile Ile Lys Thr Leu Asn Ser Leu Thr Glu Gln Lys Thr Leu Cys
        35                  40                  45

Thr Glu Leu Thr Val Thr Asp Ile Phe Ala Ala Ser Lys Asn Thr Thr
    50                  55                  60

Glu Lys Glu Thr Phe Cys Arg Ala Ala Thr Val Leu Arg Gln Phe Tyr
65                  70                  75                  80

Ser His His Glu Lys Asp Thr Arg Cys Leu Gly Ala Thr Ala Gln Gln
                85                  90                  95

Phe His Arg His Lys Gln Leu Ile Arg Phe Leu Lys Arg Leu Asp Arg
            100                 105                 110

Asn Leu Trp Gly Leu Ala Gly Leu Asn Ser Cys Pro Val Lys Glu Ala
```

115 120 125

Asn Gln Ser Thr Leu Glu Asn Phe Leu Glu Arg Leu Lys Thr Ile Met
130 135 140

Arg Glu Lys Tyr Ser Lys Cys Ser Ser
145 150

<210> 287
<211> 154
<212> PRT
<213> Homo sapiens

<400> 287

Met Val Leu Ser Gly Ala Leu Cys Phe Arg Met Lys Asp Ser Ala Leu
1 5 10 15

Lys Val Leu Tyr Leu His Asn Asn Gln Leu Leu Ala Gly Gly Leu His
20 25 30

Ala Gly Lys Val Ile Lys Gly Glu Glu Ile Ser Trp Pro Asn Arg Trp
35 40 45

Leu Asp Ala Ser Leu Ser Pro Val Ile Leu Gly Val Gln Gly Gly Ser
50 55 60

Gln Cys Leu Ser Cys Gly Val Gly Gln Glu Pro Thr Leu Thr Leu Glu
65 70 75 80

Pro Val Asn Ile Met Glu Leu Tyr Leu Gly Ala Lys Glu Ser Lys Ser
85 90 95

Phe Thr Phe Tyr Arg Arg Asp Met Gly Leu Thr Ser Ser Phe Glu Ser
100 105 110

Ala Ala Tyr Pro Gly Trp Phe Leu Cys Thr Val Pro Glu Ala Asp Gln
115 120 125

Pro Val Arg Leu Thr Gln Leu Pro Glu Asn Gly Gly Trp Asn Ala Pro
130 135 140

Ile Thr Asp Phe Tyr Phe Gln Gln Cys Asp
145 150

<210> 288
<211> 199
<212> PRT
<213> Homo sapiens

<400> 288

Met Asn Cys Val Cys Arg Leu Val Leu Val Val Leu Ser Leu Trp Pro
1 5 10 15

```
Asp Thr Ala Val Ala Pro Gly Pro Pro Pro Gly Pro Pro Arg Val Ser
            20                  25                  30

Pro Asp Pro Arg Ala Glu Leu Asp Ser Thr Val Leu Leu Thr Arg Ser
        35                  40                  45

Leu Leu Ala Asp Thr Arg Gln Leu Ala Ala Gln Leu Arg Asp Lys Phe
    50                  55                  60

Pro Ala Asp Gly Asp His Asn Leu Asp Ser Leu Pro Thr Leu Ala Met
65                  70                  75                  80

Ser Ala Gly Ala Leu Gly Ala Leu Gln Leu Pro Gly Val Leu Thr Arg
                85                  90                  95

Leu Arg Ala Asp Leu Leu Ser Tyr Leu Arg His Val Gln Trp Leu Arg
            100                 105                 110

Arg Ala Gly Gly Ser Ser Leu Lys Thr Leu Glu Pro Glu Leu Gly Thr
        115                 120                 125

Leu Gln Ala Arg Leu Asp Arg Leu Leu Arg Arg Leu Gln Leu Leu Met
    130                 135                 140

Ser Arg Leu Ala Leu Pro Gln Pro Pro Pro Asp Pro Pro Ala Pro Pro
145                 150                 155                 160

Leu Ala Pro Pro Ser Ser Ala Trp Gly Gly Ile Arg Ala Ala His Ala
                165                 170                 175

Ile Leu Gly Gly Leu His Leu Thr Leu Asp Trp Ala Val Arg Gly Leu
            180                 185                 190

Leu Leu Leu Lys Thr Arg Leu
        195


<210>  289
<211>  546
<212>  PRT
<213>  Homo sapiens

<400>  289

Met Lys Asn Gln Asp Lys Lys Asn Gly Ala Ala Lys Gln Ser Asn Pro
1               5                   10                  15

Lys Ser Ser Pro Gly Gln Pro Glu Ala Gly Pro Glu Gly Ala Gln Glu
            20                  25                  30

Arg Pro Ser Gln Ala Ala Pro Ala Val Glu Ala Glu Gly Pro Gly Ser
        35                  40                  45
```

```
Ser Gln Ala Pro Arg Lys Pro Glu Gly Ala Gln Ala Arg Thr Ala Gln
    50                  55                  60

Ser Gly Ala Leu Arg Asp Val Ser Glu Glu Leu Ser Arg Gln Leu Glu
65                  70                  75                  80

Asp Ile Leu Ser Thr Tyr Cys Val Asp Asn Asn Gln Gly Gly Pro Gly
                85                  90                  95

Glu Asp Gly Ala Gln Gly Glu Pro Ala Glu Pro Glu Asp Ala Glu Lys
            100                 105                 110

Ser Arg Thr Tyr Val Ala Arg Asn Gly Glu Pro Glu Pro Thr Pro Val
        115                 120                 125

Val Asn Gly Glu Lys Glu Pro Ser Lys Gly Asp Pro Asn Thr Glu Glu
    130                 135                 140

Ile Arg Gln Ser Asp Glu Val Gly Asp Arg Asp His Arg Arg Pro Gln
145                 150                 155                 160

Glu Lys Lys Lys Ala Lys Gly Leu Gly Lys Glu Ile Thr Leu Leu Met
                165                 170                 175

Gln Thr Leu Asn Thr Leu Ser Thr Pro Glu Glu Lys Leu Ala Ala Leu
            180                 185                 190

Cys Lys Lys Tyr Ala Glu Leu Leu Glu Glu His Arg Asn Ser Gln Lys
        195                 200                 205

Gln Met Lys Leu Leu Gln Lys Lys Gln Ser Gln Leu Val Gln Glu Lys
    210                 215                 220

Asp His Leu Arg Gly Glu His Ser Lys Ala Val Leu Ala Arg Ser Lys
225                 230                 235                 240

Leu Glu Ser Leu Cys Arg Glu Leu Gln Arg His Asn Arg Ser Leu Lys
                245                 250                 255

Glu Glu Gly Val Gln Arg Ala Arg Glu Glu Glu Glu Lys Arg Lys Glu
            260                 265                 270

Val Thr Ser His Phe Gln Val Thr Leu Asn Asp Ile Gln Leu Gln Met
        275                 280                 285

Glu Gln His Asn Glu Arg Asn Ser Lys Leu Arg Gln Glu Asn Met Glu
    290                 295                 300

Leu Ala Glu Arg Leu Lys Lys Leu Ile Glu Gln Tyr Glu Leu Arg Glu
305                 310                 315                 320
```

Glu His Ile Asp Lys Val Phe Lys His Lys Asp Leu Gln Gln Leu
325 330 335

Val Asp Ala Lys Leu Gln Gln Ala Gln Glu Met Leu Lys Glu Ala Glu
340 345 350

Glu Arg His Gln Arg Glu Lys Asp Phe Leu Leu Lys Glu Ala Val Glu
355 360 365

Ser Gln Arg Met Cys Glu Leu Met Lys Gln Gln Glu Thr His Leu Lys
370 375 380

Gln Gln Leu Ala Leu Tyr Thr Glu Lys Phe Glu Glu Phe Gln Asn Thr
385 390 395 400

Leu Ser Lys Ser Ser Glu Val Phe Thr Thr Phe Lys Gln Glu Met Glu
405 410 415

Lys Met Thr Lys Lys Ile Lys Lys Leu Glu Lys Glu Thr Thr Met Tyr
420 425 430

Arg Ser Arg Trp Glu Ser Ser Asn Lys Ala Leu Leu Glu Met Ala Glu
435 440 445

Glu Lys Thr Val Arg Asp Lys Glu Leu Glu Gly Leu Gln Val Lys Ile
450 455 460

Gln Arg Leu Glu Lys Leu Cys Arg Ala Leu Gln Thr Glu Arg Asn Asp
465 470 475 480

Leu Asn Lys Arg Val Gln Asp Leu Ser Ala Gly Gly Gln Gly Ser Leu
485 490 495

Thr Asp Ser Gly Pro Glu Arg Arg Pro Glu Gly Pro Gly Ala Gln Ala
500 505 510

Pro Ser Ser Pro Arg Val Thr Glu Ala Pro Cys Tyr Pro Gly Ala Pro
515 520 525

Ser Thr Glu Ala Ser Gly Gln Thr Gly Pro Gln Glu Pro Thr Ser Ala
530 535 540

Arg Ala
545

<210> 290
<211> 866
<212> PRT
<213> Homo sapiens

<400> 290

Met Gly Ala Ala Arg Ser Pro Pro Ser Ala Val Pro Gly Pro Leu Leu

1 5 10 15

Gly Leu Leu Leu Leu Leu Leu Gly Val Leu Ala Pro Gly Gly Ala Ser
20 25 30

Leu Arg Leu Leu Asp His Arg Ala Leu Val Cys Ser Gln Pro Gly Leu
35 40 45

Asn Cys Thr Val Lys Asn Ser Thr Cys Leu Asp Asp Ser Trp Ile His
50 55 60

Pro Arg Asn Leu Thr Pro Ser Ser Pro Lys Asp Leu Gln Ile Gln Leu
65 70 75 80

His Phe Ala His Thr Gln Gln Gly Asp Leu Phe Pro Val Ala His Ile
85 90 95

Glu Trp Thr Leu Gln Thr Asp Ala Ser Ile Leu Tyr Leu Glu Gly Ala
100 105 110

Glu Leu Ser Val Leu Gln Leu Asn Thr Asn Glu Arg Leu Cys Val Arg
115 120 125

Phe Glu Phe Leu Ser Lys Leu Arg His His His Arg Arg Trp Arg Phe
130 135 140

Thr Phe Ser His Phe Val Val Asp Pro Asp Gln Glu Tyr Glu Val Thr
145 150 155 160

Val His His Leu Pro Lys Pro Ile Pro Asp Gly Asp Pro Asn His Gln
165 170 175

Ser Lys Asn Phe Leu Val Pro Asp Cys Glu His Ala Arg Met Lys Val
180 185 190

Thr Thr Pro Cys Met Ser Ser Gly Ser Leu Trp Asp Pro Asn Ile Thr
195 200 205

Val Glu Thr Leu Glu Ala His Gln Leu Arg Val Ser Phe Thr Leu Trp
210 215 220

Asn Glu Ser Thr His Tyr Gln Ile Leu Leu Thr Ser Phe Pro His Met
225 230 235 240

Glu Asn His Ser Cys Phe Glu His Met His His Ile Pro Ala Pro Arg
245 250 255

Pro Glu Glu Phe His Gln Arg Ser Asn Val Thr Leu Thr Leu Arg Asn
260 265 270

Leu Lys Gly Cys Cys Arg His Gln Val Gln Ile Gln Pro Phe Phe Ser

275 280 285

Ser Cys Leu Asn Asp Cys Leu Arg His Ser Ala Thr Val Ser Cys Pro
290 295 300

Glu Met Pro Asp Thr Pro Glu Pro Ile Pro Asp Tyr Met Pro Leu Trp
305 310 315 320

Val Tyr Trp Phe Ile Thr Gly Ile Ser Ile Leu Leu Val Gly Ser Val
325 330 335

Ile Leu Leu Ile Val Cys Met Thr Trp Arg Leu Ala Gly Pro Gly Ser
340 345 350

Glu Lys Tyr Ser Asp Asp Thr Lys Tyr Thr Asp Gly Leu Pro Ala Ala
355 360 365

Asp Leu Ile Pro Pro Pro Leu Lys Pro Arg Lys Val Trp Ile Ile Tyr
370 375 380

Ser Ala Asp His Pro Leu Tyr Val Asp Val Val Leu Lys Phe Ala Gln
385 390 395 400

Phe Leu Leu Thr Ala Cys Gly Thr Glu Val Ala Leu Asp Leu Leu Glu
405 410 415

Glu Gln Ala Ile Ser Glu Ala Gly Val Met Thr Trp Val Gly Arg Gln
420 425 430

Lys Gln Glu Met Val Glu Ser Asn Ser Lys Ile Ile Val Leu Cys Ser
435 440 445

Arg Gly Thr Arg Ala Lys Trp Gln Ala Leu Leu Gly Arg Gly Ala Pro
450 455 460

Val Arg Leu Arg Cys Asp His Gly Lys Pro Val Gly Asp Leu Phe Thr
465 470 475 480

Ala Ala Met Asn Met Ile Leu Pro Asp Phe Lys Arg Pro Ala Cys Phe
485 490 495

Gly Thr Tyr Val Val Cys Tyr Phe Ser Glu Val Ser Cys Asp Gly Asp
500 505 510

Val Pro Asp Leu Phe Gly Ala Ala Pro Arg Tyr Pro Leu Met Asp Arg
515 520 525

Phe Glu Glu Val Tyr Phe Arg Ile Gln Asp Leu Glu Met Phe Gln Pro
530 535 540

Gly Arg Met His Arg Val Gly Glu Leu Ser Gly Asp Asn Tyr Leu Arg

```
545                 550                 555                 560

Ser Pro Gly Gly Arg Gln Leu Arg Ala Ala Leu Asp Arg Phe Arg Asp
                565                 570                 575

Trp Gln Val Arg Cys Pro Asp Trp Phe Glu Cys Glu Asn Leu Tyr Ser
            580                 585                 590

Ala Asp Asp Gln Asp Ala Pro Ser Leu Asp Glu Glu Val Phe Glu Glu
        595                 600                 605

Pro Leu Leu Pro Pro Gly Thr Gly Ile Val Lys Arg Ala Pro Leu Val
    610                 615                 620

Arg Glu Pro Gly Ser Gln Ala Cys Leu Ala Ile Asp Pro Leu Val Gly
625                 630                 635                 640

Glu Glu Gly Gly Ala Ala Val Ala Lys Leu Glu Pro His Leu Gln Pro
                645                 650                 655

Arg Gly Gln Pro Ala Pro Gln Pro Leu His Thr Leu Val Leu Ala Ala
            660                 665                 670

Glu Glu Gly Ala Leu Val Ala Ala Val Glu Pro Gly Pro Leu Ala Asp
        675                 680                 685

Gly Ala Ala Val Arg Leu Ala Leu Ala Gly Glu Gly Glu Ala Cys Pro
    690                 695                 700

Leu Leu Gly Ser Pro Gly Ala Gly Arg Asn Ser Val Leu Phe Leu Pro
705                 710                 715                 720

Val Asp Pro Glu Asp Ser Pro Leu Gly Ser Ser Thr Pro Met Ala Ser
                725                 730                 735

Pro Asp Leu Leu Pro Glu Asp Val Arg Glu His Leu Glu Gly Leu Met
            740                 745                 750

Leu Ser Leu Phe Glu Gln Ser Leu Ser Cys Gln Ala Gln Gly Gly Cys
        755                 760                 765

Ser Arg Pro Ala Met Val Leu Thr Asp Pro His Thr Pro Tyr Glu Glu
    770                 775                 780

Glu Gln Arg Gln Ser Val Gln Ser Asp Gln Gly Tyr Ile Ser Arg Ser
785                 790                 795                 800

Ser Pro Gln Pro Pro Glu Gly Leu Thr Glu Met Glu Glu Glu Glu Glu
                805                 810                 815

Glu Glu Gln Asp Pro Gly Lys Pro Ala Leu Pro Leu Ser Pro Glu Asp
```

820 825 830

Leu Glu Ser Leu Arg Ser Leu Gln Arg Gln Leu Leu Phe Arg Gln Leu
835 840 845

Gln Lys Asn Ser Gly Trp Asp Thr Met Gly Ser Glu Ser Glu Gly Pro
850 855 860

Ser Ala
865

<210> 291
<211> 155
<212> PRT
<213> Homo sapiens

<400> 291

Met Thr Pro Gly Lys Thr Ser Leu Val Ser Leu Leu Leu Leu Leu Ser
1 5 10 15

Leu Glu Ala Ile Val Lys Ala Gly Ile Thr Ile Pro Arg Asn Pro Gly
20 25 30

Cys Pro Asn Ser Glu Asp Lys Asn Phe Pro Arg Thr Val Met Val Asn
35 40 45

Leu Asn Ile His Asn Arg Asn Thr Asn Thr Asn Pro Lys Arg Ser Ser
50 55 60

Asp Tyr Tyr Asn Arg Ser Thr Ser Pro Trp Asn Leu His Arg Asn Glu
65 70 75 80

Asp Pro Glu Arg Tyr Pro Ser Val Ile Trp Glu Ala Lys Cys Arg His
85 90 95

Leu Gly Cys Ile Asn Ala Asp Gly Asn Val Asp Tyr His Met Asn Ser
100 105 110

Val Pro Ile Gln Gln Glu Ile Leu Val Leu Arg Arg Glu Pro Pro His
115 120 125

Cys Pro Asn Ser Phe Arg Leu Glu Lys Ile Leu Val Ser Val Gly Cys
130 135 140

Thr Cys Val Thr Pro Ile Val His His Val Ala
145 150 155

<210> 292
<211> 177
<212> PRT
<213> Homo sapiens

<400> 292

```
Met Lys Leu Gln Cys Val Ser Leu Trp Leu Leu Gly Thr Ile Leu Ile
1               5                  10                  15

Leu Cys Ser Val Asp Asn His Gly Leu Arg Arg Cys Leu Ile Ser Thr
            20                  25                  30

Asp Met His His Ile Glu Glu Ser Phe Gln Glu Ile Lys Arg Ala Ile
        35                  40                  45

Gln Ala Lys Asp Thr Phe Pro Asn Val Thr Ile Leu Ser Thr Leu Glu
    50                  55                  60

Thr Leu Gln Ile Ile Lys Pro Leu Asp Val Cys Cys Val Thr Lys Asn
65                  70                  75                  80

Leu Leu Ala Phe Tyr Val Asp Arg Val Phe Lys Asp His Gln Glu Pro
                85                  90                  95

Asn Pro Lys Ile Leu Arg Lys Ile Ser Ser Ile Ala Asn Ser Phe Leu
            100                 105                 110

Tyr Met Gln Lys Thr Leu Arg Gln Cys Gln Glu Gln Arg Gln Cys His
        115                 120                 125

Cys Arg Gln Glu Ala Thr Asn Ala Thr Arg Val Ile His Asp Asn Tyr
    130                 135                 140

Asp Gln Leu Glu Val His Ala Ala Ala Ile Lys Ser Leu Gly Glu Leu
145                 150                 155                 160

Asp Val Phe Leu Ala Trp Ile Asn Lys Asn His Glu Val Met Phe Ser
                165                 170                 175

Ala
```

<210> 293
<211> 155
<212> PRT
<213> Homo sapiens

<400> 293

```
Met Glu Arg Ile Val Ile Cys Leu Met Val Ile Phe Leu Gly Thr Leu
1               5                  10                  15

Val His Lys Ser Ser Ser Gln Gly Gln Asp Arg His Met Ile Arg Met
            20                  25                  30

Arg Gln Leu Ile Asp Ile Val Asp Gln Leu Lys Asn Tyr Val Asn Asp
        35                  40                  45
```

Leu Val Pro Glu Phe Leu Pro Ala Pro Glu Asp Val Glu Thr Asn Cys
50 55 60

Glu Trp Ser Ala Phe Ser Cys Phe Gln Lys Ala Gln Leu Lys Ser Ala
65 70 75 80

Asn Thr Gly Asn Asn Glu Arg Ile Ile Asn Val Ser Ile Lys Lys Leu
85 90 95

Lys Arg Lys Pro Pro Ser Thr Asn Ala Gly Arg Arg Gln Lys His Arg
100 105 110

Leu Thr Cys Pro Ser Cys Asp Ser Tyr Glu Lys Lys Pro Pro Lys Glu
115 120 125

Phe Leu Glu Arg Phe Lys Ser Leu Leu Gln Lys Met Ile His Gln His
130 135 140

Leu Ser Ser Arg Thr His Gly Ser Glu Asp Ser
145 150 155

<210> 294
<211> 350
<212> PRT
<213> Homo sapiens

<400> 294

Met Ser Asn Ile Thr Asp Pro Gln Met Trp Asp Phe Asp Asp Leu Asn
1 5 10 15

Phe Thr Gly Met Pro Pro Ala Asp Glu Asp Tyr Ser Pro Cys Met Leu
20 25 30

Glu Thr Glu Thr Leu Asn Lys Tyr Val Val Ile Ile Ala Tyr Ala Leu
35 40 45

Val Phe Leu Leu Ser Leu Leu Gly Asn Ser Leu Val Met Leu Val Ile
50 55 60

Leu Tyr Ser Arg Val Gly Arg Ser Val Thr Asp Val Tyr Leu Leu Asn
65 70 75 80

Leu Ala Leu Ala Asp Leu Leu Phe Ala Leu Thr Leu Pro Ile Trp Ala
85 90 95

Ala Ser Lys Val Asn Gly Trp Ile Phe Gly Thr Phe Leu Cys Lys Val
100 105 110

Val Ser Leu Leu Lys Glu Val Asn Phe Tyr Ser Gly Ile Leu Leu Leu
115 120 125

Ala Cys Ile Ser Val Asp Arg Tyr Leu Ala Ile Val His Ala Thr Arg

130 135 140

Thr Leu Thr Gln Lys Arg His Leu Val Lys Phe Val Cys Leu Gly Cys
145 150 155 160

Trp Gly Leu Ser Met Asn Leu Ser Leu Pro Phe Phe Leu Phe Arg Gln
165 170 175

Ala Tyr His Pro Asn Asn Ser Ser Pro Val Cys Tyr Glu Val Leu Gly
180 185 190

Asn Asp Thr Ala Lys Trp Arg Met Val Leu Arg Ile Leu Pro His Thr
195 200 205

Phe Gly Phe Ile Val Pro Leu Phe Val Met Leu Phe Cys Tyr Gly Phe
210 215 220

Thr Leu Arg Thr Leu Phe Lys Ala His Met Gly Gln Lys His Arg Ala
225 230 235 240

Met Arg Val Ile Phe Ala Val Val Leu Ile Phe Leu Leu Cys Trp Leu
245 250 255

Pro Tyr Asn Leu Val Leu Leu Ala Asp Thr Leu Met Arg Thr Gln Val
260 265 270

Ile Gln Glu Ser Cys Glu Arg Arg Asn Asn Ile Gly Arg Ala Leu Asp
275 280 285

Ala Thr Glu Ile Leu Gly Phe Leu His Ser Cys Leu Asn Pro Ile Ile
290 295 300

Tyr Ala Phe Ile Gly Gln Asn Phe Arg His Gly Phe Leu Lys Ile Leu
305 310 315 320

Ala Met His Gly Leu Val Ser Lys Glu Phe Leu Ala Arg His Arg Val
325 330 335

Thr Ser Tyr Thr Ser Ser Ser Val Asn Val Ser Ser Asn Leu
340 345 350

<210> 295
<211> 360
<212> PRT
<213> Homo sapiens

<400> 295

Met Glu Asp Phe Asn Met Glu Ser Asp Ser Phe Glu Asp Phe Trp Lys
1 5 10 15

Gly Glu Asp Leu Ser Asn Tyr Ser Tyr Ser Ser Thr Leu Pro Pro Phe
20 25 30

```
Leu Leu Asp Ala Ala Pro Cys Glu Pro Glu Ser Leu Glu Ile Asn Lys
        35                  40                  45

Tyr Phe Val Val Ile Ile Tyr Ala Leu Val Phe Leu Leu Ser Leu Leu
    50                  55                  60

Gly Asn Ser Leu Val Met Leu Val Ile Leu Tyr Ser Arg Val Gly Arg
65                  70                  75                  80

Ser Val Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ala Asp Leu Leu
                85                  90                  95

Phe Ala Leu Thr Leu Pro Ile Trp Ala Ala Ser Lys Val Asn Gly Trp
            100                 105                 110

Ile Phe Gly Thr Phe Leu Cys Lys Val Val Ser Leu Leu Lys Glu Val
        115                 120                 125

Asn Phe Tyr Ser Gly Ile Leu Leu Leu Ala Cys Ile Ser Val Asp Arg
    130                 135                 140

Tyr Leu Ala Ile Val His Ala Thr Arg Thr Leu Thr Gln Lys Arg Tyr
145                 150                 155                 160

Leu Val Lys Phe Ile Cys Leu Ser Ile Trp Gly Leu Ser Leu Leu Leu
                165                 170                 175

Ala Leu Pro Val Leu Leu Phe Arg Arg Thr Val Tyr Ser Ser Asn Val
            180                 185                 190

Ser Pro Ala Cys Tyr Glu Asp Met Gly Asn Asn Thr Ala Asn Trp Arg
        195                 200                 205

Met Leu Leu Arg Ile Leu Pro Gln Ser Phe Gly Phe Ile Val Pro Leu
    210                 215                 220

Leu Ile Met Leu Phe Cys Tyr Gly Phe Thr Leu Arg Thr Leu Phe Lys
225                 230                 235                 240

Ala His Met Gly Gln Lys His Arg Ala Met Arg Val Ile Phe Ala Val
                245                 250                 255

Val Leu Ile Phe Leu Leu Cys Trp Leu Pro Tyr Asn Leu Val Leu Leu
            260                 265                 270

Ala Asp Thr Leu Met Arg Thr Gln Val Ile Gln Glu Thr Cys Glu Arg
        275                 280                 285

Arg Asn His Ile Asp Arg Ala Leu Asp Ala Thr Glu Ile Leu Gly Ile
    290                 295                 300
```

```
Leu His Ser Cys Leu Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys
305                 310                 315                 320


Phe Arg His Gly Leu Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser
                325                 330                 335


Lys Asp Ser Leu Pro Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser
            340                 345                 350


Ser Gly His Thr Ser Thr Thr Leu
        355                 360


<210>  296
<211>  398
<212>  PRT
<213>  Homo sapiens

<400>  296

Met Leu Arg Leu Tyr Val Leu Val Met Gly Val Ser Ala Phe Thr Leu
1               5                   10                  15


Gln Pro Ala Ala His Thr Gly Ala Ala Arg Ser Cys Arg Phe Arg Gly
            20                  25                  30


Arg His Tyr Lys Arg Glu Phe Arg Leu Glu Gly Glu Pro Val Ala Leu
        35                  40                  45


Arg Cys Pro Gln Val Pro Tyr Trp Leu Trp Ala Ser Val Ser Pro Arg
    50                  55                  60


Ile Asn Leu Thr Trp His Lys Asn Asp Ser Ala Arg Thr Val Pro Gly
65                  70                  75                  80


Glu Glu Glu Thr Arg Met Trp Ala Gln Asp Gly Ala Leu Trp Leu Leu
                85                  90                  95


Pro Ala Leu Gln Glu Asp Ser Gly Thr Tyr Val Cys Thr Thr Arg Asn
            100                 105                 110


Ala Ser Tyr Cys Asp Lys Met Ser Ile Glu Leu Arg Val Phe Glu Asn
        115                 120                 125


Thr Asp Ala Phe Leu Pro Phe Ile Ser Tyr Pro Gln Ile Leu Thr Leu
    130                 135                 140


Ser Thr Ser Gly Val Leu Val Cys Pro Asp Leu Ser Glu Phe Thr Arg
145                 150                 155                 160


Asp Lys Thr Asp Val Lys Ile Gln Trp Tyr Lys Asp Ser Leu Leu Leu
                165                 170                 175
```

```
Asp Lys Asp Asn Glu Lys Phe Leu Ser Val Arg Gly Thr Thr His Leu
            180                 185                 190

Leu Val His Asp Val Ala Leu Glu Asp Ala Gly Tyr Tyr Arg Cys Val
        195                 200                 205

Leu Thr Phe Ala His Glu Gly Gln Gln Tyr Asn Ile Thr Arg Ser Ile
    210                 215                 220

Glu Leu Arg Ile Lys Lys Lys Lys Glu Glu Thr Ile Pro Val Ile Ile
225                 230                 235                 240

Ser Pro Leu Lys Thr Ile Ser Ala Ser Leu Gly Ser Arg Leu Thr Ile
                245                 250                 255

Pro Cys Lys Val Phe Leu Gly Thr Gly Thr Pro Leu Thr Thr Met Leu
            260                 265                 270

Trp Trp Thr Ala Asn Asp Thr His Ile Glu Ser Ala Tyr Pro Gly Gly
        275                 280                 285

Arg Val Thr Glu Gly Pro Arg Gln Glu Tyr Ser Glu Asn Asn Glu Asn
    290                 295                 300

Tyr Ile Glu Val Pro Leu Ile Phe Asp Pro Val Thr Arg Glu Asp Leu
305                 310                 315                 320

His Met Asp Phe Lys Cys Val Val His Asn Thr Leu Ser Phe Gln Thr
                325                 330                 335

Leu Arg Thr Thr Val Lys Glu Ala Ser Ser Thr Phe Ser Trp Gly Ile
            340                 345                 350

Val Leu Ala Pro Leu Ser Leu Ala Phe Leu Val Leu Gly Gly Ile Trp
        355                 360                 365

Met His Arg Arg Cys Lys His Arg Thr Gly Lys Ala Asp Gly Leu Thr
    370                 375                 380

Val Leu Trp Pro His His Gln Asp Phe Gln Ser Tyr Pro Lys
385                 390                 395


<210>  297
<211>  422
<212>  PRT
<213>  Homo sapiens

<400>  297

Met Ser Ser Ser Cys Ser Gly Leu Ser Arg Val Leu Val Ala Val Ala
1               5                   10                  15
```

```
Thr Ala Leu Val Ser Ala Ser Ser Pro Cys Pro Gln Ala Trp Gly Pro
            20                  25                  30

Pro Gly Val Gln Tyr Gly Gln Pro Gly Arg Ser Val Lys Leu Cys Cys
        35                  40                  45

Pro Gly Val Thr Ala Gly Asp Pro Val Ser Trp Phe Arg Asp Gly Glu
    50                  55                  60

Pro Lys Leu Leu Gln Gly Pro Asp Ser Gly Leu Gly His Glu Leu Val
65                  70                  75                  80

Leu Ala Gln Ala Asp Ser Thr Asp Glu Gly Thr Tyr Ile Cys Gln Thr
                85                  90                  95

Leu Asp Gly Ala Leu Gly Gly Thr Val Thr Leu Gln Leu Gly Tyr Pro
            100                 105                 110

Pro Ala Arg Pro Val Val Ser Cys Gln Ala Ala Asp Tyr Glu Asn Phe
        115                 120                 125

Ser Cys Thr Trp Ser Pro Ser Gln Ile Ser Gly Leu Pro Thr Arg Tyr
    130                 135                 140

Leu Thr Ser Tyr Arg Lys Lys Thr Val Leu Gly Ala Asp Ser Gln Arg
145                 150                 155                 160

Arg Ser Pro Ser Thr Gly Pro Trp Pro Cys Pro Gln Asp Pro Leu Gly
                165                 170                 175

Ala Ala Arg Cys Val Val His Gly Ala Glu Phe Trp Ser Gln Tyr Arg
            180                 185                 190

Ile Asn Val Thr Glu Val Asn Pro Leu Gly Ala Ser Thr Arg Leu Leu
        195                 200                 205

Asp Val Ser Leu Gln Ser Ile Leu Arg Pro Asp Pro Pro Gln Gly Leu
    210                 215                 220

Arg Val Glu Ser Val Pro Gly Tyr Pro Arg Arg Leu Arg Ala Ser Trp
225                 230                 235                 240

Thr Tyr Pro Ala Ser Trp Pro Cys Gln Pro His Phe Leu Leu Lys Phe
                245                 250                 255

Arg Leu Gln Tyr Arg Pro Ala Gln His Pro Ala Trp Ser Thr Val Glu
            260                 265                 270

Pro Ala Gly Leu Glu Glu Val Ile Thr Asp Ala Val Ala Gly Leu Pro
        275                 280                 285
```

```
His Ala Val Arg Val Ser Ala Arg Asp Phe Leu Asp Ala Gly Thr Trp
    290                 295                 300

Ser Thr Trp Ser Pro Glu Ala Trp Gly Thr Pro Ser Thr Gly Thr Ile
305                 310                 315                 320

Pro Lys Glu Ile Pro Ala Trp Gly Gln Leu His Thr Gln Pro Glu Val
                325                 330                 335

Glu Pro Gln Val Asp Ser Pro Ala Pro Pro Arg Pro Ser Leu Gln Pro
            340                 345                 350

His Pro Arg Leu Leu Asp His Arg Asp Ser Val Glu Gln Val Ala Val
        355                 360                 365

Leu Ala Ser Leu Gly Ile Leu Ser Phe Leu Gly Leu Val Ala Gly Ala
    370                 375                 380

Leu Ala Leu Gly Leu Trp Leu Arg Leu Arg Arg Gly Gly Lys Asp Gly
385                 390                 395                 400

Ser Pro Lys Pro Gly Phe Leu Ala Ser Val Ile Pro Val Asp Arg Arg
                405                 410                 415

Pro Gly Ala Pro Asn Leu
            420


<210>  298
<211>  427
<212>  PRT
<213>  Homo sapiens

<400>  298

Met Glu Trp Pro Ala Arg Leu Cys Gly Leu Trp Ala Leu Leu Leu Cys
1               5                   10                  15

Ala Gly Gly Gly Gly Gly Gly Gly Gly Gly Ala Ala Pro Thr Glu Thr Gln
            20                  25                  30

Pro Pro Val Thr Asn Leu Ser Val Ser Val Glu Asn Leu Cys Thr Val
        35                  40                  45

Ile Trp Thr Trp Asn Pro Pro Glu Gly Ala Ser Ser Asn Cys Ser Leu
    50                  55                  60

Trp Tyr Phe Ser His Phe Gly Asp Lys Gln Asp Lys Lys Ile Ala Pro
65                  70                  75                  80

Glu Thr Arg Arg Ser Ile Glu Val Pro Leu Asn Glu Arg Ile Cys Leu
                85                  90                  95

Gln Val Gly Ser Gln Cys Ser Thr Asn Glu Ser Glu Lys Pro Ser Ile
```

```
            100                 105                 110

Leu Val Glu Lys Cys Ile Ser Pro Pro Glu Gly Asp Pro Glu Ser Ala
        115                 120                 125

Val Thr Glu Leu Gln Cys Ile Trp His Asn Leu Ser Tyr Met Lys Cys
    130                 135                 140

Ser Trp Leu Pro Gly Arg Asn Thr Ser Pro Asp Thr Asn Tyr Thr Leu
145                 150                 155                 160

Tyr Tyr Trp His Arg Ser Leu Glu Lys Ile His Gln Cys Glu Asn Ile
                165                 170                 175

Phe Arg Glu Gly Gln Tyr Phe Gly Cys Ser Phe Asp Leu Thr Lys Val
            180                 185                 190

Lys Asp Ser Ser Phe Glu Gln His Ser Val Gln Ile Met Val Lys Asp
        195                 200                 205

Asn Ala Gly Lys Ile Lys Pro Ser Phe Asn Ile Val Pro Leu Thr Ser
    210                 215                 220

Arg Val Lys Pro Asp Pro Pro His Ile Lys Asn Leu Ser Phe His Asn
225                 230                 235                 240

Asp Asp Leu Tyr Val Gln Trp Glu Asn Pro Gln Asn Phe Ile Ser Arg
                245                 250                 255

Cys Leu Phe Tyr Glu Val Glu Val Asn Asn Ser Gln Thr Glu Thr His
            260                 265                 270

Asn Val Phe Tyr Val Gln Glu Ala Lys Cys Glu Asn Pro Glu Phe Glu
        275                 280                 285

Arg Asn Val Glu Asn Thr Ser Cys Phe Met Val Pro Gly Val Leu Pro
    290                 295                 300

Asp Thr Leu Asn Thr Val Arg Ile Arg Val Lys Thr Asn Lys Leu Cys
305                 310                 315                 320

Tyr Glu Asp Asp Lys Leu Trp Ser Asn Trp Ser Gln Glu Met Ser Ile
                325                 330                 335

Gly Lys Lys Arg Asn Ser Thr Leu Tyr Ile Thr Met Leu Leu Ile Val
            340                 345                 350

Pro Val Ile Val Ala Gly Ala Ile Ile Val Leu Leu Leu Tyr Leu Lys
        355                 360                 365

Arg Leu Lys Ile Ile Ile Phe Pro Pro Ile Pro Asp Pro Gly Lys Ile
```

370 375 380

Phe Lys Glu Met Phe Gly Asp Gln Asn Asp Asp Thr Leu His Trp Lys
385 390 395 400

Lys Tyr Asp Ile Tyr Glu Lys Gln Thr Lys Glu Glu Thr Asp Ser Val
405 410 415

Val Leu Ile Glu Asn Leu Lys Lys Ala Ser Gln
420 425

<210> 299
<211> 380
<212> PRT
<213> Homo sapiens

<400> 299

Met Ala Phe Val Cys Leu Ala Ile Gly Cys Leu Tyr Thr Phe Leu Ile
1 5 10 15

Ser Thr Thr Phe Gly Cys Thr Ser Ser Ser Asp Thr Glu Ile Lys Val
20 25 30

Asn Pro Pro Gln Asp Phe Glu Ile Val Asp Pro Gly Tyr Leu Gly Tyr
35 40 45

Leu Tyr Leu Gln Trp Gln Pro Pro Leu Ser Leu Asp His Phe Lys Glu
50 55 60

Cys Thr Val Glu Tyr Glu Leu Lys Tyr Arg Asn Ile Gly Ser Glu Thr
65 70 75 80

Trp Lys Thr Ile Ile Thr Lys Asn Leu His Tyr Lys Asp Gly Phe Asp
85 90 95

Leu Asn Lys Gly Ile Glu Ala Lys Ile His Thr Leu Leu Pro Trp Gln
100 105 110

Cys Thr Asn Gly Ser Glu Val Gln Ser Ser Trp Ala Glu Thr Thr Tyr
115 120 125

Trp Ile Ser Pro Gln Gly Ile Pro Glu Thr Lys Val Gln Asp Met Asp
130 135 140

Cys Val Tyr Tyr Asn Trp Gln Tyr Leu Leu Cys Ser Trp Lys Pro Gly
145 150 155 160

Ile Gly Val Leu Leu Asp Thr Asn Tyr Asn Leu Phe Tyr Trp Tyr Glu
165 170 175

Gly Leu Asp His Ala Leu Gln Cys Val Asp Tyr Ile Lys Ala Asp Gly
180 185 190

```
Gln Asn Ile Gly Cys Arg Phe Pro Tyr Leu Glu Ala Ser Asp Tyr Lys
        195                 200                 205

Asp Phe Tyr Ile Cys Val Asn Gly Ser Ser Glu Asn Lys Pro Ile Arg
    210                 215                 220

Ser Ser Tyr Phe Thr Phe Gln Leu Gln Asn Ile Val Lys Pro Leu Pro
225                 230                 235                 240

Pro Val Tyr Leu Thr Phe Thr Arg Glu Ser Ser Cys Glu Ile Lys Leu
                245                 250                 255

Lys Trp Ser Ile Pro Leu Gly Pro Ile Pro Ala Arg Cys Phe Asp Tyr
            260                 265                 270

Glu Ile Glu Ile Arg Glu Asp Asp Thr Thr Leu Val Thr Ala Thr Val
        275                 280                 285

Glu Asn Glu Thr Tyr Thr Leu Lys Thr Thr Asn Glu Thr Arg Gln Leu
    290                 295                 300

Cys Phe Val Val Arg Ser Lys Val Asn Ile Tyr Cys Ser Asp Asp Gly
305                 310                 315                 320

Ile Trp Ser Glu Trp Ser Asp Lys Gln Cys Trp Glu Gly Glu Asp Leu
                325                 330                 335

Ser Lys Lys Thr Leu Leu Arg Phe Trp Leu Pro Phe Gly Phe Ile Leu
            340                 345                 350

Ile Leu Val Ile Phe Val Thr Gly Leu Leu Leu Arg Lys Pro Asn Thr
        355                 360                 365

Tyr Pro Lys Met Ile Pro Glu Phe Phe Cys Asp Thr
    370                 375                 380


<210>  300
<211>  825
<212>  PRT
<213>  Homo sapiens

<400>  300

Met Gly Trp Leu Cys Ser Gly Leu Leu Phe Pro Val Ser Cys Leu Val
1               5                   10                  15

Leu Leu Gln Val Ala Ser Ser Gly Asn Met Lys Val Leu Gln Glu Pro
            20                  25                  30

Thr Cys Val Ser Asp Tyr Met Ser Ile Ser Thr Cys Glu Trp Lys Met
        35                  40                  45
```

```
Asn Gly Pro Thr Asn Cys Ser Thr Glu Leu Arg Leu Leu Tyr Gln Leu
    50                  55                  60

Val Phe Leu Leu Ser Glu Ala His Thr Cys Ile Pro Glu Asn Asn Gly
65                  70                  75                  80

Gly Ala Gly Cys Val Cys His Leu Leu Met Asp Asp Val Val Ser Ala
                85                  90                  95

Asp Asn Tyr Thr Leu Asp Leu Trp Ala Gly Gln Gln Leu Leu Trp Lys
            100                 105                 110

Gly Ser Phe Lys Pro Ser Glu His Val Lys Pro Arg Ala Pro Gly Asn
        115                 120                 125

Leu Thr Val His Thr Asn Val Ser Asp Thr Leu Leu Leu Thr Trp Ser
    130                 135                 140

Asn Pro Tyr Pro Pro Asp Asn Tyr Leu Tyr Asn His Leu Thr Tyr Ala
145                 150                 155                 160

Val Asn Ile Trp Ser Glu Asn Asp Pro Ala Asp Phe Arg Ile Tyr Asn
                165                 170                 175

Val Thr Tyr Leu Glu Pro Ser Leu Arg Ile Ala Ala Ser Thr Leu Lys
            180                 185                 190

Ser Gly Ile Ser Tyr Arg Ala Arg Val Arg Ala Trp Ala Gln Cys Tyr
        195                 200                 205

Asn Thr Thr Trp Ser Glu Trp Ser Pro Ser Thr Lys Trp His Asn Ser
    210                 215                 220

Tyr Arg Glu Pro Phe Glu Gln His Leu Leu Leu Gly Val Ser Val Ser
225                 230                 235                 240

Cys Ile Val Ile Leu Ala Val Cys Leu Leu Cys Tyr Val Ser Ile Thr
                245                 250                 255

Lys Ile Lys Lys Glu Trp Trp Asp Gln Ile Pro Asn Pro Ala Arg Ser
            260                 265                 270

Arg Leu Val Ala Ile Ile Ile Gln Asp Ala Gln Gly Ser Gln Trp Glu
        275                 280                 285

Lys Arg Ser Arg Gly Gln Glu Pro Ala Lys Cys Pro His Trp Lys Asn
    290                 295                 300

Cys Leu Thr Lys Leu Leu Pro Cys Phe Leu Glu His Asn Met Lys Arg
305                 310                 315                 320
```

```
Asp Glu Asp Pro His Lys Ala Ala Lys Glu Met Pro Phe Gln Gly Ser
                325                 330                 335

Gly Lys Ser Ala Trp Cys Pro Val Glu Ile Ser Lys Thr Val Leu Trp
            340                 345                 350

Pro Glu Ser Ile Ser Val Val Arg Cys Val Glu Leu Phe Glu Ala Pro
        355                 360                 365

Val Glu Cys Glu Glu Glu Glu Glu Val Glu Glu Glu Lys Gly Ser Phe
    370                 375                 380

Cys Ala Ser Pro Glu Ser Ser Arg Asp Asp Phe Gln Glu Gly Arg Glu
385                 390                 395                 400

Gly Ile Val Ala Arg Leu Thr Glu Ser Leu Phe Leu Asp Leu Leu Gly
                405                 410                 415

Glu Glu Asn Gly Gly Phe Cys Gln Gln Asp Met Gly Glu Ser Cys Leu
            420                 425                 430

Leu Pro Pro Ser Gly Ser Thr Ser Ala His Met Pro Trp Asp Glu Phe
        435                 440                 445

Pro Ser Ala Gly Pro Lys Glu Ala Pro Pro Trp Gly Lys Glu Gln Pro
    450                 455                 460

Leu His Leu Glu Pro Ser Pro Pro Ala Ser Pro Thr Gln Ser Pro Asp
465                 470                 475                 480

Asn Leu Thr Cys Thr Glu Thr Pro Leu Val Ile Ala Gly Asn Pro Ala
                485                 490                 495

Tyr Arg Ser Phe Ser Asn Ser Leu Ser Gln Ser Pro Cys Pro Arg Glu
            500                 505                 510

Leu Gly Pro Asp Pro Leu Leu Ala Arg His Leu Glu Glu Val Glu Pro
        515                 520                 525

Glu Met Pro Cys Val Pro Gln Leu Ser Glu Pro Thr Thr Val Pro Gln
    530                 535                 540

Pro Glu Pro Glu Thr Trp Glu Gln Ile Leu Arg Arg Asn Val Leu Gln
545                 550                 555                 560

His Gly Ala Ala Ala Ala Pro Val Ser Ala Pro Thr Ser Gly Tyr Gln
                565                 570                 575

Glu Phe Val His Ala Val Glu Gln Gly Gly Thr Gln Ala Ser Ala Val
            580                 585                 590
```

```
Val Gly Leu Gly Pro Pro Gly Glu Ala Gly Tyr Lys Ala Phe Ser Ser
        595                 600                 605

Leu Leu Ala Ser Ser Ala Val Ser Pro Glu Lys Cys Gly Phe Gly Ala
    610                 615                 620

Ser Ser Gly Glu Glu Gly Tyr Lys Pro Phe Gln Asp Leu Ile Pro Gly
625                 630                 635                 640

Cys Pro Gly Asp Pro Ala Pro Val Pro Val Pro Leu Phe Thr Phe Gly
                645                 650                 655

Leu Asp Arg Glu Pro Pro Arg Ser Pro Gln Ser Ser His Leu Pro Ser
            660                 665                 670

Ser Ser Pro Glu His Leu Gly Leu Glu Pro Gly Glu Lys Val Glu Asp
        675                 680                 685

Met Pro Lys Pro Pro Leu Pro Gln Glu Gln Ala Thr Asp Pro Leu Val
    690                 695                 700

Asp Ser Leu Gly Ser Gly Ile Val Tyr Ser Ala Leu Thr Cys His Leu
705                 710                 715                 720

Cys Gly His Leu Lys Gln Cys His Gly Gln Glu Asp Gly Gly Gln Thr
                725                 730                 735

Pro Val Met Ala Ser Pro Cys Cys Gly Cys Cys Cys Gly Asp Arg Ser
            740                 745                 750

Ser Pro Pro Thr Thr Pro Leu Arg Ala Pro Asp Pro Ser Pro Gly Gly
        755                 760                 765

Val Pro Leu Glu Ala Ser Leu Cys Pro Ala Ser Leu Ala Pro Ser Gly
    770                 775                 780

Ile Ser Glu Lys Ser Lys Ser Ser Ser Ser Phe His Pro Ala Pro Gly
785                 790                 795                 800

Asn Ala Gln Ser Ser Ser Gln Thr Pro Lys Ile Val Asn Phe Val Ser
                805                 810                 815

Val Gly Pro Thr Tyr Met Arg Val Ser
            820                 825


<210>  301
<211>  862
<212>  PRT
<213>  Homo sapiens

<400>  301
```

```
Met Ala His Thr Phe Arg Gly Cys Ser Leu Ala Phe Met Phe Ile Ile
1               5                  10                  15

Thr Trp Leu Leu Ile Lys Ala Lys Ile Asp Ala Cys Lys Arg Gly Asp
            20                  25                  30

Val Thr Val Lys Pro Ser His Val Ile Leu Leu Gly Ser Thr Val Asn
        35                  40                  45

Ile Thr Cys Ser Leu Lys Pro Arg Gln Gly Cys Phe His Tyr Ser Arg
    50                  55                  60

Arg Asn Lys Leu Ile Leu Tyr Lys Phe Asp Arg Arg Ile Asn Phe His
65                  70                  75                  80

His Gly His Ser Leu Asn Ser Gln Val Thr Gly Leu Pro Leu Gly Thr
                85                  90                  95

Thr Leu Phe Val Cys Lys Leu Ala Cys Ile Asn Ser Asp Glu Ile Gln
            100                 105                 110

Ile Cys Gly Ala Glu Ile Phe Val Gly Val Ala Pro Glu Gln Pro Gln
        115                 120                 125

Asn Leu Ser Cys Ile Gln Lys Gly Glu Gln Gly Thr Val Ala Cys Thr
    130                 135                 140

Trp Glu Arg Gly Arg Asp Thr His Leu Tyr Thr Glu Tyr Thr Leu Gln
145                 150                 155                 160

Leu Ser Gly Pro Lys Asn Leu Thr Trp Gln Lys Gln Cys Lys Asp Ile
                165                 170                 175

Tyr Cys Asp Tyr Leu Asp Phe Gly Ile Asn Leu Thr Pro Glu Ser Pro
            180                 185                 190

Glu Ser Asn Phe Thr Ala Lys Val Thr Ala Val Asn Ser Leu Gly Ser
        195                 200                 205

Ser Ser Ser Leu Pro Ser Thr Phe Thr Phe Leu Asp Ile Val Arg Pro
    210                 215                 220

Leu Pro Pro Trp Asp Ile Arg Ile Lys Phe Gln Lys Ala Ser Val Ser
225                 230                 235                 240

Arg Cys Thr Leu Tyr Trp Arg Asp Glu Gly Leu Val Leu Leu Asn Arg
                245                 250                 255

Leu Arg Tyr Arg Pro Ser Asn Ser Arg Leu Trp Asn Met Val Asn Val
            260                 265                 270
```

```
Thr Lys Ala Lys Gly Arg His Asp Leu Leu Asp Leu Lys Pro Phe Thr
        275                 280                 285

Glu Tyr Glu Phe Gln Ile Ser Ser Lys Leu His Leu Tyr Lys Gly Ser
    290                 295                 300

Trp Ser Asp Trp Ser Glu Ser Leu Arg Ala Gln Thr Pro Glu Glu Glu
305                 310                 315                 320

Pro Thr Gly Met Leu Asp Val Trp Tyr Met Lys Arg His Ile Asp Tyr
                325                 330                 335

Ser Arg Gln Gln Ile Ser Leu Phe Trp Lys Asn Leu Ser Val Ser Glu
            340                 345                 350

Ala Arg Gly Lys Ile Leu His Tyr Gln Val Thr Leu Gln Glu Leu Thr
        355                 360                 365

Gly Gly Lys Ala Met Thr Gln Asn Ile Thr Gly His Thr Ser Trp Thr
    370                 375                 380

Thr Val Ile Pro Arg Thr Gly Asn Trp Ala Val Ala Val Ser Ala Ala
385                 390                 395                 400

Asn Ser Lys Gly Ser Ser Leu Pro Thr Arg Ile Asn Ile Met Asn Leu
                405                 410                 415

Cys Glu Ala Gly Leu Leu Ala Pro Arg Gln Val Ser Ala Asn Ser Glu
            420                 425                 430

Gly Met Asp Asn Ile Leu Val Thr Trp Gln Pro Pro Arg Lys Asp Pro
        435                 440                 445

Ser Ala Val Gln Glu Tyr Val Val Glu Trp Arg Glu Leu His Pro Gly
    450                 455                 460

Gly Asp Thr Gln Val Pro Leu Asn Trp Leu Arg Ser Arg Pro Tyr Asn
465                 470                 475                 480

Val Ser Ala Leu Ile Ser Glu Asn Ile Lys Ser Tyr Ile Cys Tyr Glu
                485                 490                 495

Ile Arg Val Tyr Ala Leu Ser Gly Asp Gln Gly Gly Cys Ser Ser Ile
            500                 505                 510

Leu Gly Asn Ser Lys His Lys Ala Pro Leu Ser Gly Pro His Ile Asn
        515                 520                 525

Ala Ile Thr Glu Glu Lys Gly Ser Ile Leu Ile Ser Trp Asn Ser Ile
    530                 535                 540
```

```
Pro Val Gln Glu Gln Met Gly Cys Leu Leu His Tyr Arg Ile Tyr Trp
545                 550                 555                 560

Lys Glu Arg Asp Ser Asn Ser Gln Pro Gln Leu Cys Glu Ile Pro Tyr
                565                 570                 575

Arg Val Ser Gln Asn Ser His Pro Ile Asn Ser Leu Gln Pro Arg Val
            580                 585                 590

Thr Tyr Val Leu Trp Met Thr Ala Leu Thr Ala Ala Gly Glu Ser Ser
        595                 600                 605

His Gly Asn Glu Arg Glu Phe Cys Leu Gln Gly Lys Ala Asn Trp Met
    610                 615                 620

Ala Phe Val Ala Pro Ser Ile Cys Ile Ala Ile Ile Met Val Gly Ile
625                 630                 635                 640

Phe Ser Thr His Tyr Phe Gln Gln Lys Val Phe Val Leu Leu Ala Ala
                645                 650                 655

Leu Arg Pro Gln Trp Cys Ser Arg Glu Ile Pro Asp Pro Ala Asn Ser
            660                 665                 670

Thr Cys Ala Lys Lys Tyr Pro Ile Ala Glu Glu Lys Thr Gln Leu Pro
        675                 680                 685

Leu Asp Arg Leu Leu Ile Asp Trp Pro Thr Pro Glu Asp Pro Glu Pro
    690                 695                 700

Leu Val Ile Ser Glu Val Leu His Gln Val Thr Pro Val Phe Arg His
705                 710                 715                 720

Pro Pro Cys Ser Asn Trp Pro Gln Arg Glu Lys Gly Ile Gln Gly His
                725                 730                 735

Gln Ala Ser Glu Lys Asp Met Met His Ser Ala Ser Ser Pro Pro Pro
            740                 745                 750

Pro Arg Ala Leu Gln Ala Glu Ser Arg Gln Leu Val Asp Leu Tyr Lys
        755                 760                 765

Val Leu Glu Ser Arg Gly Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
    770                 775                 780

Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
785                 790                 795                 800

Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
                805                 810                 815
```

Asp Ser Leu Glu Glu Leu Glu Pro Gln His Ile Ser Leu Ser Val Phe
820 825 830

Pro Ser Ser Ser Leu His Pro Leu Thr Phe Ser Cys Gly Asp Lys Leu
835 840 845

Thr Leu Asp Gln Leu Lys Met Arg Cys Asp Ser Leu Met Leu
850 855 860

<210> 302
<211> 662
<212> PRT
<213> Homo sapiens

<400> 302

Met Glu Pro Leu Val Thr Trp Val Val Pro Leu Leu Phe Leu Phe Leu
1 5 10 15

Leu Ser Arg Gln Gly Ala Ala Cys Arg Thr Ser Glu Cys Cys Phe Gln
20 25 30

Asp Pro Pro Tyr Pro Asp Ala Asp Ser Gly Ser Ala Ser Gly Pro Arg
35 40 45

Asp Leu Arg Cys Tyr Arg Ile Ser Ser Asp Arg Tyr Glu Cys Ser Trp
50 55 60

Gln Tyr Glu Gly Pro Thr Ala Gly Val Ser His Phe Leu Arg Cys Cys
65 70 75 80

Leu Ser Ser Gly Arg Cys Cys Tyr Phe Ala Ala Gly Ser Ala Thr Arg
85 90 95

Leu Gln Phe Ser Asp Gln Ala Gly Val Ser Val Leu Tyr Thr Val Thr
100 105 110

Leu Trp Val Glu Ser Trp Ala Arg Asn Gln Thr Glu Lys Ser Pro Glu
115 120 125

Val Thr Leu Gln Leu Tyr Asn Ser Val Lys Tyr Glu Pro Pro Leu Gly
130 135 140

Asp Ile Lys Val Ser Lys Leu Ala Gly Gln Leu Arg Met Glu Trp Glu
145 150 155 160

Thr Pro Asp Asn Gln Val Gly Ala Glu Val Gln Phe Arg His Arg Thr
165 170 175

Pro Ser Ser Pro Trp Lys Leu Gly Asp Cys Gly Pro Gln Asp Asp Asp
180 185 190

Thr Glu Ser Cys Leu Cys Pro Leu Glu Met Asn Val Ala Gln Glu Phe

195 200 205

Gln Leu Arg Arg Arg Gln Leu Gly Ser Gln Gly Ser Ser Trp Ser Lys
210 215 220

Trp Ser Ser Pro Val Cys Val Pro Pro Glu Asn Pro Pro Gln Pro Gln
225 230 235 240

Val Arg Phe Ser Val Glu Gln Leu Gly Gln Asp Gly Arg Arg Arg Leu
245 250 255

Thr Leu Lys Glu Gln Pro Thr Gln Leu Glu Leu Pro Glu Gly Cys Gln
260 265 270

Gly Leu Ala Pro Gly Thr Glu Val Thr Tyr Arg Leu Gln Leu His Met
275 280 285

Leu Ser Cys Pro Cys Lys Ala Lys Ala Thr Arg Thr Leu His Leu Gly
290 295 300

Lys Met Pro Tyr Leu Ser Gly Ala Ala Tyr Asn Val Ala Val Ile Ser
305 310 315 320

Ser Asn Gln Phe Gly Pro Gly Leu Asn Gln Thr Trp His Ile Pro Ala
325 330 335

Asp Thr His Thr Glu Pro Val Ala Leu Asn Ile Ser Val Gly Thr Asn
340 345 350

Gly Thr Thr Met Tyr Trp Pro Ala Arg Ala Gln Ser Met Thr Tyr Cys
355 360 365

Ile Glu Trp Gln Pro Val Gly Gln Asp Gly Gly Leu Ala Thr Cys Ser
370 375 380

Leu Thr Ala Pro Gln Asp Pro Asp Pro Ala Gly Met Ala Thr Tyr Ser
385 390 395 400

Trp Ser Arg Glu Ser Gly Ala Met Gly Gln Glu Lys Cys Tyr Tyr Ile
405 410 415

Thr Ile Phe Ala Ser Ala His Pro Glu Lys Leu Thr Leu Trp Ser Thr
420 425 430

Val Leu Ser Thr Tyr His Phe Gly Gly Asn Ala Ser Ala Ala Gly Thr
435 440 445

Pro His His Val Ser Val Lys Asn His Ser Leu Asp Ser Val Ser Val
450 455 460

Asp Trp Ala Pro Ser Leu Leu Ser Thr Cys Pro Gly Val Leu Lys Glu

465 470 475 480

Tyr Val Val Arg Cys Arg Asp Glu Asp Ser Lys Gln Val Ser Glu His
485 490 495

Pro Val Gln Pro Thr Glu Thr Gln Val Thr Leu Ser Gly Leu Arg Ala
500 505 510

Gly Val Ala Tyr Thr Val Gln Val Arg Ala Asp Thr Ala Trp Leu Arg
515 520 525

Gly Val Trp Ser Gln Pro Gln Arg Phe Ser Ile Glu Val Gln Val Ser
530 535 540

Asp Trp Leu Ile Phe Phe Ala Ser Leu Gly Ser Phe Leu Ser Ile Leu
545 550 555 560

Leu Val Gly Val Leu Gly Tyr Leu Gly Leu Asn Arg Ala Ala Arg His
565 570 575

Leu Cys Pro Pro Leu Pro Thr Pro Cys Ala Ser Ser Ala Ile Glu Phe
580 585 590

Pro Gly Gly Lys Glu Thr Trp Gln Trp Ile Asn Pro Val Asp Phe Gln
595 600 605

Glu Glu Ala Ser Leu Gln Glu Ala Leu Val Val Glu Met Ser Trp Asp
610 615 620

Lys Gly Glu Arg Thr Glu Pro Leu Glu Lys Thr Glu Leu Pro Glu Gly
625 630 635 640

Ala Pro Glu Leu Ala Leu Asp Thr Glu Leu Ser Leu Glu Asp Gly Asp
645 650 655

Arg Cys Lys Ala Lys Met
660

<210> 303
<211> 521
<212> PRT
<213> Homo sapiens

<400> 303

Met Gly Leu Gly Arg Cys Ile Trp Glu Gly Trp Thr Leu Glu Ser Glu
1 5 10 15

Ala Leu Arg Arg Asp Met Gly Thr Trp Leu Leu Ala Cys Ile Cys Ile
20 25 30

Cys Thr Cys Val Cys Leu Gly Val Ser Val Thr Gly Glu Gly Gln Gly
35 40 45

```
Pro Arg Ser Arg Thr Phe Thr Cys Leu Thr Asn Asn Ile Leu Arg Ile
    50                  55                  60

Asp Cys His Trp Ser Ala Pro Glu Leu Gly Gln Gly Ser Ser Pro Trp
65                  70                  75                  80

Leu Leu Phe Thr Ser Asn Gln Ala Pro Gly Gly Thr His Lys Cys Ile
                85                  90                  95

Leu Arg Gly Ser Glu Cys Thr Val Val Leu Pro Pro Glu Ala Val Leu
            100                 105                 110

Val Pro Ser Asp Asn Phe Thr Ile Thr Phe His His Cys Met Ser Gly
        115                 120                 125

Arg Glu Gln Val Ser Leu Val Asp Pro Glu Tyr Leu Pro Arg Arg His
    130                 135                 140

Val Lys Leu Asp Pro Pro Ser Asp Leu Gln Ser Asn Ile Ser Ser Gly
145                 150                 155                 160

His Cys Ile Leu Thr Trp Ser Ile Ser Pro Ala Leu Glu Pro Met Thr
                165                 170                 175

Thr Leu Leu Ser Tyr Glu Leu Ala Phe Lys Lys Gln Glu Glu Ala Trp
            180                 185                 190

Glu Gln Ala Gln His Arg Asp His Ile Val Gly Val Thr Trp Leu Ile
        195                 200                 205

Leu Glu Ala Phe Glu Leu Asp Pro Gly Phe Ile His Glu Ala Arg Leu
    210                 215                 220

Arg Val Gln Met Ala Thr Leu Glu Asp Asp Val Val Glu Glu Glu Arg
225                 230                 235                 240

Tyr Thr Gly Gln Trp Ser Glu Trp Ser Gln Pro Val Cys Phe Gln Ala
                245                 250                 255

Pro Gln Arg Gln Gly Pro Leu Ile Pro Pro Trp Gly Trp Pro Gly Asn
            260                 265                 270

Thr Leu Val Ala Val Ser Ile Phe Leu Leu Leu Thr Gly Pro Thr Tyr
        275                 280                 285

Leu Leu Phe Lys Leu Ser Pro Arg Val Lys Arg Ile Phe Tyr Gln Asn
    290                 295                 300

Val Pro Ser Pro Ala Met Phe Phe Gln Pro Leu Tyr Ser Val His Asn
305                 310                 315                 320
```

```
Gly Asn Phe Gln Thr Trp Met Gly Ala His Gly Ala Gly Val Leu Leu
                325                 330                 335

Ser Gln Asp Cys Ala Gly Thr Pro Gln Gly Ala Leu Glu Pro Cys Val
            340                 345                 350

Gln Glu Ala Thr Ala Leu Leu Thr Cys Gly Pro Ala Arg Pro Trp Lys
        355                 360                 365

Ser Val Ala Leu Glu Glu Glu Gln Glu Gly Pro Gly Thr Arg Leu Pro
    370                 375                 380

Gly Asn Leu Ser Ser Glu Asp Val Leu Pro Ala Gly Cys Thr Glu Trp
385                 390                 395                 400

Arg Val Gln Thr Leu Ala Tyr Leu Pro Gln Glu Asp Trp Ala Pro Thr
                405                 410                 415

Ser Leu Thr Arg Pro Ala Pro Pro Asp Ser Glu Gly Ser Arg Ser Ser
            420                 425                 430

Ser Ser Ser Ser Ser Ser Asn Asn Asn Asn Tyr Cys Ala Leu Gly Cys
        435                 440                 445

Tyr Gly Gly Trp His Leu Ser Ala Leu Pro Gly Asn Thr Gln Ser Ser
    450                 455                 460

Gly Pro Ile Pro Ala Leu Ala Cys Gly Leu Ser Cys Asp His Gln Gly
465                 470                 475                 480

Leu Glu Thr Gln Gln Gly Val Ala Trp Val Leu Ala Gly His Cys Gln
                485                 490                 495

Arg Pro Gly Leu His Glu Asp Leu Gln Gly Met Leu Leu Pro Ser Val
            500                 505                 510

Leu Ser Lys Ala Arg Ser Trp Thr Phe
        515                 520


<210>  304
<211>  578
<212>  PRT
<213>  Homo sapiens

<400>  304

Met Leu Pro Cys Leu Val Val Leu Leu Ala Ala Leu Leu Ser Leu Arg
1               5                   10                  15

Leu Gly Ser Asp Ala His Gly Thr Glu Leu Pro Ser Pro Pro Ser Val
            20                  25                  30
```

```
Trp Phe Glu Ala Glu Phe Phe His His Ile Leu His Trp Thr Pro Ile
        35                  40                  45

Pro Asn Gln Ser Glu Ser Thr Cys Tyr Glu Val Ala Leu Leu Arg Tyr
    50                  55                  60

Gly Ile Glu Ser Trp Asn Ser Ile Ser Asn Cys Ser Gln Thr Leu Ser
65                  70                  75                  80

Tyr Asp Leu Thr Ala Val Thr Leu Asp Leu Tyr His Ser Asn Gly Tyr
                85                  90                  95

Arg Ala Arg Val Arg Ala Val Asp Gly Ser Arg His Ser Asn Trp Thr
            100                 105                 110

Val Thr Asn Thr Arg Phe Ser Val Asp Glu Val Thr Leu Thr Val Gly
        115                 120                 125

Ser Val Asn Leu Glu Ile His Asn Gly Phe Ile Leu Gly Lys Ile Gln
    130                 135                 140

Leu Pro Arg Pro Lys Met Ala Pro Ala Asn Asp Thr Tyr Glu Ser Ile
145                 150                 155                 160

Phe Ser His Phe Arg Glu Tyr Glu Ile Ala Ile Arg Lys Val Pro Gly
                165                 170                 175

Asn Phe Thr Phe Thr His Lys Lys Val Lys His Glu Asn Phe Ser Leu
            180                 185                 190

Leu Thr Ser Gly Glu Val Gly Glu Phe Cys Val Gln Val Lys Pro Ser
        195                 200                 205

Val Ala Ser Arg Ser Asn Lys Gly Met Trp Ser Lys Glu Glu Cys Ile
    210                 215                 220

Ser Leu Thr Arg Gln Tyr Phe Thr Val Thr Asn Val Ile Ile Phe Phe
225                 230                 235                 240

Ala Phe Val Leu Leu Leu Ser Gly Ala Leu Ala Tyr Cys Leu Ala Leu
                245                 250                 255

Gln Leu Tyr Val Arg Arg Arg Lys Lys Leu Pro Ser Val Leu Leu Phe
            260                 265                 270

Lys Lys Pro Ser Pro Phe Ile Phe Ile Ser Gln Arg Pro Ser Pro Glu
        275                 280                 285

Thr Gln Asp Thr Ile His Pro Leu Asp Glu Glu Ala Phe Leu Lys Val
    290                 295                 300
```

```
Ser Pro Glu Leu Lys Asn Leu Asp Leu His Gly Ser Thr Asp Ser Gly
305                 310                 315                 320

Phe Gly Ser Thr Lys Pro Ser Leu Gln Thr Glu Glu Pro Gln Phe Leu
                325                 330                 335

Leu Pro Asp Pro His Pro Gln Ala Asp Arg Thr Leu Gly Asn Arg Glu
            340                 345                 350

Pro Pro Val Leu Gly Asp Ser Cys Ser Ser Gly Ser Ser Asn Ser Thr
        355                 360                 365

Asp Ser Gly Ile Cys Leu Gln Glu Pro Ser Leu Ser Pro Ser Thr Gly
    370                 375                 380

Pro Thr Trp Glu Gln Gln Val Gly Ser Asn Ser Arg Gly Gln Asp Asp
385                 390                 395                 400

Ser Gly Ile Asp Leu Val Gln Asn Ser Glu Gly Arg Ala Gly Asp Thr
                405                 410                 415

Gln Gly Gly Ser Ala Leu Gly His His Ser Pro Pro Glu Pro Glu Val
            420                 425                 430

Pro Gly Glu Glu Asp Pro Ala Ala Val Ala Phe Gln Gly Tyr Leu Arg
        435                 440                 445

Gln Thr Arg Cys Ala Glu Glu Lys Ala Thr Lys Thr Gly Cys Leu Glu
    450                 455                 460

Glu Glu Ser Pro Leu Thr Asp Gly Leu Gly Pro Lys Phe Gly Arg Cys
465                 470                 475                 480

Leu Val Asp Glu Ala Gly Leu His Pro Pro Ala Leu Ala Lys Gly Tyr
                485                 490                 495

Leu Lys Gln Asp Pro Leu Glu Met Thr Leu Ala Ser Ser Gly Ala Pro
            500                 505                 510

Thr Gly Gln Trp Asn Gln Pro Thr Glu Glu Trp Ser Leu Leu Ala Leu
        515                 520                 525

Ser Ser Cys Ser Asp Leu Gly Ile Ser Asp Trp Ser Phe Ala His Asp
    530                 535                 540

Leu Ala Pro Leu Gly Cys Val Ala Ala Pro Gly Gly Leu Leu Gly Ser
545                 550                 555                 560

Phe Asn Ser Asp Leu Val Thr Leu Pro Leu Ile Ser Ser Leu Gln Ser
                565                 570                 575
```

Ser Glu

<210> 305
<211> 325
<212> PRT
<213> Homo sapiens

<400> 305

```
Met Ala Trp Ser Leu Gly Ser Trp Leu Gly Gly Cys Leu Leu Val Ser
1               5                  10                  15

Ala Leu Gly Met Val Pro Pro Pro Glu Asn Val Arg Met Asn Ser Val
            20                  25                  30

Asn Phe Lys Asn Ile Leu Gln Trp Glu Ser Pro Ala Phe Ala Lys Gly
        35                  40                  45

Asn Leu Thr Phe Thr Ala Gln Tyr Leu Ser Tyr Arg Ile Phe Gln Asp
    50                  55                  60

Lys Cys Met Asn Thr Thr Leu Thr Glu Cys Asp Phe Ser Ser Leu Ser
65                  70                  75                  80

Lys Tyr Gly Asp His Thr Leu Arg Val Arg Ala Glu Phe Ala Asp Glu
                85                  90                  95

His Ser Asp Trp Val Asn Ile Thr Phe Cys Pro Val Asp Asp Thr Ile
            100                 105                 110

Ile Gly Pro Pro Gly Met Gln Val Glu Val Leu Ala Asp Ser Leu His
        115                 120                 125

Met Arg Phe Leu Ala Pro Lys Ile Glu Asn Glu Tyr Glu Thr Trp Thr
    130                 135                 140

Met Lys Asn Val Tyr Asn Ser Trp Thr Tyr Asn Val Gln Tyr Trp Lys
145                 150                 155                 160

Asn Gly Thr Asp Glu Lys Phe Gln Ile Thr Pro Gln Tyr Asp Phe Glu
                165                 170                 175

Val Leu Arg Asn Leu Glu Pro Trp Thr Thr Tyr Cys Val Gln Val Arg
            180                 185                 190

Gly Phe Leu Pro Asp Arg Asn Lys Ala Gly Glu Trp Ser Glu Pro Val
        195                 200                 205

Cys Glu Gln Thr Thr His Asp Glu Thr Val Pro Ser Trp Met Val Ala
    210                 215                 220
```

Val Ile Leu Met Ala Ser Val Phe Met Val Cys Leu Ala Leu Leu Gly
225 230 235 240

Cys Phe Ala Leu Leu Trp Cys Val Tyr Lys Lys Thr Lys Tyr Ala Phe
245 250 255

Ser Pro Arg Asn Ser Leu Pro Gln His Leu Lys Glu Phe Leu Gly His
260 265 270

Pro His His Asn Thr Leu Leu Phe Phe Ser Phe Pro Leu Ser Asp Glu
275 280 285

Asn Asp Val Phe Asp Lys Leu Ser Val Ile Ala Glu Asp Ser Glu Ser
290 295 300

Gly Lys Gln Asn Pro Gly Asp Ser Cys Ser Leu Gly Thr Pro Pro Gly
305 310 315 320

Gln Gly Pro Gln Ser
325

<210> 306
<211> 468
<212> PRT
<213> Homo sapiens

<400> 306

Met Leu Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro
1 5 10 15

Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg
20 25 30

Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro
35 40 45

Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys
50 55 60

Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg
65 70 75 80

Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys
85 90 95

Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val
100 105 110

Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser
115 120 125

Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr

130 135 140

Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp
145 150 155 160

Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys
165 170 175

Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met
180 185 190

Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe
195 200 205

Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val
210 215 220

Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp
225 230 235 240

Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg
245 250 255

Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp
260 265 270

Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His
275 280 285

Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser
290 295 300

Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser
305 310 315 320

Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr
325 330 335

Asn Lys Asp Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr
340 345 350

Ser Leu Pro Val Gln Asp Ser Ser Ser Val Pro Leu Pro Thr Phe Leu
355 360 365

Val Ala Gly Gly Ser Leu Ala Phe Gly Thr Leu Leu Cys Ile Ala Ile
370 375 380

Val Leu Arg Phe Lys Lys Thr Trp Lys Leu Arg Ala Leu Lys Glu Gly
385 390 395 400

Lys Thr Ser Met His Pro Pro Tyr Ser Leu Gly Gln Leu Val Pro Glu

405 410 415

Arg Pro Arg Pro Thr Pro Val Leu Val Pro Leu Ile Ser Pro Pro Val
420 425 430

Ser Pro Ser Ser Leu Gly Ser Asp Asn Thr Ser Ser His Asn Arg Pro
435 440 445

Asp Ala Arg Asp Pro Arg Ser Pro Tyr Asp Ile Ser Asn Thr Asp Tyr
450 455 460

Phe Phe Pro Arg
465

<210> 307
<211> 378
<212> PRT
<213> Homo sapiens

<400> 307

Met Val Leu Leu Trp Leu Thr Leu Leu Leu Ile Ala Leu Pro Cys Leu
1 5 10 15

Leu Gln Thr Lys Glu Asp Pro Asn Pro Pro Ile Thr Asn Leu Arg Met
20 25 30

Lys Ala Lys Ala Gln Gln Leu Thr Trp Asp Leu Asn Arg Asn Val Thr
35 40 45

Asp Ile Glu Cys Val Lys Asp Ala Asp Tyr Ser Met Pro Ala Val Asn
50 55 60

Asn Ser Tyr Cys Gln Phe Gly Ala Ile Ser Leu Cys Glu Val Thr Asn
65 70 75 80

Tyr Thr Val Arg Val Ala Asn Pro Pro Phe Ser Thr Trp Ile Leu Phe
85 90 95

Pro Glu Asn Ser Gly Lys Pro Trp Ala Gly Ala Glu Asn Leu Thr Cys
100 105 110

Trp Ile His Asp Val Asp Phe Leu Ser Cys Ser Trp Ala Val Gly Pro
115 120 125

Gly Ala Pro Ala Asp Val Gln Tyr Asp Leu Tyr Leu Asn Val Ala Asn
130 135 140

Arg Arg Gln Gln Tyr Glu Cys Leu His Tyr Lys Thr Asp Ala Gln Gly
145 150 155 160

Thr Arg Ile Gly Cys Arg Phe Asp Asp Ile Ser Arg Leu Ser Ser Gly
165 170 175

```
Ser Gln Ser Ser His Ile Leu Val Arg Gly Arg Ser Ala Ala Phe Gly
            180                 185                 190

Ile Pro Cys Thr Asp Lys Phe Val Val Phe Ser Gln Ile Glu Ile Leu
        195                 200                 205

Thr Pro Pro Asn Met Thr Ala Lys Cys Asn Lys Thr His Ser Phe Met
    210                 215                 220

His Trp Lys Met Arg Ser His Phe Asn Arg Lys Phe Arg Tyr Glu Leu
225                 230                 235                 240

Gln Ile Gln Lys Arg Met Gln Pro Val Ile Thr Glu Gln Val Arg Asp
                245                 250                 255

Arg Thr Ser Phe Gln Leu Leu Asn Pro Gly Thr Tyr Thr Val Gln Ile
            260                 265                 270

Arg Ala Arg Glu Arg Val Tyr Glu Phe Leu Ser Ala Trp Ser Thr Pro
        275                 280                 285

Gln Arg Phe Glu Cys Asp Gln Glu Glu Gly Ala Asn Thr Arg Ala Trp
    290                 295                 300

Arg Thr Ser Leu Leu Ile Ala Leu Gly Thr Leu Leu Ala Leu Val Cys
305                 310                 315                 320

Val Phe Val Ile Cys Arg Arg Tyr Leu Val Met Gln Arg Leu Phe Pro
                325                 330                 335

Arg Ile Pro His Met Lys Asp Pro Ile Gly Asp Ser Phe Gln Asn Asp
            340                 345                 350

Lys Leu Val Val Trp Glu Ala Gly Lys Ala Gly Leu Glu Glu Cys Leu
        355                 360                 365

Val Thr Glu Val Gln Val Val Gln Lys Thr
    370                 375


<210>  308
<211>  400
<212>  PRT
<213>  Homo sapiens

<400>  308

Met Leu Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro
1               5                   10                  15

Ala Phe Leu Leu Ile Pro Glu Lys Ser Asp Leu Arg Thr Val Ala Pro
            20                  25                  30
```

```
Ala Ser Ser Leu Asn Val Arg Phe Asp Ser Arg Thr Met Asn Leu Ser
        35                  40                  45

Trp Asp Cys Gln Glu Asn Thr Thr Phe Ser Lys Cys Phe Leu Thr Asp
    50                  55                  60

Lys Lys Asn Arg Val Val Glu Pro Arg Leu Ser Asn Asn Glu Cys Ser
65                  70                  75                  80

Cys Thr Phe Arg Glu Ile Cys Leu His Glu Gly Val Thr Phe Glu Val
                85                  90                  95

His Val Asn Thr Ser Gln Arg Gly Phe Gln Gln Lys Leu Leu Tyr Pro
            100                 105                 110

Asn Ser Gly Arg Glu Gly Thr Ala Ala Gln Asn Phe Ser Cys Phe Ile
        115                 120                 125

Tyr Asn Ala Asp Leu Met Asn Cys Thr Trp Ala Arg Gly Pro Thr Ala
    130                 135                 140

Pro Arg Asp Val Gln Tyr Phe Leu Tyr Ile Arg Asn Ser Lys Arg Arg
145                 150                 155                 160

Arg Glu Ile Arg Cys Pro Tyr Tyr Ile Gln Asp Ser Gly Thr His Val
                165                 170                 175

Gly Cys His Leu Asp Asn Leu Ser Gly Leu Thr Ser Arg Asn Tyr Phe
            180                 185                 190

Leu Val Asn Gly Thr Ser Arg Glu Ile Gly Ile Gln Phe Phe Asp Ser
        195                 200                 205

Leu Leu Asp Thr Lys Lys Ile Glu Arg Phe Asn Pro Pro Ser Asn Val
    210                 215                 220

Thr Val Arg Cys Asn Thr Thr His Cys Leu Val Arg Trp Lys Gln Pro
225                 230                 235                 240

Arg Thr Tyr Gln Lys Leu Ser Tyr Leu Asp Phe Gln Tyr Gln Leu Asp
                245                 250                 255

Val His Arg Lys Asn Thr Gln Pro Gly Thr Glu Asn Leu Leu Ile Asn
            260                 265                 270

Val Ser Gly Asp Leu Glu Asn Arg Tyr Asn Phe Pro Ser Ser Glu Pro
        275                 280                 285

Arg Ala Lys His Ser Val Lys Ile Arg Ala Ala Asp Val Arg Ile Leu
    290                 295                 300
```

```
Asn Trp Ser Ser Trp Ser Glu Ala Ile Glu Phe Gly Ser Asp Asp Gly
305                 310                 315                 320


Asn Leu Gly Ser Val Tyr Ile Tyr Val Leu Leu Ile Val Gly Thr Leu
                325                 330                 335


Val Cys Gly Ile Val Leu Gly Phe Leu Phe Lys Arg Phe Leu Arg Ile
            340                 345                 350


Gln Arg Leu Phe Pro Pro Val Pro Gln Ile Lys Asp Lys Leu Asn Asp
        355                 360                 365


Asn His Glu Val Glu Asp Glu Ile Ile Trp Glu Glu Phe Thr Pro Glu
    370                 375                 380


Glu Gly Lys Gly Tyr Arg Glu Glu Val Leu Thr Val Lys Glu Ile Thr
385                 390                 395                 400


<210>  309
<211>  897
<212>  PRT
<213>  Homo sapiens

<400>  309

Met Val Leu Ala Gln Gly Leu Leu Ser Met Ala Leu Leu Ala Leu Cys
1               5                   10                  15


Trp Glu Arg Ser Leu Ala Gly Ala Glu Glu Thr Ile Pro Leu Gln Thr
            20                  25                  30


Leu Arg Cys Tyr Asn Asp Tyr Thr Ser His Ile Thr Cys Arg Trp Ala
        35                  40                  45


Asp Thr Gln Asp Ala Gln Arg Leu Val Asn Val Thr Leu Ile Arg Arg
    50                  55                  60


Val Asn Glu Asp Leu Leu Glu Pro Val Ser Cys Asp Leu Ser Asp Asp
65                  70                  75                  80


Met Pro Trp Ser Ala Cys Pro His Pro Arg Cys Val Pro Arg Arg Cys
                85                  90                  95


Val Ile Pro Cys Gln Ser Phe Val Val Thr Asp Val Asp Tyr Phe Ser
            100                 105                 110


Phe Gln Pro Asp Arg Pro Leu Gly Thr Arg Leu Thr Val Thr Leu Thr
        115                 120                 125


Gln His Val Gln Pro Pro Glu Pro Arg Asp Leu Gln Ile Ser Thr Asp
    130                 135                 140
```

```
Gln Asp His Phe Leu Leu Thr Trp Ser Val Ala Leu Gly Ser Pro Gln
145                 150                 155                 160

Ser His Trp Leu Ser Pro Gly Asp Leu Glu Phe Glu Val Val Tyr Lys
                165                 170                 175

Arg Leu Gln Asp Ser Trp Glu Asp Ala Ala Ile Leu Leu Ser Asn Thr
            180                 185                 190

Ser Gln Ala Thr Leu Gly Pro Glu His Leu Met Pro Ser Ser Thr Tyr
        195                 200                 205

Val Ala Arg Val Arg Thr Arg Leu Ala Pro Gly Ser Arg Leu Ser Gly
    210                 215                 220

Arg Pro Ser Lys Trp Ser Pro Glu Val Cys Trp Asp Ser Gln Pro Gly
225                 230                 235                 240

Asp Glu Ala Gln Pro Gln Asn Leu Glu Cys Phe Phe Asp Gly Ala Ala
                245                 250                 255

Val Leu Ser Cys Ser Trp Glu Val Arg Lys Glu Val Ala Ser Ser Val
            260                 265                 270

Ser Phe Gly Leu Phe Tyr Lys Pro Ser Pro Asp Ala Gly Glu Glu Glu
        275                 280                 285

Cys Ser Pro Val Leu Arg Glu Gly Leu Gly Ser Leu His Thr Arg His
    290                 295                 300

His Cys Gln Ile Pro Val Pro Asp Pro Ala Thr His Gly Gln Tyr Ile
305                 310                 315                 320

Val Ser Val Gln Pro Arg Arg Ala Glu Lys His Ile Lys Ser Ser Val
                325                 330                 335

Asn Ile Gln Met Ala Pro Pro Ser Leu Asn Val Thr Lys Asp Gly Asp
            340                 345                 350

Ser Tyr Ser Leu Arg Trp Glu Thr Met Lys Met Arg Tyr Glu His Ile
        355                 360                 365

Asp His Thr Phe Glu Ile Gln Tyr Arg Lys Asp Thr Ala Thr Trp Lys
    370                 375                 380

Asp Ser Lys Thr Glu Thr Leu Gln Asn Ala His Ser Met Ala Leu Pro
385                 390                 395                 400

Ala Leu Glu Pro Ser Thr Arg Tyr Trp Ala Arg Val Arg Val Arg Thr
                405                 410                 415
```

```
Ser Arg Thr Gly Tyr Asn Gly Ile Trp Ser Glu Trp Ser Glu Ala Arg
            420                 425                 430

Ser Trp Asp Thr Glu Ser Val Leu Pro Met Trp Val Leu Ala Leu Ile
        435                 440                 445

Val Ile Phe Leu Thr Ile Ala Val Leu Leu Ala Leu Arg Phe Cys Gly
    450                 455                 460

Ile Tyr Gly Tyr Arg Leu Arg Arg Lys Trp Glu Glu Lys Ile Pro Asn
465                 470                 475                 480

Pro Ser Lys Ser His Leu Phe Gln Asn Gly Ser Ala Glu Leu Trp Pro
                485                 490                 495

Pro Gly Ser Met Ser Ala Phe Thr Ser Gly Ser Pro Pro His Gln Gly
            500                 505                 510

Pro Trp Gly Ser Arg Phe Pro Glu Leu Glu Gly Val Phe Pro Val Gly
        515                 520                 525

Phe Gly Asp Ser Glu Val Ser Pro Leu Thr Ile Glu Asp Pro Lys His
    530                 535                 540

Val Cys Asp Pro Pro Ser Gly Pro Asp Thr Thr Pro Ala Ala Ser Asp
545                 550                 555                 560

Leu Pro Thr Glu Gln Pro Pro Ser Pro Gln Pro Gly Pro Pro Ala Ala
                565                 570                 575

Ser His Thr Pro Glu Lys Gln Ala Ser Ser Phe Asp Phe Asn Gly Pro
            580                 585                 590

Tyr Leu Gly Pro Pro His Ser Arg Ser Leu Pro Asp Ile Leu Gly Gln
        595                 600                 605

Pro Glu Pro Pro Gln Glu Gly Gly Ser Gln Lys Ser Pro Pro Pro Gly
    610                 615                 620

Ser Leu Glu Tyr Leu Cys Leu Pro Ala Gly Gly Gln Val Gln Leu Val
625                 630                 635                 640

Pro Leu Ala Gln Ala Met Gly Pro Gly Gln Ala Val Glu Val Glu Arg
                645                 650                 655

Arg Pro Ser Gln Gly Ala Ala Gly Ser Pro Ser Leu Glu Ser Gly Gly
            660                 665                 670

Gly Pro Ala Pro Pro Ala Leu Gly Pro Arg Val Gly Gly Gln Asp Gln
        675                 680                 685
```

Lys Asp Ser Pro Val Ala Ile Pro Met Ser Ser Gly Asp Thr Glu Asp
690 695 700

Pro Gly Val Ala Ser Gly Tyr Val Ser Ser Ala Asp Leu Val Phe Thr
705 710 715 720

Pro Asn Ser Gly Ala Ser Ser Val Ser Leu Val Pro Ser Leu Gly Leu
725 730 735

Pro Ser Asp Gln Thr Pro Ser Leu Cys Pro Gly Leu Ala Ser Gly Pro
740 745 750

Pro Gly Ala Pro Gly Pro Val Lys Ser Gly Phe Glu Gly Tyr Val Glu
755 760 765

Leu Pro Pro Ile Glu Gly Arg Ser Pro Arg Ser Pro Arg Asn Asn Pro
770 775 780

Val Pro Pro Glu Ala Lys Ser Pro Val Leu Asn Pro Gly Glu Arg Pro
785 790 795 800

Ala Asp Val Ser Pro Thr Ser Pro Gln Pro Glu Gly Leu Leu Val Leu
805 810 815

Gln Gln Val Gly Asp Tyr Cys Phe Leu Pro Gly Leu Gly Pro Gly Pro
820 825 830

Leu Ser Leu Arg Ser Lys Pro Ser Ser Pro Gly Pro Gly Pro Glu Ile
835 840 845

Lys Asn Leu Asp Gln Ala Phe Gln Val Lys Lys Pro Pro Gly Gln Ala
850 855 860

Val Pro Gln Val Pro Val Ile Gln Leu Phe Lys Ala Leu Lys Gln Gln
865 870 875 880

Asp Tyr Leu Ser Leu Pro Pro Trp Glu Val Asn Lys Pro Gly Glu Val
885 890 895

Cys

<210> 310
<211> 420
<212> PRT
<213> Homo sapiens

<400> 310

Met Ile Ile Val Ala His Val Leu Leu Ile Leu Leu Gly Ala Thr Glu
1 5 10 15

Ile Leu Gln Ala Asp Leu Leu Pro Asp Glu Lys Ile Ser Leu Leu Pro

20 25 30

Pro Val Asn Phe Thr Ile Lys Val Thr Gly Leu Ala Gln Val Leu Leu
35 40 45

Gln Trp Lys Pro Asn Pro Asp Gln Glu Gln Arg Asn Val Asn Leu Glu
50 55 60

Tyr Gln Val Lys Ile Asn Ala Pro Lys Glu Asp Asp Tyr Glu Thr Arg
65 70 75 80

Ile Thr Glu Ser Lys Cys Val Thr Ile Leu His Lys Gly Phe Ser Ala
85 90 95

Ser Val Arg Thr Ile Leu Gln Asn Asp His Ser Leu Leu Ala Ser Ser
100 105 110

Trp Ala Ser Ala Glu Leu His Ala Pro Pro Gly Ser Pro Gly Thr Ser
115 120 125

Ile Val Asn Leu Thr Cys Thr Thr Asn Thr Thr Glu Asp Asn Tyr Ser
130 135 140

Arg Leu Arg Ser Tyr Gln Val Ser Leu His Cys Thr Trp Leu Val Gly
145 150 155 160

Thr Asp Ala Pro Glu Asp Thr Gln Tyr Phe Leu Tyr Tyr Arg Tyr Gly
165 170 175

Ser Trp Thr Glu Glu Cys Gln Glu Tyr Ser Lys Asp Thr Leu Gly Arg
180 185 190

Asn Ile Ala Cys Trp Phe Pro Arg Thr Phe Ile Leu Ser Lys Gly Arg
195 200 205

Asp Trp Leu Ala Val Leu Val Asn Gly Ser Ser Lys His Ser Ala Ile
210 215 220

Arg Pro Phe Asp Gln Leu Phe Ala Leu His Ala Ile Asp Gln Ile Asn
225 230 235 240

Pro Pro Leu Asn Val Thr Ala Glu Ile Glu Gly Thr Arg Leu Ser Ile
245 250 255

Gln Trp Glu Lys Pro Val Ser Ala Phe Pro Ile His Cys Phe Asp Tyr
260 265 270

Glu Val Lys Ile His Asn Thr Arg Asn Gly Tyr Leu Gln Ile Glu Lys
275 280 285

Leu Met Thr Asn Ala Phe Ile Ser Ile Ile Asp Asp Leu Ser Lys Tyr

290 295 300

Asp Val Gln Val Arg Ala Ala Val Ser Ser Met Cys Arg Glu Ala Gly
305 310 315 320

Leu Trp Ser Glu Trp Ser Gln Pro Ile Tyr Val Gly Asn Asp Glu His
325 330 335

Lys Pro Leu Arg Glu Trp Phe Val Ile Val Ile Met Ala Thr Ile Cys
340 345 350

Phe Ile Leu Leu Ile Leu Ser Leu Ile Cys Lys Ile Cys His Leu Trp
355 360 365

Ile Lys Leu Phe Pro Pro Ile Pro Ala Pro Lys Ser Asn Ile Lys Asp
370 375 380

Leu Phe Val Thr Thr Asn Tyr Glu Lys Ala Gly Ser Ser Glu Thr Glu
385 390 395 400

Ile Glu Val Ile Cys Tyr Ile Glu Lys Pro Gly Val Glu Thr Leu Glu
405 410 415

Asp Ser Val Phe
420

<210> 311
<211> 459
<212> PRT
<213> Homo sapiens

<400> 311

Met Thr Ile Leu Gly Thr Thr Phe Gly Met Val Phe Ser Leu Leu Gln
1 5 10 15

Val Val Ser Gly Glu Ser Gly Tyr Ala Gln Asn Gly Asp Leu Glu Asp
20 25 30

Ala Glu Leu Asp Asp Tyr Ser Phe Ser Cys Tyr Ser Gln Leu Glu Val
35 40 45

Asn Gly Ser Gln His Ser Leu Thr Cys Ala Phe Glu Asp Pro Asp Val
50 55 60

Asn Thr Thr Asn Leu Glu Phe Glu Ile Cys Gly Ala Leu Val Glu Val
65 70 75 80

Lys Cys Leu Asn Phe Arg Lys Leu Gln Glu Ile Tyr Phe Ile Glu Thr
85 90 95

Lys Lys Phe Leu Leu Ile Gly Lys Ser Asn Ile Cys Val Lys Val Gly
100 105 110

```
Glu Lys Ser Leu Thr Cys Lys Lys Ile Asp Leu Thr Thr Ile Val Lys
        115                 120                 125

Pro Glu Ala Pro Phe Asp Leu Ser Val Ile Tyr Arg Glu Gly Ala Asn
    130                 135                 140

Asp Phe Val Val Thr Phe Asn Thr Ser His Leu Gln Lys Lys Tyr Val
145                 150                 155                 160

Lys Val Leu Met His Asp Val Ala Tyr Arg Gln Glu Lys Asp Glu Asn
                165                 170                 175

Lys Trp Thr His Val Asn Leu Ser Ser Thr Lys Leu Thr Leu Leu Gln
            180                 185                 190

Arg Lys Leu Gln Pro Ala Ala Met Tyr Glu Ile Lys Val Arg Ser Ile
        195                 200                 205

Pro Asp His Tyr Phe Lys Gly Phe Trp Ser Glu Trp Ser Pro Ser Tyr
    210                 215                 220

Tyr Phe Arg Thr Pro Glu Ile Asn Asn Ser Ser Gly Glu Met Asp Pro
225                 230                 235                 240

Ile Leu Leu Thr Ile Ser Ile Leu Ser Phe Phe Ser Val Ala Leu Leu
                245                 250                 255

Val Ile Leu Ala Cys Val Leu Trp Lys Lys Arg Ile Lys Pro Ile Val
            260                 265                 270

Trp Pro Ser Leu Pro Asp His Lys Lys Thr Leu Glu His Leu Cys Lys
        275                 280                 285

Lys Pro Arg Lys Asn Leu Asn Val Ser Phe Asn Pro Glu Ser Phe Leu
    290                 295                 300

Asp Cys Gln Ile His Arg Val Asp Asp Ile Gln Ala Arg Asp Glu Val
305                 310                 315                 320

Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
                325                 330                 335

Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
            340                 345                 350

Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
        355                 360                 365

Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
    370                 375                 380
```

```
Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
385                 390                 395                 400


Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
                405                 410                 415


Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
            420                 425                 430


Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
        435                 440                 445


Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
    450                 455


<210>  312
<211>  508
<212>  PRT
<213>  Homo sapiens

<400>  312

Met Asp His Leu Gly Ala Ser Leu Trp Pro Gln Val Gly Ser Leu Cys
1               5                   10                  15


Leu Leu Leu Ala Gly Ala Ala Trp Ala Pro Pro Pro Asn Leu Pro Asp
            20                  25                  30


Pro Lys Phe Glu Ser Lys Ala Ala Leu Leu Ala Ala Arg Gly Pro Glu
        35                  40                  45


Glu Leu Leu Cys Phe Thr Glu Arg Leu Glu Asp Leu Val Cys Phe Trp
    50                  55                  60


Glu Glu Ala Ala Ser Ala Gly Val Gly Pro Gly Asn Tyr Ser Phe Ser
65                  70                  75                  80


Tyr Gln Leu Glu Asp Glu Pro Trp Lys Leu Cys Arg Leu His Gln Ala
                85                  90                  95


Pro Thr Ala Arg Gly Ala Val Arg Phe Trp Cys Ser Leu Pro Thr Ala
            100                 105                 110


Asp Thr Ser Ser Phe Val Pro Leu Glu Leu Arg Val Thr Ala Ala Ser
        115                 120                 125


Gly Ala Pro Arg Tyr His Arg Val Ile His Ile Asn Glu Val Val Leu
    130                 135                 140


Leu Asp Ala Pro Val Gly Leu Val Ala Arg Leu Ala Asp Glu Ser Gly
145                 150                 155                 160
```

```
His Val Val Leu Arg Trp Leu Pro Pro Pro Glu Thr Pro Met Thr Ser
                165                 170                 175

His Ile Arg Tyr Glu Val Asp Val Ser Ala Gly Asn Gly Ala Gly Ser
            180                 185                 190

Val Gln Arg Val Glu Ile Leu Glu Gly Arg Thr Glu Cys Val Leu Ser
        195                 200                 205

Asn Leu Arg Gly Arg Thr Arg Tyr Thr Phe Ala Val Arg Ala Arg Met
    210                 215                 220

Ala Glu Pro Ser Phe Gly Gly Phe Trp Ser Ala Trp Ser Glu Pro Val
225                 230                 235                 240

Ser Leu Leu Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
                245                 250                 255

Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val Leu Ala Leu Leu
            260                 265                 270

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
        275                 280                 285

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
    290                 295                 300

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
305                 310                 315                 320

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
                325                 330                 335

Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
            340                 345                 350

Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
        355                 360                 365

Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
    370                 375                 380

Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
385                 390                 395                 400

Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
                405                 410                 415

Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
            420                 425                 430
```

```
Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
        435                 440                 445


Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
    450                 455                 460


Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
465                 470                 475                 480


Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala
                485                 490                 495


Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
            500                 505


<210>  313
<211>  267
<212>  PRT
<213>  Homo sapiens

<400>  313

Met Ala Pro Arg Arg Ala Arg Gly Cys Arg Thr Leu Gly Leu Pro Ala
1               5                   10                  15


Leu Leu Leu Leu Leu Leu Leu Arg Pro Pro Ala Thr Arg Gly Ile Thr
            20                  25                  30


Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val Lys Ser
        35                  40                  45


Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly Phe Lys
    50                  55                  60


Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn Lys Ala
65                  70                  75                  80


Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile Arg Asp
                85                  90                  95


Pro Ala Leu Val His Gln Arg Pro Ala Pro Pro Ser Thr Val Thr Thr
            100                 105                 110


Ala Gly Val Thr Pro Gln Pro Glu Ser Leu Ser Pro Ser Gly Lys Glu
        115                 120                 125


Pro Ala Ala Ser Ser Pro Ser Ser Asn Asn Thr Ala Ala Thr Thr Ala
    130                 135                 140


Ala Ile Val Pro Gly Ser Gln Leu Met Pro Ser Lys Ser Pro Ser Thr
145                 150                 155                 160
```

Gly Thr Thr Glu Ile Ser Ser His Glu Ser Ser His Gly Thr Pro Ser
165 170 175

Gln Thr Thr Ala Lys Asn Trp Glu Leu Thr Ala Ser Ala Ser His Gln
180 185 190

Pro Pro Gly Val Tyr Pro Gln Gly His Ser Asp Thr Thr Val Ala Ile
195 200 205

Ser Thr Ser Thr Val Leu Leu Cys Gly Leu Ser Ala Val Ser Leu Leu
210 215 220

Ala Cys Tyr Leu Lys Ser Arg Gln Thr Pro Pro Leu Ala Ser Val Glu
225 230 235 240

Met Glu Ala Met Glu Ala Leu Pro Val Thr Trp Gly Thr Ser Ser Arg
245 250 255

Asp Glu Asp Leu Glu Asn Cys Ser His His Leu
260 265

<210> 314
<211> 255
<212> PRT
<213> Homo sapiens

<400> 314

Met Gly Asn Ser Cys Tyr Asn Ile Val Ala Thr Leu Leu Leu Val Leu
1 5 10 15

Asn Phe Glu Arg Thr Arg Ser Leu Gln Asp Pro Cys Ser Asn Cys Pro
20 25 30

Ala Gly Thr Phe Cys Asp Asn Asn Arg Asn Gln Ile Cys Ser Pro Cys
35 40 45

Pro Pro Asn Ser Phe Ser Ser Ala Gly Gly Gln Arg Thr Cys Asp Ile
50 55 60

Cys Arg Gln Cys Lys Gly Val Phe Arg Thr Arg Lys Glu Cys Ser Ser
65 70 75 80

Thr Ser Asn Ala Glu Cys Asp Cys Thr Pro Gly Phe His Cys Leu Gly
85 90 95

Ala Gly Cys Ser Met Cys Glu Gln Asp Cys Lys Gln Gly Gln Glu Leu
100 105 110

Thr Lys Lys Gly Cys Lys Asp Cys Cys Phe Gly Thr Phe Asn Asp Gln
115 120 125

Lys Arg Gly Ile Cys Arg Pro Trp Thr Asn Cys Ser Leu Asp Gly Lys

130 135 140

Ser Val Leu Val Asn Gly Thr Lys Glu Arg Asp Val Val Cys Gly Pro
145 150 155 160

Ser Pro Ala Asp Leu Ser Pro Gly Ala Ser Ser Val Thr Pro Pro Ala
165 170 175

Pro Ala Arg Glu Pro Gly His Ser Pro Gln Ile Ile Ser Phe Phe Leu
180 185 190

Ala Leu Thr Ser Thr Ala Leu Leu Phe Leu Leu Phe Phe Leu Thr Leu
195 200 205

Arg Phe Ser Val Val Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe
210 215 220

Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly
225 230 235 240

Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
245 250 255

<210> 315
<211> 184
<212> PRT
<213> Homo sapiens

<400> 315

Met Leu Gln Met Ala Gly Gln Cys Ser Gln Asn Glu Tyr Phe Asp Ser
1 5 10 15

Leu Leu His Ala Cys Ile Pro Cys Gln Leu Arg Cys Ser Ser Asn Thr
20 25 30

Pro Pro Leu Thr Cys Gln Arg Tyr Cys Asn Ala Ser Val Thr Asn Ser
35 40 45

Val Lys Gly Thr Asn Ala Ile Leu Trp Thr Cys Leu Gly Leu Ser Leu
50 55 60

Ile Ile Ser Leu Ala Val Phe Val Leu Met Phe Leu Leu Arg Lys Ile
65 70 75 80

Asn Ser Glu Pro Leu Lys Asp Glu Phe Lys Asn Thr Gly Ser Gly Leu
85 90 95

Leu Gly Met Ala Asn Ile Asp Leu Glu Lys Ser Arg Thr Gly Asp Glu
100 105 110

Ile Ile Leu Pro Arg Gly Leu Glu Tyr Thr Val Glu Glu Cys Thr Cys
115 120 125

```
Glu Asp Cys Ile Lys Ser Lys Pro Lys Val Asp Ser Asp His Cys Phe
    130                 135                 140

Pro Leu Pro Ala Met Glu Glu Gly Ala Thr Ile Leu Val Thr Thr Lys
145                 150                 155                 160

Thr Asn Asp Tyr Cys Lys Ser Leu Pro Ala Ala Leu Ser Ala Thr Glu
                165                 170                 175

Ile Glu Lys Ser Ile Ser Ala Arg
            180

<210>  316
<211>  260
<212>  PRT
<213>  Homo sapiens

<400>  316

Met Ala Arg Pro His Pro Trp Trp Leu Cys Val Leu Gly Thr Leu Val
1               5                   10                  15

Gly Leu Ser Ala Thr Pro Ala Pro Lys Ser Cys Pro Glu Arg His Tyr
            20                  25                  30

Trp Ala Gln Gly Lys Leu Cys Cys Gln Met Cys Glu Pro Gly Thr Phe
        35                  40                  45

Leu Val Lys Asp Cys Asp Gln His Arg Lys Ala Ala Gln Cys Asp Pro
    50                  55                  60

Cys Ile Pro Gly Val Ser Phe Ser Pro Asp His His Thr Arg Pro His
65                  70                  75                  80

Cys Glu Ser Cys Arg His Cys Asn Ser Gly Leu Leu Val Arg Asn Cys
                85                  90                  95

Thr Ile Thr Ala Asn Ala Glu Cys Ala Cys Arg Asn Gly Trp Gln Cys
            100                 105                 110

Arg Asp Lys Glu Cys Thr Glu Cys Asp Pro Leu Pro Asn Pro Ser Leu
        115                 120                 125

Thr Ala Arg Ser Ser Gln Ala Leu Ser Pro His Pro Gln Pro Thr His
    130                 135                 140

Leu Pro Tyr Val Ser Glu Met Leu Glu Ala Arg Thr Ala Gly His Met
145                 150                 155                 160

Gln Thr Leu Ala Asp Phe Arg Gln Leu Pro Ala Arg Thr Leu Ser Thr
                165                 170                 175
```

```
His Trp Pro Pro Gln Arg Ser Leu Cys Ser Ser Asp Phe Ile Arg Ile
            180                 185                 190


Leu Val Ile Phe Ser Gly Met Phe Leu Val Phe Thr Leu Ala Gly Ala
        195                 200                 205


Leu Phe Leu His Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser
    210                 215                 220


Pro Val Glu Pro Ala Glu Pro Cys His Tyr Ser Cys Pro Arg Glu Glu
225                 230                 235                 240


Glu Gly Ser Thr Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro
                245                 250                 255


Ala Cys Ser Pro
            260


<210>  317
<211>  595
<212>  PRT
<213>  Homo sapiens

<400>  317

Met Arg Val Leu Leu Ala Ala Leu Gly Leu Leu Phe Leu Gly Ala Leu
1               5                   10                  15


Arg Ala Phe Pro Gln Asp Arg Pro Phe Glu Asp Thr Cys His Gly Asn
            20                  25                  30


Pro Ser His Tyr Tyr Asp Lys Ala Val Arg Arg Cys Cys Tyr Arg Cys
        35                  40                  45


Pro Met Gly Leu Phe Pro Thr Gln Gln Cys Pro Gln Arg Pro Thr Asp
    50                  55                  60


Cys Arg Lys Gln Cys Glu Pro Asp Tyr Tyr Leu Asp Glu Ala Asp Arg
65                  70                  75                  80


Cys Thr Ala Cys Val Thr Cys Ser Arg Asp Asp Leu Val Glu Lys Thr
                85                  90                  95


Pro Cys Ala Trp Asn Ser Ser Arg Val Cys Glu Cys Arg Pro Gly Met
            100                 105                 110


Phe Cys Ser Thr Ser Ala Val Asn Ser Cys Ala Arg Cys Phe Phe His
        115                 120                 125


Ser Val Cys Pro Ala Gly Met Ile Val Lys Phe Pro Gly Thr Ala Gln
    130                 135                 140
```

```
Lys Asn Thr Val Cys Glu Pro Ala Ser Pro Gly Val Ser Pro Ala Cys
145                 150                 155                 160

Ala Ser Pro Glu Asn Cys Lys Glu Pro Ser Ser Gly Thr Ile Pro Gln
                165                 170                 175

Ala Lys Pro Thr Pro Val Ser Pro Ala Thr Ser Ser Ala Ser Thr Met
            180                 185                 190

Pro Val Arg Gly Gly Thr Arg Leu Ala Gln Glu Ala Ala Ser Lys Leu
        195                 200                 205

Thr Arg Ala Pro Asp Ser Pro Ser Ser Val Gly Arg Pro Ser Ser Asp
    210                 215                 220

Pro Gly Leu Ser Pro Thr Gln Pro Cys Pro Glu Gly Ser Gly Asp Cys
225                 230                 235                 240

Arg Lys Gln Cys Glu Pro Asp Tyr Tyr Leu Asp Glu Ala Gly Arg Cys
                245                 250                 255

Thr Ala Cys Val Ser Cys Ser Arg Asp Asp Leu Val Glu Lys Thr Pro
            260                 265                 270

Cys Ala Trp Asn Ser Ser Arg Thr Cys Glu Cys Arg Pro Gly Met Ile
        275                 280                 285

Cys Ala Thr Ser Ala Thr Asn Ser Cys Ala Arg Cys Val Pro Tyr Pro
    290                 295                 300

Ile Cys Ala Ala Glu Thr Val Thr Lys Pro Gln Asp Met Ala Glu Lys
305                 310                 315                 320

Asp Thr Thr Phe Glu Ala Pro Pro Leu Gly Thr Gln Pro Asp Cys Asn
                325                 330                 335

Pro Thr Pro Glu Asn Gly Glu Ala Pro Ala Ser Thr Ser Pro Thr Gln
            340                 345                 350

Ser Leu Leu Val Asp Ser Gln Ala Ser Lys Thr Leu Pro Ile Pro Thr
        355                 360                 365

Ser Ala Pro Val Ala Leu Ser Ser Thr Gly Lys Pro Val Leu Asp Ala
    370                 375                 380

Gly Pro Val Leu Phe Trp Val Ile Leu Val Leu Val Val Val Val Gly
385                 390                 395                 400

Ser Ser Ala Phe Leu Leu Cys His Arg Arg Ala Cys Arg Lys Arg Ile
                405                 410                 415
```

```
Arg Gln Lys Leu His Leu Cys Tyr Pro Val Gln Thr Ser Gln Pro Lys
            420                 425                 430

Leu Glu Leu Val Asp Ser Arg Pro Arg Arg Ser Ser Thr Gln Leu Arg
        435                 440                 445

Ser Gly Ala Ser Val Thr Glu Pro Val Ala Glu Glu Arg Gly Leu Met
    450                 455                 460

Ser Gln Pro Leu Met Glu Thr Cys His Ser Val Gly Ala Ala Tyr Leu
465                 470                 475                 480

Glu Ser Leu Pro Leu Gln Asp Ala Ser Pro Ala Gly Gly Pro Ser Ser
                485                 490                 495

Pro Arg Asp Leu Pro Glu Pro Arg Val Ser Thr Glu His Thr Asn Asn
            500                 505                 510

Lys Ile Glu Lys Ile Tyr Ile Met Lys Ala Asp Thr Val Ile Val Gly
        515                 520                 525

Thr Val Lys Ala Glu Leu Pro Glu Gly Arg Gly Leu Ala Gly Pro Ala
    530                 535                 540

Glu Pro Glu Leu Glu Glu Glu Leu Glu Ala Asp His Thr Pro His Tyr
545                 550                 555                 560

Pro Glu Gln Glu Thr Glu Pro Pro Leu Gly Ser Cys Ser Asp Val Met
                565                 570                 575

Leu Ser Val Glu Glu Glu Gly Lys Glu Asp Pro Leu Pro Thr Ala Ala
            580                 585                 590

Ser Gly Lys
        595


<210>  318
<211>  277
<212>  PRT
<213>  Homo sapiens

<400>  318

Met Val Arg Leu Pro Leu Gln Cys Val Leu Trp Gly Cys Leu Leu Thr
1               5                   10                  15

Ala Val His Pro Glu Pro Pro Thr Ala Cys Arg Glu Lys Gln Tyr Leu
            20                  25                  30

Ile Asn Ser Gln Cys Cys Ser Leu Cys Gln Pro Gly Gln Lys Leu Val
        35                  40                  45

Ser Asp Cys Thr Glu Phe Thr Glu Thr Glu Cys Leu Pro Cys Gly Glu
```

50 55 60

Ser Glu Phe Leu Asp Thr Trp Asn Arg Glu Thr His Cys His Gln His
65 70 75 80

Lys Tyr Cys Asp Pro Asn Leu Gly Leu Arg Val Gln Gln Lys Gly Thr
85 90 95

Ser Glu Thr Asp Thr Ile Cys Thr Cys Glu Glu Gly Trp His Cys Thr
100 105 110

Ser Glu Ala Cys Glu Ser Cys Val Leu His Arg Ser Cys Ser Pro Gly
115 120 125

Phe Gly Val Lys Gln Ile Ala Thr Gly Val Ser Asp Thr Ile Cys Glu
130 135 140

Pro Cys Pro Val Gly Phe Phe Ser Asn Val Ser Ser Ala Phe Glu Lys
145 150 155 160

Cys His Pro Trp Thr Ser Cys Glu Thr Lys Asp Leu Val Val Gln Gln
165 170 175

Ala Gly Thr Asn Lys Thr Asp Val Val Cys Gly Pro Gln Asp Arg Leu
180 185 190

Arg Ala Leu Val Val Ile Pro Ile Ile Phe Gly Ile Leu Phe Ala Ile
195 200 205

Leu Leu Val Leu Val Phe Ile Lys Lys Val Ala Lys Lys Pro Thr Asn
210 215 220

Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn Phe Pro Asp
225 230 235 240

Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu Thr Leu His
245 250 255

Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser
260 265 270

Val Gln Glu Arg Gln
275

<210> 319
<211> 448
<212> PRT
<213> Homo sapiens

<400> 319

Met Ala His Val Gly Asp Cys Thr Gln Thr Pro Trp Leu Pro Val Leu
1 5 10 15

```
Val Val Ser Leu Met Cys Ser Ala Arg Ala Glu Tyr Ser Asn Cys Gly
            20                  25                  30

Glu Asn Glu Tyr Tyr Asn Gln Thr Thr Gly Leu Cys Gln Glu Cys Pro
        35                  40                  45

Pro Cys Gly Pro Gly Glu Glu Pro Tyr Leu Ser Cys Gly Tyr Gly Thr
    50                  55                  60

Lys Asp Glu Asp Tyr Gly Cys Val Pro Cys Pro Ala Glu Lys Phe Ser
65                  70                  75                  80

Lys Gly Gly Tyr Gln Ile Cys Arg Arg His Lys Asp Cys Glu Gly Phe
                85                  90                  95

Phe Arg Ala Thr Val Leu Thr Pro Gly Asp Met Glu Asn Asp Ala Glu
            100                 105                 110

Cys Gly Pro Cys Leu Pro Gly Tyr Tyr Met Leu Glu Asn Arg Pro Arg
        115                 120                 125

Asn Ile Tyr Gly Met Val Cys Tyr Ser Cys Leu Leu Ala Pro Pro Asn
    130                 135                 140

Thr Lys Glu Cys Val Gly Ala Thr Ser Gly Ala Ser Ala Asn Phe Pro
145                 150                 155                 160

Gly Thr Ser Gly Ser Ser Thr Leu Ser Pro Phe Gln His Ala His Lys
                165                 170                 175

Glu Leu Ser Gly Gln Gly His Leu Ala Thr Ala Leu Ile Ile Ala Met
            180                 185                 190

Ser Thr Ile Phe Ile Met Ala Ile Ala Ile Val Leu Ile Ile Met Phe
        195                 200                 205

Tyr Ile Leu Lys Thr Lys Pro Ser Ala Pro Ala Cys Cys Thr Ser His
    210                 215                 220

Pro Gly Lys Ser Val Glu Ala Gln Val Ser Lys Asp Glu Glu Lys Lys
225                 230                 235                 240

Glu Ala Pro Asp Asn Val Val Met Phe Ser Glu Lys Asp Glu Phe Glu
                245                 250                 255

Lys Leu Thr Ala Thr Pro Ala Lys Pro Thr Lys Ser Glu Asn Asp Ala
            260                 265                 270

Ser Ser Glu Asn Glu Gln Leu Leu Ser Arg Ser Val Asp Ser Asp Glu
        275                 280                 285
```

```
Glu Pro Ala Pro Asp Lys Gln Gly Ser Pro Glu Leu Cys Leu Leu Ser
    290                 295                 300

Leu Val His Leu Ala Arg Glu Lys Ser Ala Thr Ser Asn Lys Ser Ala
305                 310                 315                 320

Gly Ile Gln Ser Arg Arg Lys Lys Ile Leu Asp Val Tyr Ala Asn Val
                325                 330                 335

Cys Gly Val Val Glu Gly Leu Ser Pro Thr Glu Leu Pro Phe Asp Cys
            340                 345                 350

Leu Glu Lys Thr Ser Arg Met Leu Ser Ser Thr Tyr Asn Ser Glu Lys
        355                 360                 365

Ala Val Val Lys Thr Trp Arg His Leu Ala Glu Ser Phe Gly Leu Lys
    370                 375                 380

Arg Asp Glu Ile Gly Gly Met Thr Asp Gly Met Gln Leu Phe Asp Arg
385                 390                 395                 400

Ile Ser Thr Ala Gly Tyr Ser Ile Pro Glu Leu Leu Thr Lys Leu Val
                405                 410                 415

Gln Ile Glu Arg Leu Asp Ala Val Glu Ser Leu Cys Ala Asp Ile Leu
            420                 425                 430

Glu Trp Ala Gly Val Val Pro Pro Ala Ser Gln Pro His Ala Ala Ser
        435                 440                 445


<210>  320
<211>  277
<212>  PRT
<213>  Homo sapiens

<400>  320

Met Cys Val Gly Ala Arg Arg Leu Gly Arg Gly Pro Cys Ala Ala Leu
1               5                   10                  15

Leu Leu Leu Gly Leu Gly Leu Ser Thr Val Thr Gly Leu His Cys Val
            20                  25                  30

Gly Asp Thr Tyr Pro Ser Asn Asp Arg Cys Cys His Glu Cys Arg Pro
        35                  40                  45

Gly Asn Gly Met Val Ser Arg Cys Ser Arg Ser Gln Asn Thr Val Cys
    50                  55                  60

Arg Pro Cys Gly Pro Gly Phe Tyr Asn Asp Val Val Ser Ser Lys Pro
65                  70                  75                  80
```

```
Cys Lys Pro Cys Thr Trp Cys Asn Leu Arg Ser Gly Ser Glu Arg Lys
                85                  90                  95

Gln Leu Cys Thr Ala Thr Gln Asp Thr Val Cys Arg Cys Arg Ala Gly
            100                 105                 110

Thr Gln Pro Leu Asp Ser Tyr Lys Pro Gly Val Asp Cys Ala Pro Cys
        115                 120                 125

Pro Pro Gly His Phe Ser Pro Gly Asp Asn Gln Ala Cys Lys Pro Trp
    130                 135                 140

Thr Asn Cys Thr Leu Ala Gly Lys His Thr Leu Gln Pro Ala Ser Asn
145                 150                 155                 160

Ser Ser Asp Ala Ile Cys Glu Asp Arg Asp Pro Pro Ala Thr Gln Pro
                165                 170                 175

Gln Glu Thr Gln Gly Pro Pro Ala Arg Pro Ile Thr Val Gln Pro Thr
            180                 185                 190

Glu Ala Trp Pro Arg Thr Ser Gln Gly Pro Ser Thr Arg Pro Val Glu
        195                 200                 205

Val Pro Gly Gly Arg Ala Val Ala Ala Ile Leu Gly Leu Gly Leu Val
    210                 215                 220

Leu Gly Leu Leu Gly Pro Leu Ala Ile Leu Leu Ala Leu Tyr Leu Leu
225                 230                 235                 240

Arg Arg Asp Gln Arg Leu Pro Pro Asp Ala His Lys Pro Pro Gly Gly
                245                 250                 255

Gly Ser Phe Arg Thr Pro Ile Gln Glu Glu Gln Ala Asp Ala His Ser
            260                 265                 270

Thr Leu Ala Lys Ile
        275


<210>  321
<211>  293
<212>  PRT
<213>  Homo sapiens

<400>  321

Met Ser Gly Leu Gly Arg Ser Arg Arg Gly Gly Arg Ser Arg Val Asp
1               5                   10                  15

Gln Glu Glu Arg Phe Pro Gln Gly Leu Trp Thr Gly Val Ala Met Arg
            20                  25                  30
```

```
Ser Cys Pro Glu Glu Gln Tyr Trp Asp Pro Leu Leu Gly Thr Cys Met
        35                  40                  45

Ser Cys Lys Thr Ile Cys Asn His Gln Ser Gln Arg Thr Cys Ala Ala
    50                  55                  60

Phe Cys Arg Ser Leu Ser Cys Arg Lys Glu Gln Gly Lys Phe Tyr Asp
65                  70                  75                  80

His Leu Leu Arg Asp Cys Ile Ser Cys Ala Ser Ile Cys Gly Gln His
                85                  90                  95

Pro Lys Gln Cys Ala Tyr Phe Cys Glu Asn Lys Leu Arg Ser Pro Val
            100                 105                 110

Asn Leu Pro Pro Glu Leu Arg Arg Gln Arg Ser Gly Glu Val Glu Asn
        115                 120                 125

Asn Ser Asp Asn Ser Gly Arg Tyr Gln Gly Leu Glu His Arg Gly Ser
    130                 135                 140

Glu Ala Ser Pro Ala Leu Pro Gly Leu Lys Leu Ser Ala Asp Gln Val
145                 150                 155                 160

Ala Leu Val Tyr Ser Thr Leu Gly Leu Cys Leu Cys Ala Val Leu Cys
                165                 170                 175

Cys Phe Leu Val Ala Val Ala Cys Phe Leu Lys Lys Arg Gly Asp Pro
            180                 185                 190

Cys Ser Cys Gln Pro Arg Ser Arg Pro Arg Gln Ser Pro Ala Lys Ser
        195                 200                 205

Ser Gln Asp His Ala Met Glu Ala Gly Ser Pro Val Ser Thr Ser Pro
    210                 215                 220

Glu Pro Val Glu Thr Cys Ser Phe Cys Phe Pro Glu Cys Arg Ala Pro
225                 230                 235                 240

Thr Gln Glu Ser Ala Val Thr Pro Gly Thr Pro Asp Pro Thr Cys Ala
                245                 250                 255

Gly Arg Trp Gly Cys His Thr Arg Thr Thr Val Leu Gln Pro Cys Pro
            260                 265                 270

His Ile Pro Asp Ser Gly Leu Gly Ile Val Cys Val Pro Ala Gln Glu
        275                 280                 285

Gly Gly Pro Gly Ala
    290
```

<210> 322
<211> 455
<212> PRT
<213> Homo sapiens

<400> 322

```
Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu
1               5                  10                  15

Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro
            20                  25                  30

His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys
        35                  40                  45

Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys
    50                  55                  60

Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp
65                  70                  75                  80

Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu
                85                  90                  95

Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val
            100                 105                 110

Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg
        115                 120                 125

Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe
    130                 135                 140

Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu
145                 150                 155                 160

Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu
                165                 170                 175

Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr
            180                 185                 190

Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser
        195                 200                 205

Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu
    210                 215                 220

Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys
225                 230                 235                 240

Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu
```

245 250 255

Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser
260 265 270

Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val
275 280 285

Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys
290 295 300

Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly
305 310 315 320

Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn
325 330 335

Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp
340 345 350

Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro
355 360 365

Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu
370 375 380

Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln
385 390 395 400

Tyr Ser Met Leu Ala Thr Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala
405 410 415

Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly
420 425 430

Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys Gly Pro Ala Ala Leu Pro
435 440 445

Pro Ala Pro Ser Leu Leu Arg
450 455

<210> 323
<211> 461
<212> PRT
<213> Homo sapiens

<400> 323

Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu
1 5 10 15

Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr
20 25 30

```
Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln
        35                  40                  45

Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys
    50                  55                  60

Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp
65                  70                  75                  80

Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys
                85                  90                  95

Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg
            100                 105                 110

Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu
        115                 120                 125

Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg
    130                 135                 140

Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val
145                 150                 155                 160

Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr
                165                 170                 175

Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly
            180                 185                 190

Asn Ala Ser Met Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser
        195                 200                 205

Met Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser
    210                 215                 220

Gln His Thr Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser
225                 230                 235                 240

Phe Leu Leu Pro Met Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly
                245                 250                 255

Asp Phe Ala Leu Pro Val Gly Leu Ile Val Gly Val Thr Ala Leu Gly
            260                 265                 270

Leu Leu Ile Ile Gly Val Val Asn Cys Val Ile Met Thr Gln Val Lys
        275                 280                 285

Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys Val Pro His Leu Pro
    290                 295                 300
```

```
Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln His Leu Leu
305                 310                 315                 320


Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala Ser
                325                 330                 335


Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly
            340                 345                 350


Val Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser
        355                 360                 365


Asp Ser Ser Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile
    370                 375                 380


Val Asn Val Cys Ser Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln
385                 390                 395                 400


Ala Ser Ser Thr Met Gly Asp Thr Asp Ser Ser Pro Ser Glu Ser Pro
                405                 410                 415


Lys Asp Glu Gln Val Pro Phe Ser Lys Glu Glu Cys Ala Phe Arg Ser
            420                 425                 430


Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser Thr Glu Glu Lys Pro
        435                 440                 445


Leu Pro Leu Gly Val Pro Asp Ala Gly Met Lys Pro Ser
    450                 455                 460


<210>  324
<211>  423
<212>  PRT
<213>  Homo sapiens

<400>  324

Met Ala Leu Lys Val Leu Leu Glu Gln Glu Lys Thr Phe Phe Thr Leu
1               5                   10                  15


Leu Val Leu Leu Gly Tyr Leu Ser Cys Lys Val Thr Cys Glu Ser Gly
            20                  25                  30


Asp Cys Arg Gln Gln Glu Phe Arg Asp Arg Ser Gly Asn Cys Val Pro
        35                  40                  45


Cys Asn Gln Cys Gly Pro Gly Met Glu Leu Ser Lys Glu Cys Gly Phe
    50                  55                  60


Gly Tyr Gly Glu Asp Ala Gln Cys Val Thr Cys Arg Leu His Arg Phe
65                  70                  75                  80
```

```
Lys Glu Asp Trp Gly Phe Gln Lys Cys Lys Pro Cys Leu Asp Cys Ala
                85                  90                  95

Val Val Asn Arg Phe Gln Lys Ala Asn Cys Ser Ala Thr Ser Asp Ala
            100                 105                 110

Ile Cys Gly Asp Cys Leu Pro Gly Phe Tyr Arg Lys Thr Lys Leu Val
        115                 120                 125

Gly Phe Gln Asp Met Glu Cys Val Pro Cys Gly Asp Pro Pro Pro Pro
    130                 135                 140

Tyr Glu Pro His Cys Ala Ser Lys Val Asn Leu Val Lys Ile Ala Ser
145                 150                 155                 160

Thr Ala Ser Ser Pro Arg Asp Thr Ala Leu Ala Ala Val Ile Cys Ser
                165                 170                 175

Ala Leu Ala Thr Val Leu Leu Ala Leu Leu Ile Leu Cys Val Ile Tyr
            180                 185                 190

Cys Lys Arg Gln Phe Met Glu Lys Lys Pro Ser Trp Ser Leu Arg Ser
        195                 200                 205

Gln Asp Ile Gln Tyr Asn Gly Ser Glu Leu Ser Cys Phe Asp Arg Pro
    210                 215                 220

Gln Leu His Glu Tyr Ala His Arg Ala Cys Cys Gln Cys Arg Arg Asp
225                 230                 235                 240

Ser Val Gln Thr Cys Gly Pro Val Arg Leu Leu Pro Ser Met Cys Cys
                245                 250                 255

Glu Glu Ala Cys Ser Pro Asn Pro Ala Thr Leu Gly Cys Gly Val His
            260                 265                 270

Ser Ala Ala Ser Leu Gln Ala Arg Asn Ala Gly Pro Ala Gly Glu Met
        275                 280                 285

Val Pro Thr Phe Phe Gly Ser Leu Thr Gln Ser Ile Cys Gly Glu Phe
    290                 295                 300

Ser Asp Ala Trp Pro Leu Met Gln Asn Pro Met Gly Gly Asp Asn Ile
305                 310                 315                 320

Ser Phe Cys Asp Ser Tyr Pro Glu Leu Thr Gly Glu Asp Ile His Ser
                325                 330                 335

Leu Asn Pro Glu Leu Glu Ser Ser Thr Ser Leu Asp Ser Asn Ser Ser
            340                 345                 350
```

```
Gln Asp Leu Val Gly Gly Ala Val Pro Val Gln Ser His Ser Glu Asn
        355                 360                 365


Phe Thr Ala Ala Thr Asp Leu Ser Arg Tyr Asn Asn Thr Leu Val Glu
    370                 375                 380


Ser Ala Ser Thr Gln Asp Ala Leu Thr Met Arg Ser Gln Leu Asp Gln
385                 390                 395                 400


Glu Ser Gly Ala Val Ile His Pro Ala Thr Gln Thr Ser Leu Gln Val
                405                 410                 415


Arg Gln Arg Leu Gly Ser Leu
            420


<210>  325
<211>  233
<212>  PRT
<213>  Homo sapiens

<400>  325

Met Ser Thr Glu Ser Met Ile Arg Asp Val Glu Leu Ala Glu Glu Ala
1               5                   10                  15


Leu Pro Lys Lys Thr Gly Gly Pro Gln Gly Ser Arg Arg Cys Leu Phe
            20                  25                  30


Leu Ser Leu Phe Ser Phe Leu Ile Val Ala Gly Ala Thr Thr Leu Phe
        35                  40                  45


Cys Leu Leu His Phe Gly Val Ile Gly Pro Gln Arg Glu Glu Phe Pro
    50                  55                  60


Arg Asp Leu Ser Leu Ile Ser Pro Leu Ala Gln Ala Val Arg Ser Ser
65                  70                  75                  80


Ser Arg Thr Pro Ser Asp Lys Pro Val Ala His Val Val Ala Asn Pro
                85                  90                  95


Gln Ala Glu Gly Gln Leu Gln Trp Leu Asn Arg Arg Ala Asn Ala Leu
            100                 105                 110


Leu Ala Asn Gly Val Glu Leu Arg Asp Asn Gln Leu Val Val Pro Ser
        115                 120                 125


Glu Gly Leu Tyr Leu Ile Tyr Ser Gln Val Leu Phe Lys Gly Gln Gly
    130                 135                 140


Cys Pro Ser Thr His Val Leu Leu Thr His Thr Ile Ser Arg Ile Ala
145                 150                 155                 160
```

```
Val Ser Tyr Gln Thr Lys Val Asn Leu Leu Ser Ala Ile Lys Ser Pro
                165                 170                 175


Cys Gln Arg Glu Thr Pro Glu Gly Ala Glu Ala Lys Pro Trp Tyr Glu
            180                 185                 190


Pro Ile Tyr Leu Gly Gly Val Phe Gln Leu Glu Lys Gly Asp Arg Leu
        195                 200                 205


Ser Ala Glu Ile Asn Arg Pro Asp Tyr Leu Asp Phe Ala Glu Ser Gly
    210                 215                 220


Gln Val Tyr Phe Gly Ile Ile Ala Leu
225                 230


<210>  326
<211>  205
<212>  PRT
<213>  Homo sapiens

<400>  326

Met Thr Pro Pro Glu Arg Leu Phe Leu Pro Arg Val Cys Gly Thr Thr
1               5                   10                  15


Leu His Leu Leu Leu Leu Gly Leu Leu Leu Val Leu Leu Pro Gly Ala
            20                  25                  30


Gln Gly Leu Pro Gly Val Gly Leu Thr Pro Ser Ala Ala Gln Thr Ala
        35                  40                  45


Arg Gln His Pro Lys Met His Leu Ala His Ser Thr Leu Lys Pro Ala
    50                  55                  60


Ala His Leu Ile Gly Asp Pro Ser Lys Gln Asn Ser Leu Leu Trp Arg
65                  70                  75                  80


Ala Asn Thr Asp Arg Ala Phe Leu Gln Asp Gly Phe Ser Leu Ser Asn
                85                  90                  95


Asn Ser Leu Leu Val Pro Thr Ser Gly Ile Tyr Phe Val Tyr Ser Gln
            100                 105                 110


Val Val Phe Ser Gly Lys Ala Tyr Ser Pro Lys Ala Thr Ser Ser Pro
        115                 120                 125


Leu Tyr Leu Ala His Glu Val Gln Leu Phe Ser Ser Gln Tyr Pro Phe
    130                 135                 140


His Val Pro Leu Leu Ser Ser Gln Lys Met Val Tyr Pro Gly Leu Gln
145                 150                 155                 160


Glu Pro Trp Leu His Ser Met Tyr His Gly Ala Ala Phe Gln Leu Thr
```

165 170 175

Gln Gly Asp Gln Leu Ser Thr His Thr Asp Gly Ile Pro His Leu Val
180 185 190

Leu Ser Pro Ser Thr Val Phe Phe Gly Ala Phe Ala Leu
195 200 205

<210> 327
<211> 244
<212> PRT
<213> Homo sapiens

<400> 327

Met Gly Ala Leu Gly Leu Glu Gly Arg Gly Gly Arg Leu Gln Gly Arg
1 5 10 15

Gly Ser Leu Leu Leu Ala Val Ala Gly Ala Thr Ser Leu Val Thr Leu
20 25 30

Leu Leu Ala Val Pro Ile Thr Val Leu Ala Val Leu Ala Leu Val Pro
35 40 45

Gln Asp Gln Gly Gly Leu Val Thr Glu Thr Ala Asp Pro Gly Ala Gln
50 55 60

Ala Gln Gln Gly Leu Gly Phe Gln Lys Leu Pro Glu Glu Glu Pro Glu
65 70 75 80

Thr Asp Leu Ser Pro Gly Leu Pro Ala Ala His Leu Ile Gly Ala Pro
85 90 95

Leu Lys Gly Gln Gly Leu Gly Trp Glu Thr Thr Lys Glu Gln Ala Phe
100 105 110

Leu Thr Ser Gly Thr Gln Phe Ser Asp Ala Glu Gly Leu Ala Leu Pro
115 120 125

Gln Asp Gly Leu Tyr Tyr Leu Tyr Cys Leu Val Gly Tyr Arg Gly Arg
130 135 140

Ala Pro Pro Gly Gly Gly Asp Pro Gln Gly Arg Ser Val Thr Leu Arg
145 150 155 160

Ser Ser Leu Tyr Arg Ala Gly Gly Ala Tyr Gly Pro Gly Thr Pro Glu
165 170 175

Leu Leu Leu Glu Gly Ala Glu Thr Val Thr Pro Val Leu Asp Pro Ala
180 185 190

Arg Arg Gln Gly Tyr Gly Pro Leu Trp Tyr Thr Ser Val Gly Phe Gly
195 200 205

```
Gly Leu Val Gln Leu Arg Arg Gly Glu Arg Val Tyr Val Asn Ile Ser
    210                 215                 220

His Pro Asp Met Val Asp Phe Ala Arg Gly Lys Thr Phe Phe Gly Ala
225                 230                 235                 240

Val Met Val Gly
```

<210> 328
<211> 317
<212> PRT
<213> Homo sapiens

<400> 328

```
Met Arg Arg Ala Ser Arg Asp Tyr Thr Lys Tyr Leu Arg Gly Ser Glu
1               5                   10                  15

Glu Met Gly Gly Gly Pro Gly Ala Pro His Glu Gly Pro Leu His Ala
            20                  25                  30

Pro Pro Pro Pro Ala Pro His Gln Pro Pro Ala Ala Ser Arg Ser Met
        35                  40                  45

Phe Val Ala Leu Leu Gly Leu Gly Leu Gly Gln Val Val Cys Ser Val
    50                  55                  60

Ala Leu Phe Phe Tyr Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser
65                  70                  75                  80

Glu Asp Gly Thr His Cys Ile Tyr Arg Ile Leu Arg Leu His Glu Asn
                85                  90                  95

Ala Asp Phe Gln Asp Thr Thr Leu Glu Ser Gln Asp Thr Lys Leu Ile
            100                 105                 110

Pro Asp Ser Cys Arg Arg Ile Lys Gln Ala Phe Gln Gly Ala Val Gln
        115                 120                 125

Lys Glu Leu Gln His Ile Val Gly Ser Gln His Ile Arg Ala Glu Lys
    130                 135                 140

Ala Met Val Asp Gly Ser Trp Leu Asp Leu Ala Lys Arg Ser Lys Leu
145                 150                 155                 160

Glu Ala Gln Pro Phe Ala His Leu Thr Ile Asn Ala Thr Asp Ile Pro
                165                 170                 175

Ser Gly Ser His Lys Val Ser Leu Ser Ser Trp Tyr His Asp Arg Gly
            180                 185                 190
```

```
Trp Ala Lys Ile Ser Asn Met Thr Phe Ser Asn Gly Lys Leu Ile Val
        195                 200                 205

Asn Gln Asp Gly Phe Tyr Tyr Leu Tyr Ala Asn Ile Cys Phe Arg His
    210                 215                 220

His Glu Thr Ser Gly Asp Leu Ala Thr Glu Tyr Leu Gln Leu Met Val
225                 230                 235                 240

Tyr Val Thr Lys Thr Ser Ile Lys Ile Pro Ser Ser His Thr Leu Met
                245                 250                 255

Lys Gly Gly Ser Thr Lys Tyr Trp Ser Gly Asn Ser Glu Phe His Phe
            260                 265                 270

Tyr Ser Ile Asn Val Gly Gly Phe Phe Lys Leu Arg Ser Gly Glu Glu
        275                 280                 285

Ile Ser Ile Glu Val Ser Asn Pro Ser Leu Leu Asp Pro Asp Gln Asp
    290                 295                 300

Ala Thr Tyr Phe Gly Ala Phe Lys Val Arg Asp Ile Asp
305                 310                 315


<210>  329
<211>  281
<212>  PRT
<213>  Homo sapiens

<400>  329

Met Gln Gln Pro Phe Asn Tyr Pro Tyr Pro Gln Ile Tyr Trp Val Asp
1               5                   10                  15

Ser Ser Ala Ser Ser Pro Trp Ala Pro Pro Gly Thr Val Leu Pro Cys
            20                  25                  30

Pro Thr Ser Val Pro Arg Arg Pro Gly Gln Arg Arg Pro Pro Pro Pro
        35                  40                  45

Pro Pro Pro Pro Pro Leu Pro Pro Pro Pro Pro Pro Pro Pro Leu Pro
    50                  55                  60

Pro Leu Pro Leu Pro Pro Leu Lys Lys Arg Gly Asn His Ser Thr Gly
65                  70                  75                  80

Leu Cys Leu Leu Val Met Phe Phe Met Val Leu Val Ala Leu Val Gly
                85                  90                  95

Leu Gly Leu Gly Met Phe Gln Leu Phe His Leu Gln Lys Glu Leu Ala
            100                 105                 110
```

Glu Leu Arg Glu Ser Thr Ser Gln Met His Thr Ala Ser Ser Leu Glu
115 120 125

Lys Gln Ile Gly His Pro Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg
130 135 140

Lys Val Ala His Leu Thr Gly Lys Ser Asn Ser Arg Ser Met Pro Leu
145 150 155 160

Glu Trp Glu Asp Thr Tyr Gly Ile Val Leu Leu Ser Gly Val Lys Tyr
165 170 175

Lys Lys Gly Gly Leu Val Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr
180 185 190

Ser Lys Val Tyr Phe Arg Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser
195 200 205

His Lys Val Tyr Met Arg Asn Ser Lys Tyr Pro Gln Asp Leu Val Met
210 215 220

Met Glu Gly Lys Met Met Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala
225 230 235 240

Arg Ser Ser Tyr Leu Gly Ala Val Phe Asn Leu Thr Ser Ala Asp His
245 250 255

Leu Tyr Val Asn Val Ser Glu Leu Ser Leu Val Asn Phe Glu Glu Ser
260 265 270

Gln Thr Phe Phe Gly Leu Tyr Lys Leu
275 280

<210> 330
<211> 193
<212> PRT
<213> Homo sapiens

<400> 330

Met Pro Glu Glu Gly Ser Gly Cys Ser Val Arg Arg Arg Pro Tyr Gly
1 5 10 15

Cys Val Leu Arg Ala Ala Leu Val Pro Leu Val Ala Gly Leu Val Ile
20 25 30

Cys Leu Val Val Cys Ile Gln Arg Phe Ala Gln Ala Gln Gln Gln Leu
35 40 45

Pro Leu Glu Ser Leu Gly Trp Asp Val Ala Glu Leu Gln Leu Asn His
50 55 60

Thr Gly Pro Gln Gln Asp Pro Arg Leu Tyr Trp Gln Gly Gly Pro Ala

65 70 75 80

Leu Gly Arg Ser Phe Leu His Gly Pro Glu Leu Asp Lys Gly Gln Leu
85 90 95

Arg Ile His Arg Asp Gly Ile Tyr Met Val His Ile Gln Val Thr Leu
100 105 110

Ala Ile Cys Ser Ser Thr Thr Ala Ser Arg His His Pro Thr Thr Leu
115 120 125

Ala Val Gly Ile Cys Ser Pro Ala Ser Arg Ser Ile Ser Leu Leu Arg
130 135 140

Leu Ser Phe His Gln Gly Cys Thr Ile Ala Ser Gln Arg Leu Thr Pro
145 150 155 160

Leu Ala Arg Gly Asp Thr Leu Cys Thr Asn Leu Thr Gly Thr Leu Leu
165 170 175

Pro Ser Arg Asn Thr Asp Glu Thr Phe Phe Gly Val Gln Trp Val Arg
180 185 190

Pro

<210> 331
<211> 234
<212> PRT
<213> Homo sapiens

<400> 331

Met Asp Pro Gly Leu Gln Gln Ala Leu Asn Gly Met Ala Pro Pro Gly
1 5 10 15

Asp Thr Ala Met His Val Pro Ala Gly Ser Val Ala Ser His Leu Gly
20 25 30

Thr Thr Ser Arg Ser Tyr Phe Tyr Leu Thr Thr Ala Thr Leu Ala Leu
35 40 45

Cys Leu Val Phe Thr Val Ala Thr Ile Met Val Leu Val Val Gln Arg
50 55 60

Thr Asp Ser Ile Pro Asn Ser Pro Asp Asn Val Pro Leu Lys Gly Gly
65 70 75 80

Asn Cys Ser Glu Asp Leu Leu Cys Ile Leu Lys Arg Ala Pro Phe Lys
85 90 95

Lys Ser Trp Ala Tyr Leu Gln Val Ala Lys His Leu Asn Lys Thr Lys
100 105 110

```
Leu Ser Trp Asn Lys Asp Gly Ile Leu His Gly Val Arg Tyr Gln Asp
        115                 120                 125

Gly Asn Leu Val Ile Gln Phe Pro Gly Leu Tyr Phe Ile Ile Cys Gln
    130                 135                 140

Leu Gln Phe Leu Val Gln Cys Pro Asn Asn Ser Val Asp Leu Lys Leu
145                 150                 155                 160

Glu Leu Leu Ile Asn Lys His Ile Lys Lys Gln Ala Leu Val Thr Val
                165                 170                 175

Cys Glu Ser Gly Met Gln Thr Lys His Val Tyr Gln Asn Leu Ser Gln
            180                 185                 190

Phe Leu Leu Asp Tyr Leu Gln Val Asn Thr Thr Ile Ser Val Asn Val
        195                 200                 205

Asp Thr Phe Gln Tyr Ile Asp Thr Ser Thr Phe Pro Leu Glu Asn Val
    210                 215                 220

Leu Ser Ile Phe Leu Tyr Ser Asn Ser Asp
225                 230


<210>  332
<211>  261
<212>  PRT
<213>  Homo sapiens

<400>  332

Met Ile Glu Thr Tyr Asn Gln Thr Ser Pro Arg Ser Ala Ala Thr Gly
1               5                   10                  15

Leu Pro Ile Ser Met Lys Ile Phe Met Tyr Leu Leu Thr Val Phe Leu
            20                  25                  30

Ile Thr Gln Met Ile Gly Ser Ala Leu Phe Ala Val Tyr Leu His Arg
        35                  40                  45

Arg Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu His Glu Asp Phe Val
    50                  55                  60

Phe Met Lys Thr Ile Gln Arg Cys Asn Thr Gly Glu Arg Ser Leu Ser
65                  70                  75                  80

Leu Leu Asn Cys Glu Glu Ile Lys Ser Gln Phe Glu Gly Phe Val Lys
                85                  90                  95

Asp Ile Met Leu Asn Lys Glu Glu Thr Lys Lys Glu Asn Ser Phe Glu
            100                 105                 110
```

```
Met Gln Lys Gly Asp Gln Asn Pro Gln Ile Ala Ala His Val Ile Ser
        115                 120                 125

Glu Ala Ser Ser Lys Thr Thr Ser Val Leu Gln Trp Ala Glu Lys Gly
    130                 135                 140

Tyr Tyr Thr Met Ser Asn Asn Leu Val Thr Leu Glu Asn Gly Lys Gln
145                 150                 155                 160

Leu Thr Val Lys Arg Gln Gly Leu Tyr Tyr Ile Tyr Ala Gln Val Thr
                165                 170                 175

Phe Cys Ser Asn Arg Glu Ala Ser Ser Gln Ala Pro Phe Ile Ala Ser
            180                 185                 190

Leu Cys Leu Lys Ser Pro Gly Arg Phe Glu Arg Ile Leu Leu Arg Ala
        195                 200                 205

Ala Asn Thr His Ser Ser Ala Lys Pro Cys Gly Gln Gln Ser Ile His
    210                 215                 220

Leu Gly Gly Val Phe Glu Leu Gln Pro Gly Ala Ser Val Phe Val Asn
225                 230                 235                 240

Val Thr Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe
                245                 250                 255

Gly Leu Leu Lys Leu
            260


<210>  333
<211>  254
<212>  PRT
<213>  Homo sapiens

<400>  333

Met Glu Tyr Ala Ser Asp Ala Ser Leu Asp Pro Glu Ala Pro Trp Pro
1               5                   10                  15

Pro Ala Pro Arg Ala Arg Ala Cys Arg Val Leu Pro Trp Ala Leu Val
            20                  25                  30

Ala Gly Leu Leu Leu Leu Leu Leu Leu Ala Ala Ala Cys Ala Val Phe
        35                  40                  45

Leu Ala Cys Pro Trp Ala Val Ser Gly Ala Arg Ala Ser Pro Gly Ser
    50                  55                  60

Ala Ala Ser Pro Arg Leu Arg Glu Gly Pro Glu Leu Ser Pro Asp Asp
65                  70                  75                  80
```

```
Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu Val
                85                  90                  95

Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser Asp
            100                 105                 110

Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys Glu
        115                 120                 125

Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val Phe
    130                 135                 140

Phe Gln Leu Glu Leu Arg Arg Val Val Ala Gly Glu Gly Ser Gly Ser
145                 150                 155                 160

Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly Ala
                165                 170                 175

Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu Ala
            180                 185                 190

Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser Ala
        195                 200                 205

Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg His
    210                 215                 220

Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg Val
225                 230                 235                 240

Thr Pro Glu Ile Pro Ala Gly Leu Pro Ser Pro Arg Ser Glu
                245                 250


<210>  334
<211>  300
<212>  PRT
<213>  Homo sapiens

<400>  334

Met Arg Ala Leu Glu Gly Pro Gly Leu Ser Leu Leu Cys Leu Val Leu
1               5                   10                  15

Ala Leu Pro Ala Leu Leu Pro Val Pro Ala Val Arg Gly Val Ala Glu
            20                  25                  30

Thr Pro Thr Tyr Pro Trp Arg Asp Ala Glu Thr Gly Glu Arg Leu Val
        35                  40                  45

Cys Ala Gln Cys Pro Pro Gly Thr Phe Val Gln Arg Pro Cys Arg Arg
    50                  55                  60

Asp Ser Pro Thr Thr Cys Gly Pro Cys Pro Pro Arg His Tyr Thr Gln
```

65 70 75 80

Phe Trp Asn Tyr Leu Glu Arg Cys Arg Tyr Cys Asn Val Leu Cys Gly
85 90 95

Glu Arg Glu Glu Glu Ala Arg Ala Cys His Ala Thr His Asn Arg Ala
100 105 110

Cys Arg Cys Arg Thr Gly Phe Phe Ala His Ala Gly Phe Cys Leu Glu
115 120 125

His Ala Ser Cys Pro Pro Gly Ala Gly Val Ile Ala Pro Gly Thr Pro
130 135 140

Ser Gln Asn Thr Gln Cys Gln Pro Cys Pro Pro Gly Thr Phe Ser Ala
145 150 155 160

Ser Ser Ser Ser Ser Glu Gln Cys Gln Pro His Arg Asn Cys Thr Ala
165 170 175

Leu Gly Leu Ala Leu Asn Val Pro Gly Ser Ser Ser His Asp Thr Leu
180 185 190

Cys Thr Ser Cys Thr Gly Phe Pro Leu Ser Thr Arg Val Pro Gly Ala
195 200 205

Glu Glu Cys Glu Arg Ala Val Ile Asp Phe Val Ala Phe Gln Asp Ile
210 215 220

Ser Ile Lys Arg Leu Gln Arg Leu Leu Gln Ala Leu Glu Ala Pro Glu
225 230 235 240

Gly Trp Gly Pro Thr Pro Arg Ala Gly Arg Ala Ala Leu Gln Leu Lys
245 250 255

Leu Arg Arg Arg Leu Thr Glu Leu Leu Gly Ala Gln Asp Gly Ala Leu
260 265 270

Leu Val Arg Leu Leu Gln Ala Leu Arg Val Ala Arg Met Pro Gly Leu
275 280 285

Glu Arg Ser Val Arg Glu Arg Phe Leu Pro Val His
290 295 300

<210> 335
<211> 183
<212> PRT
<213> Homo sapiens

<400> 335

Met Glu Arg Val Gln Pro Leu Glu Glu Asn Val Gly Asn Ala Ala Arg
1 5 10 15

```
Pro Arg Phe Glu Arg Asn Lys Leu Leu Leu Val Ala Ser Val Ile Gln
            20                  25                  30

Gly Leu Gly Leu Leu Leu Cys Phe Thr Tyr Ile Cys Leu His Phe Ser
        35                  40                  45

Ala Leu Gln Val Ser His Arg Tyr Pro Arg Ile Gln Ser Ile Lys Val
    50                  55                  60

Gln Phe Thr Glu Tyr Lys Lys Glu Lys Gly Phe Ile Leu Thr Ser Gln
65                  70                  75                  80

Lys Glu Asp Glu Ile Met Lys Val Gln Asn Asn Ser Val Ile Ile Asn
                85                  90                  95

Cys Asp Gly Phe Tyr Leu Ile Ser Leu Lys Gly Tyr Phe Ser Gln Glu
            100                 105                 110

Val Asn Ile Ser Leu His Tyr Gln Lys Asp Glu Glu Pro Leu Phe Gln
        115                 120                 125

Leu Lys Lys Val Arg Ser Val Asn Ser Leu Met Val Ala Ser Leu Thr
    130                 135                 140

Tyr Lys Asp Lys Val Tyr Leu Asn Val Thr Thr Asp Asn Thr Ser Leu
145                 150                 155                 160

Asp Asp Phe His Val Asn Gly Gly Glu Leu Ile Leu Ile His Gln Asn
                165                 170                 175

Pro Gly Glu Phe Cys Val Leu
            180


<210>  336
<211>  99
<212>  PRT
<213>  Homo sapiens

<400>  336

Met Lys Ala Ser Ala Ala Leu Leu Cys Leu Leu Leu Thr Ala Ala Ala
1               5                   10                  15

Phe Ser Pro Gln Gly Leu Ala Gln Pro Val Gly Ile Asn Thr Ser Thr
            20                  25                  30

Thr Cys Cys Tyr Arg Phe Ile Asn Lys Lys Ile Pro Lys Gln Arg Leu
        35                  40                  45

Glu Ser Tyr Arg Arg Thr Thr Ser Ser His Cys Pro Arg Glu Ala Val
    50                  55                  60
```

Ile Phe Lys Thr Lys Leu Asp Lys Glu Ile Cys Ala Asp Pro Thr Gln
65 70 75 80

Lys Trp Val Gln Asp Phe Met Lys His Leu Asp Lys Lys Thr Gln Thr
85 90 95

Pro Lys Leu

<210> 337
<211> 99
<212> PRT
<213> Homo sapiens

<400> 337

Met Lys Val Ser Ala Ala Leu Leu Cys Leu Leu Leu Ile Ala Ala Thr
1 5 10 15

Phe Ile Pro Gln Gly Leu Ala Gln Pro Asp Ala Ile Asn Ala Pro Val
20 25 30

Thr Cys Cys Tyr Asn Phe Thr Asn Arg Lys Ile Ser Val Gln Arg Leu
35 40 45

Ala Ser Tyr Arg Arg Ile Thr Ser Ser Lys Cys Pro Lys Glu Ala Val
50 55 60

Ile Phe Lys Thr Ile Val Ala Lys Glu Ile Cys Ala Asp Pro Lys Gln
65 70 75 80

Lys Trp Val Gln Asp Ser Met Asp His Leu Asp Lys Gln Thr Gln Thr
85 90 95

Pro Lys Thr

<210> 338
<211> 107
<212> PRT
<213> Homo sapiens

<400> 338

Met Ala Arg Ala Thr Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
1 5 10 15

Arg Val Ala Leu Leu Leu Leu Leu Leu Val Ala Ala Ser Arg Arg Ala
20 25 30

Ala Gly Ala Pro Leu Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr
35 40 45

Leu Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Lys Val Lys Ser

50 55 60

Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn
65 70 75 80

Gly Gln Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Lys Lys Ile
85 90 95

Ile Glu Lys Met Leu Lys Asn Gly Lys Ser Asn
100 105

<210> 339
<211> 107
<212> PRT
<213> Homo sapiens

<400> 339

Met Ala His Ala Thr Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
1 5 10 15

Arg Val Ala Leu Leu Leu Leu Leu Leu Val Ala Ala Ser Arg Arg Ala
20 25 30

Ala Gly Ala Ser Val Val Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr
35 40 45

Leu Gln Gly Ile His Leu Lys Asn Ile Gln Ser Val Asn Val Arg Ser
50 55 60

Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn
65 70 75 80

Gly Lys Lys Ala Cys Leu Asn Pro Ala Ser Pro Met Val Gln Lys Ile
85 90 95

Ile Glu Lys Ile Leu Asn Lys Gly Ser Thr Asn
100 105

<210> 340
<211> 107
<212> PRT
<213> Homo sapiens

<400> 340

Met Ala Arg Ala Ala Leu Ser Ala Ala Pro Ser Asn Pro Arg Leu Leu
1 5 10 15

Arg Val Ala Leu Leu Leu Leu Leu Leu Val Ala Ala Gly Arg Arg Ala
20 25 30

Ala Gly Ala Ser Val Ala Thr Glu Leu Arg Cys Gln Cys Leu Gln Thr
35 40 45

```
Leu Gln Gly Ile His Pro Lys Asn Ile Gln Ser Val Asn Val Lys Ser
    50                  55                  60

Pro Gly Pro His Cys Ala Gln Thr Glu Val Ile Ala Thr Leu Lys Asn
65                  70                  75                  80

Gly Arg Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile
                85                  90                  95

Ile Glu Lys Met Leu Asn Ser Asp Lys Ser Asn
            100                 105
```

<210> 341
<211> 99
<212> PRT
<213> Homo sapiens

<400> 341

```
Met Thr Ser Lys Leu Ala Val Ala Leu Leu Ala Ala Phe Leu Ile Ser
1               5                   10                  15

Ala Ala Leu Cys Glu Gly Ala Val Leu Pro Arg Ser Ala Lys Glu Leu
            20                  25                  30

Arg Cys Gln Cys Ile Lys Thr Tyr Ser Lys Pro Phe His Pro Lys Phe
        35                  40                  45

Ile Lys Glu Leu Arg Val Ile Glu Ser Gly Pro His Cys Ala Asn Thr
    50                  55                  60

Glu Ile Ile Val Lys Leu Ser Asp Gly Arg Glu Leu Cys Leu Asp Pro
65                  70                  75                  80

Lys Glu Asn Trp Val Gln Arg Val Val Glu Lys Phe Leu Lys Arg Ala
                85                  90                  95

Glu Asn Ser
```

<210> 342
<211> 113
<212> PRT
<213> Homo sapiens

<400> 342

```
Met Lys Val Ser Val Ala Ala Leu Ser Cys Leu Met Leu Val Ala Val
1               5                   10                  15

Leu Gly Ser Gln Ala Gln Phe Ile Asn Asp Ala Glu Thr Glu Leu Met
            20                  25                  30

Met Ser Lys Leu Pro Leu Glu Asn Pro Val Val Leu Asn Ser Phe His
```

35 40 45

Phe Ala Ala Asp Cys Cys Thr Ser Tyr Ile Ser Gln Ser Ile Pro Cys
50 55 60

Ser Leu Met Lys Ser Tyr Phe Glu Thr Ser Ser Glu Cys Ser Lys Pro
65 70 75 80

Gly Val Ile Phe Leu Thr Lys Lys Gly Arg Gln Val Cys Ala Lys Pro
85 90 95

Ser Gly Pro Gly Val Gln Asp Cys Met Lys Lys Leu Lys Pro Tyr Ser
100 105 110

Ile

<210> 343
<211> 93
<212> PRT
<213> Homo sapiens

<400> 343

Met Lys Ile Ser Val Ala Ala Ile Pro Phe Phe Leu Leu Ile Thr Ile
1 5 10 15

Ala Leu Gly Thr Lys Thr Glu Ser Ser Ser Arg Gly Pro Tyr His Pro
20 25 30

Ser Glu Cys Cys Phe Thr Tyr Thr Thr Tyr Lys Ile Pro Arg Gln Arg
35 40 45

Ile Met Asp Tyr Tyr Glu Thr Asn Ser Gln Cys Ser Lys Pro Gly Ile
50 55 60

Val Phe Ile Thr Lys Arg Gly His Ser Val Cys Thr Asn Pro Ser Asp
65 70 75 80

Lys Trp Val Gln Asp Tyr Ile Lys Asp Met Lys Glu Asn
85 90

<210> 344
<211> 99
<212> PRT
<213> Homo sapiens

<400> 344

Met Lys Val Ser Ala Ala Leu Leu Cys Leu Leu Leu Met Ala Ala Thr
1 5 10 15

Phe Ser Pro Gln Gly Leu Ala Gln Pro Asp Ser Val Ser Ile Pro Ile
20 25 30

```
Thr Cys Cys Phe Asn Val Ile Asn Arg Lys Ile Pro Ile Gln Arg Leu
        35                  40                  45

Glu Ser Tyr Thr Arg Ile Thr Asn Ile Gln Cys Pro Lys Glu Ala Val
    50                  55                  60

Ile Phe Lys Thr Lys Arg Gly Lys Glu Val Cys Ala Asp Pro Lys Glu
65                  70                  75                  80

Arg Trp Val Arg Asp Ser Met Lys His Leu Asp Gln Ile Phe Gln Asn
                85                  90                  95

Leu Lys Pro
```

<210> 345
<211> 93
<212> PRT
<213> Homo sapiens

<400> 345

```
Met Asp Arg Leu Gln Thr Ala Leu Leu Val Val Leu Val Leu Leu Ala
1               5                   10                  15

Val Ala Leu Gln Ala Thr Glu Ala Gly Pro Tyr Gly Ala Asn Met Glu
            20                  25                  30

Asp Ser Val Cys Cys Arg Asp Tyr Val Arg Tyr Arg Leu Pro Leu Arg
        35                  40                  45

Val Val Lys His Phe Tyr Trp Thr Ser Asp Ser Cys Pro Arg Pro Gly
    50                  55                  60

Val Val Leu Leu Thr Phe Arg Asp Lys Glu Ile Cys Ala Asp Pro Arg
65                  70                  75                  80

Val Pro Trp Val Lys Met Ile Leu Asn Lys Leu Ser Gln
                85                  90
```

<210> 346
<211> 134
<212> PRT
<213> Homo sapiens

<400> 346

```
Met Ala Gln Ser Leu Ala Leu Ser Leu Leu Ile Leu Val Leu Ala Phe
1               5                   10                  15

Gly Ile Pro Arg Thr Gln Gly Ser Asp Gly Gly Ala Gln Asp Cys Cys
            20                  25                  30

Leu Lys Tyr Ser Gln Arg Lys Ile Pro Ala Lys Val Val Arg Ser Tyr
```

35 40 45

Arg Lys Gln Glu Pro Ser Leu Gly Cys Ser Ile Pro Ala Ile Leu Phe
50 55 60

Leu Pro Arg Lys Arg Ser Gln Ala Glu Leu Cys Ala Asp Pro Lys Glu
65 70 75 80

Leu Trp Val Gln Gln Leu Met Gln His Leu Asp Lys Thr Pro Ser Pro
85 90 95

Gln Lys Pro Ala Gln Gly Cys Arg Lys Asp Arg Gly Ala Ser Lys Thr
100 105 110

Gly Lys Lys Gly Lys Gly Ser Lys Gly Cys Lys Arg Thr Glu Arg Ser
115 120 125

Gln Thr Pro Lys Gly Pro
130

<210> 347
<211> 98
<212> PRT
<213> Homo sapiens

<400> 347

Met Lys Val Ser Ala Val Leu Leu Cys Leu Leu Leu Met Thr Ala Ala
1 5 10 15

Phe Asn Pro Gln Gly Leu Ala Gln Pro Asp Ala Leu Asn Val Pro Ser
20 25 30

Thr Cys Cys Phe Thr Phe Ser Ser Lys Lys Ile Ser Leu Gln Arg Leu
35 40 45

Lys Ser Tyr Val Ile Thr Thr Ser Arg Cys Pro Gln Lys Ala Val Ile
50 55 60

Phe Arg Thr Lys Leu Gly Lys Glu Ile Cys Ala Asp Pro Lys Glu Lys
65 70 75 80

Trp Val Gln Asn Tyr Met Lys His Leu Gly Arg Lys Ala His Thr Leu
85 90 95

Lys Thr

<210> 348
<211> 150
<212> PRT
<213> Homo sapiens

<400> 348

```
Met Asn Leu Trp Leu Leu Ala Cys Leu Val Ala Gly Phe Leu Gly Ala
1               5                  10                  15

Trp Ala Pro Ala Val His Thr Gln Gly Val Phe Glu Asp Cys Cys Leu
            20                  25                  30

Ala Tyr His Tyr Pro Ile Gly Trp Ala Val Leu Arg Arg Ala Trp Thr
        35                  40                  45

Tyr Arg Ile Gln Glu Val Ser Gly Ser Cys Asn Leu Pro Ala Ala Ile
    50                  55                  60

Phe Tyr Leu Pro Lys Arg His Arg Lys Val Cys Gly Asn Pro Lys Ser
65                  70                  75                  80

Arg Glu Val Gln Arg Ala Met Lys Leu Leu Asp Ala Arg Asn Lys Val
                85                  90                  95

Phe Ala Lys Leu His His Asn Thr Gln Thr Phe Gln Ala Gly Pro His
            100                 105                 110

Ala Val Lys Lys Leu Ser Ser Gly Asn Ser Lys Leu Ser Ser Ser Lys
        115                 120                 125

Phe Ser Asn Pro Ile Ser Ser Ser Lys Arg Asn Val Ser Leu Leu Ile
    130                 135                 140

Ser Ala Asn Ser Gly Leu
145                 150


<210>  349
<211>  94
<212>  PRT
<213>  Homo sapiens

<400>  349

Met Met Gly Leu Ser Leu Ala Ser Ala Val Leu Leu Ala Ser Leu Leu
1               5                  10                  15

Ser Leu His Leu Gly Thr Ala Thr Arg Gly Ser Asp Ile Ser Lys Thr
            20                  25                  30

Cys Cys Phe Gln Tyr Ser His Lys Pro Leu Pro Trp Thr Trp Val Arg
        35                  40                  45

Ser Tyr Glu Phe Thr Ser Asn Ser Cys Ser Gln Arg Ala Val Ile Phe
    50                  55                  60

Thr Thr Lys Arg Gly Lys Lys Val Cys Thr His Pro Arg Lys Lys Trp
65                  70                  75                  80
```

Val Gln Lys Tyr Ile Ser Leu Leu Lys Thr Pro Lys Gln Leu
85 90

<210> 350
<211> 111
<212> PRT
<213> Homo sapiens

<400> 350

Met Ser Leu Leu Pro Arg Arg Ala Pro Pro Val Ser Met Arg Leu Leu
1 5 10 15

Ala Ala Ala Leu Leu Leu Leu Leu Leu Ala Leu Tyr Thr Ala Arg Val
20 25 30

Asp Gly Ser Lys Cys Lys Cys Ser Arg Lys Gly Pro Lys Ile Arg Tyr
35 40 45

Ser Asp Val Lys Lys Leu Glu Met Lys Pro Lys Tyr Pro His Cys Glu
50 55 60

Glu Lys Met Val Ile Ile Thr Thr Lys Ser Val Ser Arg Tyr Arg Gly
65 70 75 80

Gln Glu His Cys Leu His Pro Lys Leu Gln Ser Thr Lys Arg Phe Ile
85 90 95

Lys Trp Tyr Asn Ala Trp Asn Glu Lys Arg Arg Val Tyr Glu Glu
100 105 110

<210> 351
<211> 125
<212> PRT
<213> Homo sapiens

<400> 351

Met Lys Lys Ser Gly Val Leu Phe Leu Leu Gly Ile Ile Leu Leu Val
1 5 10 15

Leu Ile Gly Val Gln Gly Thr Pro Val Val Arg Lys Gly Arg Cys Ser
20 25 30

Cys Ile Ser Thr Asn Gln Gly Thr Ile His Leu Gln Ser Leu Lys Asp
35 40 45

Leu Lys Gln Phe Ala Pro Ser Pro Ser Cys Glu Lys Ile Glu Ile Ile
50 55 60

Ala Thr Leu Lys Asn Gly Val Gln Thr Cys Leu Asn Pro Asp Ser Ala
65 70 75 80

Asp Val Lys Glu Leu Ile Lys Lys Trp Glu Lys Gln Val Ser Gln Lys
85 90 95

Lys Lys Gln Lys Asn Gly Lys Lys His Gln Lys Lys Lys Val Leu Lys
100 105 110

Val Arg Lys Ser Gln Arg Ser Arg Gln Lys Lys Thr Thr
115 120 125

<210> 352
<211> 114
<212> PRT
<213> Homo sapiens

<400> 352

Met Ser Leu Leu Ser Ser Arg Ala Ala Arg Val Pro Gly Pro Ser Ser
1 5 10 15

Ser Leu Cys Ala Leu Leu Val Leu Leu Leu Leu Leu Thr Gln Pro Gly
20 25 30

Pro Ile Ala Ser Ala Gly Pro Ala Ala Ala Val Leu Arg Glu Leu Arg
35 40 45

Cys Val Cys Leu Gln Thr Thr Gln Gly Val His Pro Lys Met Ile Ser
50 55 60

Asn Leu Gln Val Phe Ala Ile Gly Pro Gln Cys Ser Lys Val Glu Val
65 70 75 80

Val Ala Ser Leu Lys Asn Gly Lys Glu Ile Cys Leu Asp Pro Glu Ala
85 90 95

Pro Phe Leu Lys Lys Val Ile Gln Lys Ile Leu Asp Gly Gly Asn Lys
100 105 110

Glu Asn

<210> 353
<211> 128
<212> PRT
<213> Homo sapiens

<400> 353

Met Ser Leu Arg Leu Asp Thr Thr Pro Ser Cys Asn Ser Ala Arg Pro
1 5 10 15

Leu His Ala Leu Gln Val Leu Leu Leu Leu Ser Leu Leu Leu Thr Ala
20 25 30

Leu Ala Ser Ser Thr Lys Gly Gln Thr Lys Arg Asn Leu Ala Lys Gly
35 40 45

Lys Glu Glu Ser Leu Asp Ser Asp Leu Tyr Ala Glu Leu Arg Cys Met
50 55 60

Cys Ile Lys Thr Thr Ser Gly Ile His Pro Lys Asn Ile Gln Ser Leu
65 70 75 80

Glu Val Ile Gly Lys Gly Thr His Cys Asn Gln Val Glu Val Ile Ala
85 90 95

Thr Leu Lys Asp Gly Arg Lys Ile Cys Leu Asp Pro Asp Ala Pro Arg
100 105 110

Ile Lys Lys Ile Val Gln Lys Lys Leu Ala Gly Asp Glu Ser Ala Asp
115 120 125

<210> 354
<211> 85
<212> PRT
<213> Homo sapiens

<400> 354

Asn Leu Ala Lys Gly Lys Glu Glu Ser Leu Asp Ser Asp Leu Tyr Ala
1 5 10 15

Glu Leu Arg Cys Met Cys Ile Lys Thr Thr Ser Gly Ile His Pro Lys
20 25 30

Asn Ile Gln Ser Leu Glu Val Ile Gly Lys Gly Thr His Cys Asn Gln
35 40 45

Val Glu Val Ile Ala Thr Leu Lys Asp Gly Arg Lys Ile Cys Leu Asp
50 55 60

Pro Asp Ala Pro Arg Ile Lys Lys Ile Val Gln Lys Lys Leu Ala Gly
65 70 75 80

Asp Glu Ser Ala Asp
85

<210> 355
<211> 81
<212> PRT
<213> Homo sapiens

<400> 355

Gly Lys Glu Glu Ser Leu Asp Ser Asp Leu Tyr Ala Glu Leu Arg Cys
1 5 10 15

Met Cys Ile Lys Thr Thr Ser Gly Ile His Pro Lys Asn Ile Gln Ser
20 25 30

Leu Glu Val Ile Gly Lys Gly Thr His Cys Asn Gln Val Glu Val Ile
35 40 45

Ala Thr Leu Lys Asp Gly Arg Lys Ile Cys Leu Asp Pro Asp Ala Pro
    50   55   60

Arg Ile Lys Lys Ile Val Gln Lys Lys Leu Ala Gly Asp Glu Ser Ala
65   70   75   80

Asp

<210> 356
<211> 70
<212> PRT
<213> Homo sapiens

<400> 356

Ala Glu Leu Arg Cys Met Cys Ile Lys Thr Thr Ser Gly Ile His Pro
1   5   10   15

Lys Asn Ile Gln Ser Leu Glu Val Ile Gly Lys Gly Thr His Cys Asn
            20   25   30

Gln Val Glu Val Ile Ala Thr Leu Lys Asp Gly Arg Lys Ile Cys Leu
        35   40   45

Asp Pro Asp Ala Pro Arg Ile Lys Lys Ile Val Gln Lys Lys Leu Ala
    50   55   60

Gly Asp Glu Ser Ala Asp
65   70

<210> 357
<211> 114
<212> PRT
<213> Homo sapiens

<400> 357

Met Ser Leu Pro Ser Ser Arg Ala Ala Arg Val Pro Gly Pro Ser Gly
1   5   10   15

Ser Leu Cys Ala Leu Leu Ala Leu Leu Leu Leu Leu Thr Pro Pro Gly
            20   25   30

Pro Leu Ala Ser Ala Gly Pro Val Ser Ala Val Leu Thr Glu Leu Arg
        35   40   45

Cys Thr Cys Leu Arg Val Thr Leu Arg Val Asn Pro Lys Thr Ile Gly
    50   55   60

Lys Leu Gln Val Phe Pro Ala Gly Pro Gln Cys Ser Lys Val Glu Val
65   70   75   80

Val Ala Ser Leu Lys Asn Gly Lys Gln Val Cys Leu Asp Pro Glu Ala
85 90 95

Pro Phe Leu Lys Lys Val Ile Gln Lys Ile Leu Asp Ser Gly Asn Lys
100 105 110

Lys Asn

<210> 358
<211> 92
<212> PRT
<213> Homo sapiens

<400> 358

Met Lys Leu Cys Val Thr Val Leu Ser Leu Leu Met Leu Val Ala Ala
1 5 10 15

Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr
20 25 30

Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val
35 40 45

Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val
50 55 60

Phe Gln Thr Lys Arg Ser Lys Gln Val Cys Ala Asp Pro Ser Glu Ser
65 70 75 80

Trp Val Gln Glu Tyr Val Tyr Asp Leu Glu Leu Asn
85 90

<210> 359
<211> 101
<212> PRT
<213> Homo sapiens

<400> 359

Met Ser Ser Ala Ala Gly Phe Cys Ala Ser Arg Pro Gly Leu Leu Phe
1 5 10 15

Leu Gly Leu Leu Leu Leu Pro Leu Val Val Ala Phe Ala Ser Ala Glu
20 25 30

Ala Glu Glu Asp Gly Asp Leu Gln Cys Leu Cys Val Lys Thr Thr Ser
35 40 45

Gln Val Arg Pro Arg His Ile Thr Ser Leu Glu Val Ile Lys Ala Gly
50 55 60

Pro His Cys Pro Thr Ala Gln Leu Ile Ala Thr Leu Lys Asn Gly Arg
65 70 75 80

```
Lys Ile Cys Leu Asp Leu Gln Ala Pro Leu Tyr Lys Lys Ile Ile Lys
                85                  90                  95


Lys Leu Leu Glu Ser
            100


<210>  360
<211>  96
<212>  PRT
<213>  Homo sapiens

<400>  360

Met Gln Ile Ile Thr Thr Ala Leu Val Cys Leu Leu Leu Ala Gly Met
1               5                  10                  15


Trp Pro Glu Asp Val Asp Ser Lys Ser Met Gln Val Pro Phe Ser Arg
            20                  25                  30


Cys Cys Phe Ser Phe Ala Glu Gln Glu Ile Pro Leu Arg Ala Ile Leu
        35                  40                  45


Cys Tyr Arg Asn Thr Ser Ser Ile Cys Ser Asn Glu Gly Leu Ile Phe
    50                  55                  60


Lys Leu Lys Arg Gly Lys Glu Ala Cys Ala Leu Asp Thr Val Gly Trp
65                  70                  75                  80


Val Gln Arg His Arg Lys Met Leu Arg His Cys Pro Ser Lys Arg Lys
                85                  90                  95


<210>  361
<211>  93
<212>  PRT
<213>  Homo sapiens

<400>  361

Met Lys Ile Ser Val Ala Ala Ile Pro Phe Phe Leu Leu Ile Thr Ile
1               5                  10                  15


Ala Leu Gly Thr Lys Thr Glu Ser Ser Ser Arg Gly Pro Tyr His Pro
            20                  25                  30


Ser Glu Cys Cys Phe Thr Tyr Thr Thr Tyr Lys Ile Pro Arg Gln Arg
        35                  40                  45


Ile Met Asp Tyr Tyr Glu Thr Asn Ser Gln Cys Ser Lys Pro Gly Ile
    50                  55                  60


Val Phe Ile Thr Lys Arg Gly His Ser Val Cys Thr Asn Pro Ser Asp
65                  70                  75                  80
```

Lys Trp Val Gln Asp Tyr Ile Lys Asp Met Lys Glu Asn
85 90

<210> 362
<211> 374
<212> PRT
<213> Homo sapiens

<400> 362

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
1 5 10 15

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
20 25 30

His Lys Phe Asp Val Lys Gln Ile Gly Ala Gln Leu Leu Pro Pro Leu
35 40 45

Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn Met Leu Val Val
50 55 60

Leu Ile Leu Ile Asn Cys Lys Lys Leu Lys Cys Leu Thr Asp Ile Tyr
65 70 75 80

Leu Leu Asn Leu Ala Ile Ser Asp Leu Leu Phe Leu Ile Thr Leu Pro
85 90 95

Leu Trp Ala His Ser Ala Ala Asn Glu Trp Val Phe Gly Asn Ala Met
100 105 110

Cys Lys Leu Phe Thr Gly Leu Tyr His Ile Gly Tyr Phe Gly Gly Ile
115 120 125

Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu Ala Ile Val His
130 135 140

Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe Gly Val Val Thr
145 150 155 160

Ser Val Ile Thr Trp Leu Val Ala Val Phe Ala Ser Val Pro Gly Ile
165 170 175

Ile Phe Thr Lys Cys Gln Lys Glu Asp Ser Val Tyr Val Cys Gly Pro
180 185 190

Tyr Phe Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg Asn Ile
195 200 205

Leu Gly Leu Val Leu Pro Leu Leu Ile Met Val Ile Cys Tyr Ser Gly
210 215 220

Ile Leu Lys Thr Leu Leu Arg Cys Arg Asn Glu Lys Lys Arg His Arg

225 230 235 240

Ala Val Arg Val Ile Phe Thr Ile Met Ile Val Tyr Phe Leu Phe Trp
245 250 255

Thr Pro Tyr Asn Ile Val Ile Leu Leu Asn Thr Phe Gln Glu Phe Phe
260 265 270

Gly Leu Ser Asn Cys Glu Ser Thr Ser Gln Leu Asp Gln Ala Thr Gln
275 280 285

Val Thr Glu Thr Leu Gly Met Thr His Cys Cys Ile Asn Pro Ile Ile
290 295 300

Tyr Ala Phe Val Gly Glu Lys Phe Arg Ser Leu Phe His Ile Ala Leu
305 310 315 320

Gly Cys Arg Ile Ala Pro Leu Gln Lys Pro Val Cys Gly Gly Pro Gly
325 330 335

Val Arg Pro Gly Lys Asn Val Lys Val Thr Thr Gln Gly Leu Leu Asp
340 345 350

Gly Arg Gly Lys Gly Lys Ser Ile Gly Arg Ala Pro Glu Ala Ser Leu
355 360 365

Gln Asp Lys Glu Gly Ala
370

<210> 363
<211> 94
<212> PRT
<213> Homo sapiens

<400> 363

Met Ser Val Lys Gly Met Ala Ile Ala Leu Ala Val Ile Leu Cys Ala
1 5 10 15

Thr Val Val Gln Gly Phe Pro Met Phe Lys Arg Gly Arg Cys Leu Cys
20 25 30

Ile Gly Pro Gly Val Lys Ala Val Lys Val Ala Asp Ile Glu Lys Ala
35 40 45

Ser Ile Met Tyr Pro Ser Asn Asn Cys Asp Lys Ile Glu Val Ile Ile
50 55 60

Thr Leu Lys Glu Asn Lys Gly Gln Arg Cys Leu Asn Pro Lys Ser Lys
65 70 75 80

Gln Ala Arg Leu Ile Ile Lys Lys Val Glu Arg Lys Asn Phe
85 90

<210> 364
<211> 92
<212> PRT
<213> Homo sapiens

<400> 364

```
Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
1               5                  10                  15


Leu Cys Asn Gln Phe Ser Ala Ser Leu Ala Ala Asp Thr Pro Thr Ala
            20                  25                  30


Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile Ala
        35                  40                  45


Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Gly Val Ile Phe
    50                  55                  60


Leu Thr Lys Arg Ser Arg Gln Val Cys Ala Asp Pro Ser Glu Glu Trp
65                  70                  75                  80


Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
                85                  90
```

<210> 365
<211> 180
<212> PRT
<213> Homo sapiens

<400> 365

```
Met Leu Cys Leu Leu Leu Thr Leu Gly Val Ala Leu Val Cys Gly Val
1               5                  10                  15


Pro Ala Met Asp Ile Pro Gln Thr Lys Gln Asp Leu Glu Leu Pro Lys
            20                  25                  30


Leu Ala Gly Thr Trp His Ser Met Ala Met Ala Thr Asn Asn Ile Ser
        35                  40                  45


Leu Met Ala Thr Leu Lys Ala Pro Leu Arg Val His Ile Thr Ser Leu
    50                  55                  60


Leu Pro Thr Pro Glu Asp Asn Leu Glu Ile Val Leu His Arg Trp Glu
65                  70                  75                  80


Asn Asn Ser Cys Val Glu Lys Lys Val Leu Gly Glu Lys Thr Glu Asn
                85                  90                  95


Pro Lys Lys Phe Lys Ile Asn Tyr Thr Val Ala Asn Glu Ala Thr Leu
            100                 105                 110
```

Leu Asp Thr Asp Tyr Asp Asn Phe Leu Phe Leu Cys Leu Gln Asp Thr
        115   120   125

Thr Thr Pro Ile Gln Ser Met Met Cys Gln Tyr Leu Ala Arg Val Leu
    130   135   140

Val Glu Asp Asp Glu Ile Met Gln Gly Phe Ile Arg Ala Phe Arg Pro
145   150   155   160

Leu Pro Arg His Leu Trp Tyr Leu Leu Asp Leu Lys Gln Met Glu Glu
                165   170   175

Pro Cys Arg Phe
            180

<210> 366
<211> 1192
<212> PRT
<213> Homo sapiens

<400> 366

Met Glu Asp Leu Asp Gln Ser Pro Leu Val Ser Ser Ser Asp Ser Pro
1   5   10   15

Pro Arg Pro Gln Pro Ala Phe Lys Tyr Gln Phe Val Arg Glu Pro Glu
            20   25   30

Asp Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Asp Glu Asp Glu Asp
        35   40   45

Leu Glu Glu Leu Glu Val Leu Glu Arg Lys Pro Ala Ala Gly Leu Ser
    50   55   60

Ala Ala Pro Val Pro Thr Ala Pro Ala Ala Gly Ala Pro Leu Met Asp
65   70   75   80

Phe Gly Asn Asp Phe Val Pro Pro Ala Pro Arg Gly Pro Leu Pro Ala
                85   90   95

Ala Pro Pro Val Ala Pro Glu Arg Gln Pro Ser Trp Asp Pro Ser Pro
            100   105   110

Val Ser Ser Thr Val Pro Ala Pro Ser Pro Leu Ser Ala Ala Ala Val
        115   120   125

Ser Pro Ser Lys Leu Pro Glu Asp Asp Glu Pro Pro Ala Arg Pro Pro
    130   135   140

Pro Pro Pro Pro Ala Ser Val Ser Pro Gln Ala Glu Pro Val Trp Thr
145   150   155   160

Pro Pro Ala Pro Ala Pro Ala Ala Pro Pro Ser Thr Pro Ala Ala Pro

165 170 175

Lys Arg Arg Gly Ser Ser Gly Ser Val Asp Glu Thr Leu Phe Ala Leu
180 185 190

Pro Ala Ala Ser Glu Pro Val Ile Arg Ser Ser Ala Glu Asn Met Asp
195 200 205

Leu Lys Glu Gln Pro Gly Asn Thr Ile Ser Ala Gly Gln Glu Asp Phe
210 215 220

Pro Ser Val Leu Leu Glu Thr Ala Ala Ser Leu Pro Ser Leu Ser Pro
225 230 235 240

Leu Ser Ala Ala Ser Phe Lys Glu His Glu Tyr Leu Gly Asn Leu Ser
245 250 255

Thr Val Leu Pro Thr Glu Gly Thr Leu Gln Glu Asn Val Ser Glu Ala
260 265 270

Ser Lys Glu Val Ser Glu Lys Ala Lys Thr Leu Leu Ile Asp Arg Asp
275 280 285

Leu Thr Glu Phe Ser Glu Leu Glu Tyr Ser Glu Met Gly Ser Ser Phe
290 295 300

Ser Val Ser Pro Lys Ala Glu Ser Ala Val Ile Val Ala Asn Pro Arg
305 310 315 320

Glu Glu Ile Ile Val Lys Asn Lys Asp Glu Glu Glu Lys Leu Val Ser
325 330 335

Asn Asn Ile Leu His Asn Gln Gln Glu Leu Pro Thr Ala Leu Thr Lys
340 345 350

Leu Val Lys Glu Asp Glu Val Val Ser Ser Glu Lys Ala Lys Asp Ser
355 360 365

Phe Asn Glu Lys Arg Val Ala Val Glu Ala Pro Met Arg Glu Glu Tyr
370 375 380

Ala Asp Phe Lys Pro Phe Glu Arg Val Trp Glu Val Lys Asp Ser Lys
385 390 395 400

Glu Asp Ser Asp Met Leu Ala Ala Gly Gly Lys Ile Glu Ser Asn Leu
405 410 415

Glu Ser Lys Val Asp Lys Lys Cys Phe Ala Asp Ser Leu Glu Gln Thr
420 425 430

Asn His Glu Lys Asp Ser Glu Ser Ser Asn Asp Asp Thr Ser Phe Pro

```
        435                 440                 445

Ser Thr Pro Glu Gly Ile Lys Asp Arg Pro Gly Ala Tyr Ile Thr Cys
    450                 455                 460

Ala Pro Phe Asn Pro Ala Ala Thr Glu Ser Ile Ala Thr Asn Ile Phe
465                 470                 475                 480

Pro Leu Leu Gly Asp Pro Thr Ser Glu Asn Lys Thr Asp Glu Lys Lys
                485                 490                 495

Ile Glu Glu Lys Lys Ala Gln Ile Val Thr Glu Lys Asn Thr Ser Thr
            500                 505                 510

Lys Thr Ser Asn Pro Phe Leu Val Ala Ala Gln Asp Ser Glu Thr Asp
        515                 520                 525

Tyr Val Thr Thr Asp Asn Leu Thr Lys Val Thr Glu Glu Val Val Ala
    530                 535                 540

Asn Met Pro Glu Gly Leu Thr Pro Asp Leu Val Gln Glu Ala Cys Glu
545                 550                 555                 560

Ser Glu Leu Asn Glu Val Thr Gly Thr Lys Ile Ala Tyr Glu Thr Lys
                565                 570                 575

Met Asp Leu Val Gln Thr Ser Glu Val Met Gln Glu Ser Leu Tyr Pro
            580                 585                 590

Ala Ala Gln Leu Cys Pro Ser Phe Glu Glu Ser Glu Ala Thr Pro Ser
        595                 600                 605

Pro Val Leu Pro Asp Ile Val Met Glu Ala Pro Leu Asn Ser Ala Val
    610                 615                 620

Pro Ser Ala Gly Ala Ser Val Ile Gln Pro Ser Ser Ser Pro Leu Glu
625                 630                 635                 640

Ala Ser Ser Val Asn Tyr Glu Ser Ile Lys His Glu Pro Glu Asn Pro
                645                 650                 655

Pro Pro Tyr Glu Glu Ala Met Ser Val Ser Leu Lys Lys Val Ser Gly
            660                 665                 670

Ile Lys Glu Glu Ile Lys Glu Pro Glu Asn Ile Asn Ala Ala Leu Gln
        675                 680                 685

Glu Thr Glu Ala Pro Tyr Ile Ser Ile Ala Cys Asp Leu Ile Lys Glu
    690                 695                 700

Thr Lys Leu Ser Ala Glu Pro Ala Pro Asp Phe Ser Asp Tyr Ser Glu
```

```
705                 710                 715                 720

Met Ala Lys Val Glu Gln Pro Val Pro Asp His Ser Glu Leu Val Glu
                725                 730                 735

Asp Ser Ser Pro Asp Ser Glu Pro Val Asp Leu Phe Ser Asp Asp Ser
            740                 745                 750

Ile Pro Asp Val Pro Gln Lys Gln Asp Glu Thr Val Met Leu Val Lys
        755                 760                 765

Glu Ser Leu Thr Glu Thr Ser Phe Glu Ser Met Ile Glu Tyr Glu Asn
    770                 775                 780

Lys Glu Lys Leu Ser Ala Leu Pro Pro Glu Gly Gly Lys Pro Tyr Leu
785                 790                 795                 800

Glu Ser Phe Lys Leu Ser Leu Asp Asn Thr Lys Asp Thr Leu Leu Pro
                805                 810                 815

Asp Glu Val Ser Thr Leu Ser Lys Lys Glu Lys Ile Pro Leu Gln Met
            820                 825                 830

Glu Glu Leu Ser Thr Ala Val Tyr Ser Asn Asp Asp Leu Phe Ile Ser
        835                 840                 845

Lys Glu Ala Gln Ile Arg Glu Thr Glu Thr Phe Ser Asp Ser Ser Pro
    850                 855                 860

Ile Glu Ile Ile Asp Glu Phe Pro Thr Leu Ile Ser Ser Lys Thr Asp
865                 870                 875                 880

Ser Phe Ser Lys Leu Ala Arg Glu Tyr Thr Asp Leu Glu Val Ser His
                885                 890                 895

Lys Ser Glu Ile Ala Asn Ala Pro Asp Gly Ala Gly Ser Leu Pro Cys
            900                 905                 910

Thr Glu Leu Pro His Asp Leu Ser Leu Lys Asn Ile Gln Pro Lys Val
        915                 920                 925

Glu Glu Lys Ile Ser Phe Ser Asp Asp Phe Ser Lys Asn Gly Ser Ala
    930                 935                 940

Thr Ser Lys Val Leu Leu Leu Pro Pro Asp Val Ser Ala Leu Ala Thr
945                 950                 955                 960

Gln Ala Glu Ile Glu Ser Ile Val Lys Pro Lys Val Leu Val Lys Glu
                965                 970                 975

Ala Glu Lys Lys Leu Pro Ser Asp Thr Glu Lys Glu Asp Arg Ser Pro
```

980 985 990

Ser Ala Ile Phe Ser Ala Glu Leu Ser Lys Thr Ser Val Val Asp Leu
995 1000 1005

Leu Tyr Trp Arg Asp Ile Lys Lys Thr Gly Val Val Phe Gly Ala
1010 1015 1020

Ser Leu Phe Leu Leu Leu Ser Leu Thr Val Phe Ser Ile Val Ser
1025 1030 1035

Val Thr Ala Tyr Ile Ala Leu Ala Leu Leu Ser Val Thr Ile Ser
1040 1045 1050

Phe Arg Ile Tyr Lys Gly Val Ile Gln Ala Ile Gln Lys Ser Asp
1055 1060 1065

Glu Gly His Pro Phe Arg Ala Tyr Leu Glu Ser Glu Val Ala Ile
1070 1075 1080

Ser Glu Glu Leu Val Gln Lys Tyr Ser Asn Ser Ala Leu Gly His
1085 1090 1095

Val Asn Cys Thr Ile Lys Glu Leu Arg Arg Leu Phe Leu Val Asp
1100 1105 1110

Asp Leu Val Asp Ser Leu Lys Phe Ala Val Leu Met Trp Val Phe
1115 1120 1125

Thr Tyr Val Gly Ala Leu Phe Asn Gly Leu Thr Leu Leu Ile Leu
1130 1135 1140

Ala Leu Ile Ser Leu Phe Ser Val Pro Val Ile Tyr Glu Arg His
1145 1150 1155

Gln Ala Gln Ile Asp His Tyr Leu Gly Leu Ala Asn Lys Asn Val
1160 1165 1170

Lys Asp Ala Met Ala Lys Ile Gln Ala Lys Ile Pro Gly Leu Lys
1175 1180 1185

Arg Lys Ala Glu
1190

<210> 367
<211> 373
<212> PRT
<213> Homo sapiens

<400> 367

Met Glu Asp Leu Asp Gln Ser Pro Leu Val Ser Ser Ser Asp Ser Pro
1 5 10 15

```
Pro Arg Pro Gln Pro Ala Phe Lys Tyr Gln Phe Val Arg Glu Pro Glu
            20                  25                  30

Asp Glu Glu Glu Glu Glu Glu Glu Glu Glu Glu Asp Glu Asp Glu Asp
        35                  40                  45

Leu Glu Glu Leu Glu Val Leu Glu Arg Lys Pro Ala Ala Gly Leu Ser
    50                  55                  60

Ala Ala Pro Val Pro Thr Ala Pro Ala Ala Gly Ala Pro Leu Met Asp
65                  70                  75                  80

Phe Gly Asn Asp Phe Val Pro Pro Ala Pro Arg Gly Pro Leu Pro Ala
                85                  90                  95

Ala Pro Pro Val Ala Pro Glu Arg Gln Pro Ser Trp Asp Pro Ser Pro
            100                 105                 110

Val Ser Ser Thr Val Pro Ala Pro Ser Pro Leu Ser Ala Ala Ala Val
        115                 120                 125

Ser Pro Ser Lys Leu Pro Glu Asp Asp Glu Pro Pro Ala Arg Pro Pro
    130                 135                 140

Pro Pro Pro Pro Ala Ser Val Ser Pro Gln Ala Glu Pro Val Trp Thr
145                 150                 155                 160

Pro Pro Ala Pro Ala Pro Ala Ala Pro Pro Ser Thr Pro Ala Ala Pro
                165                 170                 175

Lys Arg Arg Gly Ser Ser Gly Ser Val Val Val Asp Leu Leu Tyr Trp
            180                 185                 190

Arg Asp Ile Lys Lys Thr Gly Val Val Phe Gly Ala Ser Leu Phe Leu
        195                 200                 205

Leu Leu Ser Leu Thr Val Phe Ser Ile Val Ser Val Thr Ala Tyr Ile
    210                 215                 220

Ala Leu Ala Leu Leu Ser Val Thr Ile Ser Phe Arg Ile Tyr Lys Gly
225                 230                 235                 240

Val Ile Gln Ala Ile Gln Lys Ser Asp Glu Gly His Pro Phe Arg Ala
                245                 250                 255

Tyr Leu Glu Ser Glu Val Ala Ile Ser Glu Glu Leu Val Gln Lys Tyr
            260                 265                 270

Ser Asn Ser Ala Leu Gly His Val Asn Cys Thr Ile Lys Glu Leu Arg
        275                 280                 285
```

```
Arg Leu Phe Leu Val Asp Asp Leu Val Asp Ser Leu Lys Phe Ala Val
    290                 295                 300

Leu Met Trp Val Phe Thr Tyr Val Gly Ala Leu Phe Asn Gly Leu Thr
305                 310                 315                 320

Leu Leu Ile Leu Ala Leu Ile Ser Leu Phe Ser Val Pro Val Ile Tyr
                325                 330                 335

Glu Arg His Gln Ala Gln Ile Asp His Tyr Leu Gly Leu Ala Asn Lys
            340                 345                 350

Asn Val Lys Asp Ala Met Ala Lys Ile Gln Ala Lys Ile Pro Gly Leu
        355                 360                 365

Lys Arg Lys Ala Glu
    370
```

<210> 368
<211> 199
<212> PRT
<213> Homo sapiens

<400> 368

```
Met Asp Gly Gln Lys Lys Asn Trp Lys Asp Lys Val Val Asp Leu Leu
1               5                   10                  15

Tyr Trp Arg Asp Ile Lys Lys Thr Gly Val Val Phe Gly Ala Ser Leu
            20                  25                  30

Phe Leu Leu Leu Ser Leu Thr Val Phe Ser Ile Val Ser Val Thr Ala
        35                  40                  45

Tyr Ile Ala Leu Ala Leu Leu Ser Val Thr Ile Ser Phe Arg Ile Tyr
    50                  55                  60

Lys Gly Val Ile Gln Ala Ile Gln Lys Ser Asp Glu Gly His Pro Phe
65                  70                  75                  80

Arg Ala Tyr Leu Glu Ser Glu Val Ala Ile Ser Glu Glu Leu Val Gln
                85                  90                  95

Lys Tyr Ser Asn Ser Ala Leu Gly His Val Asn Cys Thr Ile Lys Glu
            100                 105                 110

Leu Arg Arg Leu Phe Leu Val Asp Asp Leu Val Asp Ser Leu Lys Phe
        115                 120                 125

Ala Val Leu Met Trp Val Phe Thr Tyr Val Gly Ala Leu Phe Asn Gly
    130                 135                 140
```

```
Leu Thr Leu Leu Ile Leu Ala Leu Ile Ser Leu Phe Ser Val Pro Val
145                 150                 155                 160


Ile Tyr Glu Arg His Gln Ala Gln Ile Asp His Tyr Leu Gly Leu Ala
                165                 170                 175


Asn Lys Asn Val Lys Asp Ala Met Ala Lys Ile Gln Ala Lys Ile Pro
            180                 185                 190


Gly Leu Lys Arg Lys Ala Glu
        195


<210>  369
<211>  473
<212>  PRT
<213>  Homo sapiens

<400>  369

Met Lys Arg Ala Ser Ala Gly Gly Ser Arg Leu Leu Ala Trp Val Leu
1               5                   10                  15


Trp Leu Gln Ala Trp Gln Val Ala Ala Pro Cys Pro Gly Ala Cys Val
            20                  25                  30


Cys Tyr Asn Glu Pro Lys Val Thr Thr Ser Cys Pro Gln Gln Gly Leu
        35                  40                  45


Gln Ala Val Pro Val Gly Ile Pro Ala Ala Ser Gln Arg Ile Phe Leu
    50                  55                  60


His Gly Asn Arg Ile Ser His Val Pro Ala Ala Ser Phe Arg Ala Cys
65                  70                  75                  80


Arg Asn Leu Thr Ile Leu Trp Leu His Ser Asn Val Leu Ala Arg Ile
                85                  90                  95


Asp Ala Ala Ala Phe Thr Gly Leu Ala Leu Leu Glu Gln Leu Asp Leu
            100                 105                 110


Ser Asp Asn Ala Gln Leu Arg Ser Val Asp Pro Ala Thr Phe His Gly
        115                 120                 125


Leu Gly Arg Leu His Thr Leu His Leu Asp Arg Cys Gly Leu Gln Glu
    130                 135                 140


Leu Gly Pro Gly Leu Phe Arg Gly Leu Ala Ala Leu Gln Tyr Leu Tyr
145                 150                 155                 160


Leu Gln Asp Asn Ala Leu Gln Ala Leu Pro Asp Asp Thr Phe Arg Asp
                165                 170                 175
```

```
Leu Gly Asn Leu Thr His Leu Phe Leu His Gly Asn Arg Ile Ser Ser
            180                 185                 190

Val Pro Glu Arg Ala Phe Arg Gly Leu His Ser Leu Asp Arg Leu Leu
        195                 200                 205

Leu His Gln Asn Arg Val Ala His Val His Pro His Ala Phe Arg Asp
    210                 215                 220

Leu Gly Arg Leu Met Thr Leu Tyr Leu Phe Ala Asn Asn Leu Ser Ala
225                 230                 235                 240

Leu Pro Thr Glu Ala Leu Ala Pro Leu Arg Ala Leu Gln Tyr Leu Arg
                245                 250                 255

Leu Asn Asp Asn Pro Trp Val Cys Asp Cys Arg Ala Arg Pro Leu Trp
            260                 265                 270

Ala Trp Leu Gln Lys Phe Arg Gly Ser Ser Ser Glu Val Pro Cys Ser
        275                 280                 285

Leu Pro Gln Arg Leu Ala Gly Arg Asp Leu Lys Arg Leu Ala Ala Asn
    290                 295                 300

Asp Leu Gln Gly Cys Ala Val Ala Thr Gly Pro Tyr His Pro Ile Trp
305                 310                 315                 320

Thr Gly Arg Ala Thr Asp Glu Glu Pro Leu Gly Leu Pro Lys Cys Cys
                325                 330                 335

Gln Pro Asp Ala Ala Asp Lys Ala Ser Val Leu Glu Pro Gly Arg Pro
            340                 345                 350

Ala Ser Ala Gly Asn Ala Leu Lys Gly Arg Val Pro Pro Gly Asp Ser
        355                 360                 365

Pro Pro Gly Asn Gly Ser Gly Pro Arg His Ile Asn Asp Ser Pro Phe
    370                 375                 380

Gly Thr Leu Pro Gly Ser Ala Glu Pro Pro Leu Thr Ala Val Arg Pro
385                 390                 395                 400

Glu Gly Ser Glu Pro Pro Gly Phe Pro Thr Ser Gly Pro Arg Arg Arg
                405                 410                 415

Pro Gly Cys Ser Arg Lys Asn Arg Thr Arg Ser His Cys Arg Leu Gly
            420                 425                 430

Gln Ala Gly Ser Gly Gly Gly Gly Thr Gly Asp Ser Glu Gly Ser Gly
        435                 440                 445
```

Ala Leu Pro Ser Leu Thr Cys Ser Leu Thr Pro Leu Gly Leu Ala Leu
450 455 460

Val Leu Trp Thr Val Leu Gly Pro Cys
465 470

<210> 370
<211> 317
<212> PRT
<213> Homo sapiens

<400> 370

Met Ala Lys Asn Pro Pro Glu Asn Cys Glu Asp Cys His Ile Leu Asn
1 5 10 15

Ala Glu Ala Phe Lys Ser Lys Lys Ile Cys Lys Ser Leu Lys Ile Cys
20 25 30

Gly Leu Val Phe Gly Ile Leu Ala Leu Thr Leu Ile Val Leu Phe Trp
35 40 45

Gly Ser Lys His Phe Trp Pro Glu Val Pro Lys Lys Ala Tyr Asp Met
50 55 60

Glu His Thr Phe Tyr Ser Asn Gly Glu Lys Lys Lys Ile Tyr Met Glu
65 70 75 80

Ile Asp Pro Val Thr Arg Thr Glu Ile Phe Arg Ser Gly Asn Gly Thr
85 90 95

Asp Glu Thr Leu Glu Val His Asp Phe Lys Asn Gly Tyr Thr Gly Ile
100 105 110

Tyr Phe Val Gly Leu Gln Lys Cys Phe Ile Lys Thr Gln Ile Lys Val
115 120 125

Ile Pro Glu Phe Ser Glu Pro Glu Glu Glu Ile Asp Glu Asn Glu Glu
130 135 140

Ile Thr Thr Thr Phe Phe Glu Gln Ser Val Ile Trp Val Pro Ala Glu
145 150 155 160

Lys Pro Ile Glu Asn Arg Asp Phe Leu Lys Asn Ser Lys Ile Leu Glu
165 170 175

Ile Cys Asp Asn Val Thr Met Tyr Trp Ile Asn Pro Thr Leu Ile Ser
180 185 190

Val Ser Glu Leu Gln Asp Phe Glu Glu Glu Gly Glu Asp Leu His Phe
195 200 205

Pro Ala Asn Glu Lys Lys Gly Ile Glu Gln Asn Glu Gln Trp Val Val

210 215 220

Pro Gln Val Lys Val Glu Lys Thr Arg His Ala Arg Gln Ala Ser Glu
225 230 235 240

Glu Glu Leu Pro Ile Asn Asp Tyr Thr Glu Asn Gly Ile Glu Phe Asp
245 250 255

Pro Met Leu Asp Glu Arg Gly Tyr Cys Cys Ile Tyr Cys Arg Arg Gly
260 265 270

Asn Arg Tyr Cys Arg Arg Val Cys Glu Pro Leu Leu Gly Tyr Tyr Pro
275 280 285

Tyr Pro Tyr Cys Tyr Gln Gly Gly Arg Val Ile Cys Arg Val Ile Met
290 295 300

Pro Cys Asn Trp Trp Val Ala Arg Met Leu Gly Arg Val
305 310 315

<210> 371
<211> 164
<212> PRT
<213> Homo sapiens

<400> 371

Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1 5 10 15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
20 25 30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
35 40 45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
50 55 60

Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65 70 75 80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
85 90 95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
100 105 110

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
115 120 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Tyr Val Gly
130 135 140

```
Ala Arg Cys Cys Leu Met Pro Trp Ser Leu Pro Gly Pro Gln Cys Asp
145                 150                 155                 160


Lys Pro Arg Arg



<210>  372
<211>  188
<212>  PRT
<213>  Homo sapiens

<400>  372

Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1               5                   10                  15


Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
            20                  25                  30


Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
        35                  40                  45


Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
    50                  55                  60


Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65                  70                  75                  80


Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
                85                  90                  95


Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
            100                 105                 110


Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
        115                 120                 125


Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val
    130                 135                 140


Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr
145                 150                 155                 160


Lys Ser Trp Ser Val Tyr Val Gly Ala Arg Cys Cys Leu Met Pro Trp
                165                 170                 175


Ser Leu Pro Gly Pro Gln Cys Asp Lys Pro Arg Arg
            180                 185


<210>  373
<211>  208
<212>  PRT
```

<213> Homo sapiens

<400> 373

```
Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1               5                  10                  15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
            20                  25                  30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
        35                  40                  45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
    50                  55                  60

Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65                  70                  75                  80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
                85                  90                  95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
            100                 105                 110

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
        115                 120                 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Tyr Val Gly
    130                 135                 140

Ala Arg Cys Cys Leu Met Pro Trp Ser Leu Pro Gly Pro His Pro Cys
145                 150                 155                 160

Gly Pro Cys Ser Glu Arg Arg Lys His Leu Phe Val Gln Asp Pro Gln
                165                 170                 175

Thr Cys Lys Cys Ser Cys Lys Asn Thr Asp Ser Arg Cys Lys Ala Arg
            180                 185                 190

Gln Leu Glu Leu Asn Glu Arg Thr Cys Arg Cys Asp Lys Pro Arg Arg
        195                 200                 205
```

<210> 374
<211> 354
<212> PRT
<213> Homo sapiens

<400> 374

```
Met Tyr Arg Glu Trp Val Val Val Asn Val Phe Met Met Leu Tyr Val
1               5                  10                  15

Gln Leu Val Gln Gly Ser Ser Asn Glu His Gly Pro Val Lys Arg Ser
```

20 25 30

Ser Gln Ser Thr Leu Glu Arg Ser Glu Gln Gln Ile Arg Ala Ala Ser
35 40 45

Ser Leu Glu Glu Leu Leu Arg Ile Thr His Ser Glu Asp Trp Lys Leu
50 55 60

Trp Arg Cys Arg Leu Arg Leu Lys Ser Phe Thr Ser Met Asp Ser Arg
65 70 75 80

Ser Ala Ser His Arg Ser Thr Arg Phe Ala Ala Thr Phe Tyr Asp Ile
85 90 95

Glu Thr Leu Lys Val Ile Asp Glu Glu Trp Gln Arg Thr Gln Cys Ser
100 105 110

Pro Arg Glu Thr Cys Val Glu Val Ala Ser Glu Leu Gly Lys Ser Thr
115 120 125

Asn Thr Phe Phe Lys Pro Pro Cys Val Asn Val Phe Arg Cys Gly Gly
130 135 140

Cys Cys Asn Glu Glu Ser Leu Ile Cys Met Asn Thr Ser Thr Ser Tyr
145 150 155 160

Ile Ser Lys Gln Leu Phe Glu Ile Ser Val Pro Leu Thr Ser Val Pro
165 170 175

Glu Leu Val Pro Val Lys Val Ala Asn His Thr Gly Cys Lys Cys Leu
180 185 190

Pro Thr Ala Pro Arg His Pro Tyr Ser Ile Ile Arg Arg Ser Ile Gln
195 200 205

Ile Pro Glu Glu Asp Arg Cys Ser His Ser Lys Lys Leu Cys Pro Ile
210 215 220

Asp Met Leu Trp Asp Ser Asn Lys Cys Lys Cys Val Leu Gln Glu Glu
225 230 235 240

Asn Pro Leu Ala Gly Thr Glu Asp His Ser His Leu Gln Glu Pro Ala
245 250 255

Leu Cys Gly Pro His Met Met Phe Asp Glu Asp Arg Cys Glu Cys Val
260 265 270

Cys Lys Thr Pro Cys Pro Lys Asp Leu Ile Gln His Pro Lys Asn Cys
275 280 285

Ser Cys Phe Glu Cys Lys Glu Ser Leu Glu Thr Cys Cys Gln Lys His

290 295 300

Lys Leu Phe His Pro Asp Thr Cys Ser Cys Glu Asp Arg Cys Pro Phe
305 310 315 320

His Thr Arg Pro Cys Ala Ser Gly Lys Thr Ala Cys Ala Lys His Cys
325 330 335

Arg Phe Pro Lys Glu Lys Arg Ala Ala Gln Gly Pro His Ser Arg Lys
340 345 350

Asn Pro

<210> 375
<211> 160
<212> PRT
<213> Homo sapiens

<400> 375

Met Thr Asp Gln Gln Ala Glu Ala Arg Ser Tyr Leu Ser Glu Glu Met
1 5 10 15

Ile Ala Glu Phe Lys Ala Ala Phe Asp Met Phe Asp Ala Asp Gly Gly
20 25 30

Gly Asp Ile Ser Val Lys Glu Leu Gly Thr Val Met Arg Met Leu Gly
35 40 45

Gln Thr Pro Thr Lys Glu Glu Leu Asp Ala Ile Ile Glu Glu Val Asp
50 55 60

Glu Asp Gly Ser Gly Thr Ile Asp Phe Glu Glu Phe Leu Val Met Met
65 70 75 80

Val Arg Gln Met Lys Glu Asp Ala Lys Gly Lys Ser Glu Glu Glu Leu
85 90 95

Ala Glu Cys Phe Arg Ile Phe Asp Arg Asn Ala Asp Gly Tyr Ile Asp
100 105 110

Pro Glu Glu Leu Ala Glu Ile Phe Arg Ala Ser Gly Glu His Val Thr
115 120 125

Asp Glu Glu Ile Glu Ser Leu Met Lys Asp Gly Asp Lys Asn Asn Asp
130 135 140

Gly Arg Ile Asp Phe Asp Glu Phe Leu Lys Met Met Glu Gly Val Gln
145 150 155 160

<210> 376
<211> 182

<212> PRT
<213> Homo sapiens

<400> 376

```
Met Gly Asp Glu Glu Lys Arg Asn Arg Ala Ile Thr Ala Arg Arg Gln
1               5                  10                  15

His Leu Lys Ser Val Met Leu Gln Ile Ala Ala Thr Glu Leu Glu Lys
            20                  25                  30

Glu Glu Ser Arg Arg Glu Ala Glu Lys Gln Asn Tyr Leu Ala Glu His
        35                  40                  45

Cys Pro Pro Leu His Ile Pro Gly Ser Met Ser Glu Val Gln Glu Leu
    50                  55                  60

Cys Lys Gln Leu His Ala Lys Ile Asp Ala Ala Glu Glu Glu Lys Tyr
65                  70                  75                  80

Asp Met Glu Val Arg Val Gln Lys Thr Ser Lys Glu Leu Glu Asp Met
                85                  90                  95

Asn Gln Lys Leu Phe Asp Leu Arg Gly Lys Phe Lys Arg Pro Pro Leu
            100                 105                 110

Arg Arg Val Arg Met Ser Ala Asp Ala Met Leu Lys Ala Leu Leu Gly
        115                 120                 125

Ser Lys His Lys Val Cys Met Asp Leu Arg Ala Asn Leu Lys Gln Val
    130                 135                 140

Lys Lys Glu Asp Thr Glu Lys Glu Arg Asp Leu Arg Asp Val Gly Asp
145                 150                 155                 160

Trp Arg Lys Asn Ile Glu Glu Lys Ser Gly Met Glu Gly Arg Lys Lys
                165                 170                 175

Met Phe Glu Ser Glu Ser
            180
```

<210> 377
<211> 258
<212> PRT
<213> Homo sapiens

<400> 377

```
Met Ser Asp Glu Glu Val Glu Gln Val Glu Glu Gln Tyr Glu Glu Glu
1               5                  10                  15

Glu Glu Ala Gln Glu Glu Glu Glu Val Gln Glu Asp Thr Ala Glu Glu
            20                  25                  30
```

```
Asp Ala Glu Glu Glu Lys Pro Arg Pro Lys Leu Thr Ala Pro Lys Ile
        35                  40                  45

Pro Glu Gly Glu Lys Val Asp Phe Asp Asp Ile Gln Lys Lys Arg Gln
    50                  55                  60

Asn Lys Asp Leu Met Glu Leu Gln Ala Leu Ile Asp Ser His Phe Glu
65                  70                  75                  80

Ala Arg Lys Lys Glu Glu Glu Glu Leu Val Ala Leu Lys Glu Arg Ile
                85                  90                  95

Glu Lys Arg Arg Ala Glu Arg Ala Glu Gln Gln Arg Ile Arg Ala Glu
            100                 105                 110

Lys Glu Arg Glu Arg Gln Asn Arg Leu Ala Glu Glu Lys Ala Arg Arg
        115                 120                 125

Glu Glu Glu Asp Ala Lys Arg Arg Ala Glu Asp Asp Leu Lys Lys Lys
    130                 135                 140

Lys Ala Leu Ser Ser Met Gly Ala Asn Tyr Ser Ser Tyr Leu Ala Lys
145                 150                 155                 160

Ala Asp Gln Lys Arg Gly Lys Lys Gln Thr Ala Arg Glu Met Lys Lys
                165                 170                 175

Lys Ile Leu Ala Glu Arg Arg Lys Pro Leu Asn Ile Asp His Leu Gly
            180                 185                 190

Glu Asp Lys Leu Arg Asp Lys Ala Lys Glu Leu Trp Glu Thr Leu His
        195                 200                 205

Gln Leu Glu Ile Asp Lys Phe Glu Phe Gly Glu Lys Leu Lys Arg Gln
    210                 215                 220

Lys Tyr Asp Ile Thr Thr Leu Arg Ser Arg Ile Asp Gln Ala Gln Lys
225                 230                 235                 240

His Ser Lys Lys Ala Gly Thr Pro Ala Lys Gly Lys Val Gly Gly Arg
                245                 250                 255

Trp Lys


<210>  378
<211>  355
<212>  PRT
<213>  Homo sapiens

<400>  378

Met Asp Tyr Thr Leu Asp Leu Ser Val Thr Thr Val Thr Asp Tyr Tyr
```

1 5 10 15

Tyr Pro Asp Ile Phe Ser Ser Pro Cys Asp Ala Glu Leu Ile Gln Thr
20 25 30

Asn Gly Lys Leu Leu Leu Ala Val Phe Tyr Cys Leu Leu Phe Val Phe
35 40 45

Ser Leu Leu Gly Asn Ser Leu Val Ile Leu Val Leu Glu Val Cys Lys
50 55 60

Lys Leu Arg Ser Ile Thr Asp Val Tyr Leu Leu Asn Leu Ala Leu Ser
65 70 75 80

Asp Leu Leu Phe Val Phe Ser Phe Pro Phe Gln Thr Tyr Tyr Leu Leu
85 90 95

Asp Gln Trp Val Phe Gly Thr Val Met Cys Lys Val Val Ser Gly Phe
100 105 110

Tyr Tyr Ile Gly Phe Tyr Ser Ser Met Phe Phe Ile Thr Leu Met Ser
115 120 125

Val Asp Arg Tyr Leu Ala Val Val His Ala Val Tyr Ala Leu Lys Val
130 135 140

Arg Thr Ile Arg Met Gly Thr Thr Leu Cys Leu Ala Val Trp Leu Thr
145 150 155 160

Ala Ile Met Ala Thr Ile Pro Leu Leu Val Phe Tyr Gln Val Ala Ser
165 170 175

Glu Asp Gly Val Leu Gln Cys Tyr Ser Phe Tyr Asn Gln Gln Thr Leu
180 185 190

Lys Trp Lys Ile Phe Thr Asn Phe Lys Met Asn Ile Leu Gly Leu Leu
195 200 205

Ile Pro Phe Thr Ile Phe Met Phe Cys Tyr Ile Lys Ile Leu His Gln
210 215 220

Leu Lys Arg Cys Gln Asn His Asn Lys Thr Lys Ala Ile Arg Leu Val
225 230 235 240

Leu Ile Val Val Ile Ala Ser Leu Leu Phe Trp Val Pro Phe Asn Val
245 250 255

Val Leu Phe Leu Thr Ser Leu His Ser Met His Ile Leu Asp Gly Cys
260 265 270

Ser Ile Ser Gln Gln Leu Thr Tyr Ala Thr His Val Thr Glu Ile Ile

275 280 285

Ser Phe Thr His Cys Cys Val Asn Pro Val Ile Tyr Ala Phe Val Gly
290 295 300

Glu Lys Phe Lys Lys His Leu Ser Glu Ile Phe Gln Lys Ser Cys Ser
305 310 315 320

Gln Ile Phe Asn Tyr Leu Gly Arg Gln Met Pro Arg Glu Ser Cys Glu
325 330 335

Lys Ser Ser Ser Cys Gln Gln His Ser Ser Arg Ser Ser Asn Val Asp
340 345 350

Tyr Ile Leu
355

<210> 379
<211> 355
<212> PRT
<213> Homo sapiens

<400> 379

Met Glu Thr Pro Asn Thr Thr Glu Asp Tyr Asp Thr Thr Thr Glu Phe
1 5 10 15

Asp Tyr Gly Asp Ala Thr Pro Cys Gln Lys Val Asn Glu Arg Ala Phe
20 25 30

Gly Ala Gln Leu Leu Pro Pro Leu Tyr Ser Leu Val Phe Val Ile Gly
35 40 45

Leu Val Gly Asn Ile Leu Val Val Leu Val Leu Val Gln Tyr Lys Arg
50 55 60

Leu Lys Asn Met Thr Ser Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp
65 70 75 80

Leu Leu Phe Leu Phe Thr Leu Pro Phe Trp Ile Asp Tyr Lys Leu Lys
85 90 95

Asp Asp Trp Val Phe Gly Asp Ala Met Cys Lys Ile Leu Ser Gly Phe
100 105 110

Tyr Tyr Thr Gly Leu Tyr Ser Glu Ile Phe Phe Ile Ile Leu Leu Thr
115 120 125

Ile Asp Arg Tyr Leu Ala Ile Val His Ala Val Phe Ala Leu Arg Ala
130 135 140

Arg Thr Val Thr Phe Gly Val Ile Thr Ser Ile Ile Ile Trp Ala Leu
145 150 155 160

```
Ala Ile Leu Ala Ser Met Pro Gly Leu Tyr Phe Ser Lys Thr Gln Trp
                165                 170                 175

Glu Phe Thr His His Thr Cys Ser Leu His Phe Pro His Glu Ser Leu
            180                 185                 190

Arg Glu Trp Lys Leu Phe Gln Ala Leu Lys Leu Asn Leu Phe Gly Leu
        195                 200                 205

Val Leu Pro Leu Leu Val Met Ile Ile Cys Tyr Thr Gly Ile Ile Lys
    210                 215                 220

Ile Leu Leu Arg Arg Pro Asn Glu Lys Lys Ser Lys Ala Val Arg Leu
225                 230                 235                 240

Ile Phe Val Ile Met Ile Ile Phe Phe Leu Phe Trp Thr Pro Tyr Asn
                245                 250                 255

Leu Thr Ile Leu Ile Ser Val Phe Gln Asp Phe Leu Phe Thr His Glu
            260                 265                 270

Cys Glu Gln Ser Arg His Leu Asp Leu Ala Val Gln Val Thr Glu Val
        275                 280                 285

Ile Ala Tyr Thr His Cys Cys Val Asn Pro Val Ile Tyr Ala Phe Val
    290                 295                 300

Gly Glu Arg Phe Arg Lys Tyr Leu Arg Gln Leu Phe His Arg Arg Val
305                 310                 315                 320

Ala Val His Leu Val Lys Trp Leu Pro Phe Leu Ser Val Asp Arg Leu
                325                 330                 335

Glu Arg Val Ser Ser Thr Ser Pro Ser Thr Gly Glu His Glu Leu Ser
            340                 345                 350

Ala Gly Phe
        355


<210>  380
<211>  92
<212>  PRT
<213>  Homo sapiens

<400>  380

Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
1               5                   10                  15

Leu Cys Asn Gln Phe Ser Ala Ser Leu Ala Ala Asp Thr Pro Thr Ala
            20                  25                  30
```

```
Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile Ala
        35                  40                  45


Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Gly Val Ile Phe
    50                  55                  60


Leu Thr Lys Arg Ser Arg Gln Val Cys Ala Asp Pro Ser Glu Glu Trp
65                  70                  75                  80


Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
                85                  90


<210>  381
<211>  93
<212>  PRT
<213>  Homo sapiens

<400>  381

Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
1               5                   10                  15


Leu Cys Asn Gln Val Leu Ser Ala Pro Leu Ala Ala Asp Thr Pro Thr
            20                  25                  30


Ala Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile
        35                  40                  45


Ala Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Ser Val Ile
    50                  55                  60


Phe Leu Thr Lys Arg Gly Arg Gln Val Cys Ala Asp Pro Ser Glu Glu
65                  70                  75                  80


Trp Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
                85                  90


<210>  382
<211>  211
<212>  PRT
<213>  Homo sapiens

<400>  382

Met Arg Thr Leu Ala Cys Leu Leu Leu Leu Gly Cys Gly Tyr Leu Ala
1               5                   10                  15


His Val Leu Ala Glu Glu Ala Glu Ile Pro Arg Glu Val Ile Glu Arg
            20                  25                  30


Leu Ala Arg Ser Gln Ile His Ser Ile Arg Asp Leu Gln Arg Leu Leu
        35                  40                  45


Glu Ile Asp Ser Val Gly Ser Glu Asp Ser Leu Asp Thr Ser Leu Arg
```

50 55 60

Ala His Gly Val His Ala Thr Lys His Val Pro Glu Lys Arg Pro Leu
65 70 75 80

Pro Ile Arg Arg Lys Arg Ser Ile Glu Glu Ala Val Pro Ala Val Cys
85 90 95

Lys Thr Arg Thr Val Ile Tyr Glu Ile Pro Arg Ser Gln Val Asp Pro
100 105 110

Thr Ser Ala Asn Phe Leu Ile Trp Pro Pro Cys Val Glu Val Lys Arg
115 120 125

Cys Thr Gly Cys Cys Asn Thr Ser Ser Val Lys Cys Gln Pro Ser Arg
130 135 140

Val His His Arg Ser Val Lys Val Ala Lys Val Glu Tyr Val Arg Lys
145 150 155 160

Lys Pro Lys Leu Lys Glu Val Gln Val Arg Leu Glu Glu His Leu Glu
165 170 175

Cys Ala Cys Ala Thr Thr Ser Leu Asn Pro Asp Tyr Arg Glu Glu Asp
180 185 190

Thr Gly Arg Pro Arg Glu Ser Gly Lys Lys Arg Lys Arg Lys Arg Leu
195 200 205

Lys Pro Thr
210

<210> 383
<211> 196
<212> PRT
<213> Homo sapiens

<400> 383

Met Arg Thr Leu Ala Cys Leu Leu Leu Leu Gly Cys Gly Tyr Leu Ala
1 5 10 15

His Val Leu Ala Glu Glu Ala Glu Ile Pro Arg Glu Val Ile Glu Arg
20 25 30

Leu Ala Arg Ser Gln Ile His Ser Ile Arg Asp Leu Gln Arg Leu Leu
35 40 45

Glu Ile Asp Ser Val Gly Ser Glu Asp Ser Leu Asp Thr Ser Leu Arg
50 55 60

Ala His Gly Val His Ala Thr Lys His Val Pro Glu Lys Arg Pro Leu
65 70 75 80

```
Pro Ile Arg Arg Lys Arg Ser Ile Glu Glu Ala Val Pro Ala Val Cys
                85                  90                  95

Lys Thr Arg Thr Val Ile Tyr Glu Ile Pro Arg Ser Gln Val Asp Pro
            100                 105                 110

Thr Ser Ala Asn Phe Leu Ile Trp Pro Pro Cys Val Glu Val Lys Arg
        115                 120                 125

Cys Thr Gly Cys Cys Asn Thr Ser Ser Val Lys Cys Gln Pro Ser Arg
    130                 135                 140

Val His His Arg Ser Val Lys Val Ala Lys Val Glu Tyr Val Arg Lys
145                 150                 155                 160

Lys Pro Lys Leu Lys Glu Val Gln Val Arg Leu Glu Glu His Leu Glu
                165                 170                 175

Cys Ala Cys Ala Thr Thr Ser Leu Asn Pro Asp Tyr Arg Glu Glu Asp
            180                 185                 190

Thr Asp Val Arg
        195


<210>  384
<211>  271
<212>  PRT
<213>  Homo sapiens

<400>  384

Met Leu Leu Thr Ser Ser Leu His His Pro Arg His Gln Met Ser Pro
1               5                   10                  15

Gly Ser Trp Lys Lys Leu Ile Ile Leu Leu Ser Cys Val Phe Gly Gly
            20                  25                  30

Gly Gly Thr Ser Leu Gln Asn Lys Asn Pro His Gln Pro Met Thr Leu
        35                  40                  45

Thr Trp Gln Gly Asp Pro Ile Pro Glu Glu Leu Tyr Lys Met Leu Ser
    50                  55                  60

Gly His Ser Ile Arg Ser Phe Asn Asp Leu Gln Arg Leu Leu Gln Gly
65                  70                  75                  80

Asp Ser Gly Lys Glu Asp Gly Ala Glu Leu Asp Leu Asn Met Thr Arg
                85                  90                  95

Ser His Ser Gly Gly Glu Leu Glu Ser Leu Ala Arg Gly Lys Arg Ser
            100                 105                 110
```

```
Leu Gly Ser Leu Ser Val Ala Glu Pro Ala Met Ile Ala Glu Cys Lys
        115                 120                 125


Thr Arg Thr Glu Val Phe Glu Ile Ser Arg Arg Leu Ile Asp Arg Thr
    130                 135                 140


Asn Ala Asn Phe Leu Val Trp Pro Pro Cys Val Glu Val Gln Arg Cys
145                 150                 155                 160


Ser Gly Cys Cys Asn Asn Arg Asn Val Gln Cys Arg Pro Thr Gln Val
                165                 170                 175


Gln Leu Arg Pro Val Gln Val Arg Lys Ile Glu Ile Val Arg Lys Lys
            180                 185                 190


Pro Ile Phe Lys Lys Ala Thr Val Thr Leu Glu Asp His Leu Ala Cys
        195                 200                 205


Lys Cys Glu Ile Val Ala Ala Ala Arg Ala Val Thr Arg Ser Pro Gly
    210                 215                 220


Thr Ser Gln Glu Gln Arg Ala Lys Thr Thr Gln Ser Arg Val Thr Ile
225                 230                 235                 240


Arg Thr Val Arg Val Arg Arg Pro Pro Lys Gly Lys His Arg Lys Cys
                245                 250                 255


Lys His Thr His Asp Lys Thr Ala Leu Lys Glu Thr Leu Gly Ala
            260                 265                 270


<210>  385
<211>  11
<212>  PRT
<213>  Homo sapiens

<400>  385

Arg Pro Lys Pro Gln Gln Phe Phe Gly Leu Met
1               5                   10


<210>  386
<211>  153
<212>  PRT
<213>  Homo sapiens

<400>  386

Ala Pro Val Arg Ser Leu Asn Cys Thr Leu Arg Asp Ser Gln Gln Lys
1               5                   10                  15


Ser Leu Val Met Ser Gly Pro Tyr Glu Leu Lys Ala Leu His Leu Gln
            20                  25                  30


Gly Gln Asp Met Glu Gln Gln Val Val Phe Ser Met Ser Phe Val Gln
```

35 40 45

Gly Glu Glu Ser Asn Asp Lys Ile Pro Val Ala Leu Gly Leu Lys Glu
50 55 60

Lys Asn Leu Tyr Leu Ser Cys Val Leu Lys Asp Asp Lys Pro Thr Leu
65 70 75 80

Gln Leu Glu Ser Val Asp Pro Lys Asn Tyr Pro Lys Lys Lys Met Glu
85 90 95

Lys Arg Phe Val Phe Asn Lys Ile Glu Ile Asn Asn Lys Leu Glu Phe
100 105 110

Glu Ser Ala Gln Phe Pro Asn Trp Tyr Ile Ser Thr Ser Gln Ala Glu
115 120 125

Asn Met Pro Val Phe Leu Gly Gly Thr Lys Gly Gly Gln Asp Ile Thr
130 135 140

Asp Phe Thr Met Gln Phe Val Ser Ser
145 150

<210> 387
<211> 144
<212> PRT
<213> Homo sapiens

<400> 387

Met Leu Leu Ala Met Val Leu Thr Ser Ala Leu Leu Leu Cys Ser Val
1 5 10 15

Ala Gly Gln Gly Cys Pro Thr Leu Ala Gly Ile Leu Asp Ile Asn Phe
20 25 30

Leu Ile Asn Lys Met Gln Glu Asp Pro Ala Ser Lys Cys His Cys Ser
35 40 45

Ala Asn Val Thr Ser Cys Leu Cys Leu Gly Ile Pro Ser Asp Asn Cys
50 55 60

Thr Arg Pro Cys Phe Ser Glu Arg Leu Ser Gln Met Thr Asn Thr Thr
65 70 75 80

Met Gln Thr Arg Tyr Pro Leu Ile Phe Ser Arg Val Lys Lys Ser Val
85 90 95

Glu Val Leu Lys Asn Asn Lys Cys Pro Tyr Phe Ser Cys Glu Gln Pro
100 105 110

Cys Asn Gln Thr Thr Ala Gly Asn Ala Leu Thr Phe Leu Lys Ser Leu
115 120 125

```
Leu Glu Ile Phe Gln Lys Glu Lys Met Arg Gly Met Arg Gly Lys Ile
    130                 135                 140


<210>  388
<211>  144
<212>  PRT
<213>  Homo sapiens

<400>  388

Met Leu Leu Ala Met Val Leu Thr Ser Ala Leu Leu Leu Cys Ser Val
1               5                   10                  15


Ala Gly Gln Gly Cys Pro Thr Leu Ala Gly Ile Leu Asp Ile Asn Phe
            20                  25                  30


Leu Ile Asn Lys Met Gln Glu Asp Pro Ala Ser Lys Cys His Cys Ser
        35                  40                  45


Ala Asn Val Thr Ser Cys Leu Cys Leu Gly Ile Pro Ser Asp Asn Cys
    50                  55                  60


Thr Arg Pro Cys Phe Ser Glu Arg Leu Ser Gln Met Thr Asn Thr Thr
65                  70                  75                  80


Met Gln Thr Arg Tyr Pro Leu Ile Phe Ser Arg Val Lys Lys Ser Val
                85                  90                  95


Glu Val Leu Lys Asn Asn Lys Cys Pro Tyr Phe Ser Cys Glu Gln Pro
            100                 105                 110


Cys Asn Gln Thr Met Ala Gly Asn Ala Leu Thr Phe Leu Lys Ser Leu
        115                 120                 125


Leu Glu Ile Phe Gln Lys Glu Lys Met Arg Gly Met Arg Gly Lys Ile
    130                 135                 140


<210>  389
<211>  126
<212>  PRT
<213>  Homo sapiens

<400>  389

Gln Gly Cys Pro Thr Leu Ala Gly Ile Leu Asp Ile Asn Phe Leu Ile
1               5                   10                  15


Asn Lys Met Gln Glu Asp Pro Ala Ser Lys Cys His Cys Ser Ala Asn
            20                  25                  30


Val Thr Ser Cys Leu Cys Leu Gly Ile Pro Ser Asp Asn Cys Thr Arg
        35                  40                  45
```

```
Pro Cys Phe Ser Glu Arg Leu Ser Gln Met Thr Asn Thr Thr Met Gln
    50                  55                  60

Thr Arg Tyr Pro Leu Ile Phe Ser Arg Val Lys Lys Ser Val Glu Val
65                  70                  75                  80

Leu Lys Asn Asn Lys Cys Pro Tyr Phe Ser Cys Glu Gln Pro Cys Asn
                85                  90                  95

Gln Thr Thr Ala Gly Asn Ala Leu Thr Phe Leu Lys Ser Leu Leu Glu
            100                 105                 110

Ile Phe Gln Lys Glu Lys Met Arg Gly Met Arg Gly Lys Ile
        115                 120                 125


<210>  390
<211>  126
<212>  PRT
<213>  Homo sapiens

<400>  390

Gln Gly Cys Pro Thr Leu Ala Gly Ile Leu Asp Ile Asn Phe Leu Ile
1               5                   10                  15

Asn Lys Met Gln Glu Asp Pro Ala Ser Lys Cys His Cys Ser Ala Asn
            20                  25                  30

Val Thr Ser Cys Leu Cys Leu Gly Ile Pro Ser Asp Asn Cys Thr Arg
        35                  40                  45

Pro Cys Phe Ser Glu Arg Leu Ser Gln Met Thr Asn Thr Thr Met Gln
    50                  55                  60

Thr Arg Tyr Pro Leu Ile Phe Ser Arg Val Lys Lys Ser Val Glu Val
65                  70                  75                  80

Leu Lys Asn Asn Lys Cys Pro Tyr Phe Ser Cys Glu Gln Pro Cys Asn
                85                  90                  95

Gln Thr Met Ala Gly Asn Ala Leu Thr Phe Leu Lys Ser Leu Leu Glu
            100                 105                 110

Ile Phe Gln Lys Glu Lys Met Arg Gly Met Arg Gly Lys Ile
        115                 120                 125


<210>  391
<211>  261
<212>  PRT
<213>  Homo sapiens

<400>  391

Met Leu Gln Ala Glu Ala Val Gln Ser Pro Cys Gly Arg Lys Glu His
1               5                   10                  15
```

```
Ala Glu Cys Lys Thr Glu Arg Arg Pro Glu Ala Gly Thr His Lys Arg
            20                  25                  30

Glu Glu Thr Gly Gly Asn Leu Arg Arg Glu Ser Trp Gly Met Val Gly
        35                  40                  45

Arg Val Arg Pro Glu Pro Gly Arg Pro Leu Arg Ala Met Gly Lys Gly
    50                  55                  60

Pro Trp Thr Pro Ser Leu Gly Pro Asp Arg Asp Leu Ala Leu Pro Pro
65                  70                  75                  80

Leu Thr Cys Gly Phe Pro Pro Gln Leu Phe Leu Leu Thr Ile Ser Ile
                85                  90                  95

Phe Leu Gly Leu Gly Gln Pro Arg Ser Pro Lys Ser Lys Arg Lys Gly
            100                 105                 110

Gln Gly Arg Pro Gly Pro Leu Ala Pro Gly Pro His Gln Val Pro Leu
        115                 120                 125

Asp Leu Val Ser Arg Met Lys Pro Tyr Ala Arg Met Glu Glu Tyr Glu
    130                 135                 140

Arg Asn Ile Glu Glu Met Val Ala Gln Leu Arg Asn Ser Ser Glu Leu
145                 150                 155                 160

Ala Gln Arg Lys Cys Glu Val Asn Leu Gln Leu Trp Met Ser Asn Lys
                165                 170                 175

Arg Ser Leu Ser Pro Trp Gly Tyr Ser Ile Asn His Asp Pro Ser Arg
            180                 185                 190

Ile Pro Val Asp Leu Pro Glu Ala Arg Cys Leu Cys Leu Gly Cys Val
        195                 200                 205

Asn Pro Phe Thr Met Gln Glu Asp Arg Ser Met Val Ser Val Pro Val
    210                 215                 220

Phe Ser Gln Val Pro Val Arg Arg Arg Leu Cys Pro Pro Pro Pro Arg
225                 230                 235                 240

Thr Gly Pro Cys Arg Gln Arg Ala Val Met Glu Thr Ile Ala Val Gly
                245                 250                 255

Cys Thr Cys Ile Phe
            260
```

<210> 392
<211> 180

<212> PRT
<213> Homo sapiens

<400> 392

```
Met Asp Trp Pro His Asn Leu Leu Phe Leu Leu Thr Ile Ser Ile Phe
1               5                  10                  15

Leu Gly Leu Gly Gln Pro Arg Ser Pro Lys Ser Lys Arg Lys Gly Gln
            20                  25                  30

Gly Arg Pro Gly Pro Leu Ala Pro Gly Pro His Gln Val Pro Leu Asp
        35                  40                  45

Leu Val Ser Arg Met Lys Pro Tyr Ala Arg Met Glu Glu Tyr Glu Arg
    50                  55                  60

Asn Ile Glu Glu Met Val Ala Gln Leu Arg Asn Ser Ser Glu Leu Ala
65                  70                  75                  80

Gln Arg Lys Cys Glu Val Asn Leu Gln Leu Trp Met Ser Asn Lys Arg
                85                  90                  95

Ser Leu Ser Pro Trp Gly Tyr Ser Ile Asn His Asp Pro Ser Arg Ile
            100                 105                 110

Pro Val Asp Leu Pro Glu Ala Arg Cys Leu Cys Leu Gly Cys Val Asn
        115                 120                 125

Pro Phe Thr Met Gln Glu Asp Arg Ser Met Val Ser Val Pro Val Phe
    130                 135                 140

Ser Gln Val Pro Val Arg Arg Arg Leu Cys Pro Pro Pro Pro Arg Thr
145                 150                 155                 160

Gly Pro Cys Arg Gln Arg Ala Val Met Glu Thr Ile Ala Val Gly Cys
                165                 170                 175

Thr Cys Ile Phe
            180
```

<210> 393
<211> 662
<212> PRT
<213> Homo sapiens

<400> 393

```
Met Glu Pro Leu Val Thr Trp Val Val Pro Leu Leu Phe Leu Phe Leu
1               5                  10                  15

Leu Ser Arg Gln Gly Ala Ala Cys Arg Thr Ser Glu Cys Cys Phe Gln
            20                  25                  30
```

```
Asp Pro Pro Tyr Pro Asp Ala Asp Ser Gly Ser Ala Ser Gly Pro Arg
        35                  40                  45

Asp Leu Arg Cys Tyr Arg Ile Ser Ser Asp Arg Tyr Glu Cys Ser Trp
    50                  55                  60

Gln Tyr Glu Gly Pro Thr Ala Gly Val Ser His Phe Leu Arg Cys Cys
65                  70                  75                  80

Leu Ser Ser Gly Arg Cys Cys Tyr Phe Ala Ala Gly Ser Ala Thr Arg
                85                  90                  95

Leu Gln Phe Ser Asp Gln Ala Gly Val Ser Val Leu Tyr Thr Val Thr
            100                 105                 110

Leu Trp Val Glu Ser Trp Ala Arg Asn Gln Thr Glu Lys Ser Pro Glu
        115                 120                 125

Val Thr Leu Gln Leu Tyr Asn Ser Val Lys Tyr Glu Pro Pro Leu Gly
    130                 135                 140

Asp Ile Lys Val Ser Lys Leu Ala Gly Gln Leu Arg Met Glu Trp Glu
145                 150                 155                 160

Thr Pro Asp Asn Gln Val Gly Ala Glu Val Gln Phe Arg His Arg Thr
                165                 170                 175

Pro Ser Ser Pro Trp Lys Leu Gly Asp Cys Gly Pro Gln Asp Asp Asp
            180                 185                 190

Thr Glu Ser Cys Leu Cys Pro Leu Glu Met Asn Val Ala Gln Glu Phe
        195                 200                 205

Gln Leu Arg Arg Arg Gln Leu Gly Ser Gln Gly Ser Ser Trp Ser Lys
    210                 215                 220

Trp Ser Ser Pro Val Cys Val Pro Pro Glu Asn Pro Pro Gln Pro Gln
225                 230                 235                 240

Val Arg Phe Ser Val Glu Gln Leu Gly Gln Asp Gly Arg Arg Arg Leu
                245                 250                 255

Thr Leu Lys Glu Gln Pro Thr Gln Leu Glu Leu Pro Glu Gly Cys Gln
            260                 265                 270

Gly Leu Ala Pro Gly Thr Glu Val Thr Tyr Arg Leu Gln Leu His Met
        275                 280                 285

Leu Ser Cys Pro Cys Lys Ala Lys Ala Thr Arg Thr Leu His Leu Gly
    290                 295                 300
```

```
Lys Met Pro Tyr Leu Ser Gly Ala Ala Tyr Asn Val Ala Val Ile Ser
305                 310                 315                 320

Ser Asn Gln Phe Gly Pro Gly Leu Asn Gln Thr Trp His Ile Pro Ala
                325                 330                 335

Asp Thr His Thr Glu Pro Val Ala Leu Asn Ile Ser Val Gly Thr Asn
            340                 345                 350

Gly Thr Thr Met Tyr Trp Pro Ala Arg Ala Gln Ser Met Thr Tyr Cys
        355                 360                 365

Ile Glu Trp Gln Pro Val Gly Gln Asp Gly Gly Leu Ala Thr Cys Ser
    370                 375                 380

Leu Thr Ala Pro Gln Asp Pro Asp Pro Ala Gly Met Ala Thr Tyr Ser
385                 390                 395                 400

Trp Ser Arg Glu Ser Gly Ala Met Gly Gln Glu Lys Cys Tyr Tyr Ile
                405                 410                 415

Thr Ile Phe Ala Ser Ala His Pro Glu Lys Leu Thr Leu Trp Ser Thr
            420                 425                 430

Val Leu Ser Thr Tyr His Phe Gly Gly Asn Ala Ser Ala Ala Gly Thr
        435                 440                 445

Pro His His Val Ser Val Lys Asn His Ser Leu Asp Ser Val Ser Val
    450                 455                 460

Asp Trp Ala Pro Ser Leu Leu Ser Thr Cys Pro Gly Val Leu Lys Glu
465                 470                 475                 480

Tyr Val Val Arg Cys Arg Asp Glu Asp Ser Lys Gln Val Ser Glu His
                485                 490                 495

Pro Val Gln Pro Thr Glu Thr Gln Val Thr Leu Ser Gly Leu Arg Ala
            500                 505                 510

Gly Val Ala Tyr Thr Val Gln Val Arg Ala Asp Thr Ala Trp Leu Arg
        515                 520                 525

Gly Val Trp Ser Gln Pro Gln Arg Phe Ser Ile Glu Val Gln Val Ser
    530                 535                 540

Asp Trp Leu Ile Phe Phe Ala Ser Leu Gly Ser Phe Leu Ser Ile Leu
545                 550                 555                 560

Leu Val Gly Val Leu Gly Tyr Leu Gly Leu Asn Arg Ala Ala Arg His
                565                 570                 575
```

Leu Cys Pro Pro Leu Pro Thr Pro Cys Ala Ser Ser Ala Ile Glu Phe
580 585 590

Pro Gly Gly Lys Glu Thr Trp Gln Trp Ile Asn Pro Val Asp Phe Gln
595 600 605

Glu Glu Ala Ser Leu Gln Glu Ala Leu Val Val Glu Met Ser Trp Asp
610 615 620

Lys Gly Glu Arg Thr Glu Pro Leu Glu Lys Thr Glu Leu Pro Glu Gly
625 630 635 640

Ala Pro Glu Leu Ala Leu Asp Thr Glu Leu Ser Leu Glu Asp Gly Asp
645 650 655

Arg Cys Lys Ala Lys Met
660

<210> 394
<211> 862
<212> PRT
<213> Homo sapiens

<400> 394

Met Ala His Thr Phe Arg Gly Cys Ser Leu Ala Phe Met Phe Ile Ile
1 5 10 15

Thr Trp Leu Leu Ile Lys Ala Lys Ile Asp Ala Cys Lys Arg Gly Asp
20 25 30

Val Thr Val Lys Pro Ser His Val Ile Leu Leu Gly Ser Thr Val Asn
35 40 45

Ile Thr Cys Ser Leu Lys Pro Arg Gln Gly Cys Phe His Tyr Ser Arg
50 55 60

Arg Asn Lys Leu Ile Leu Tyr Lys Phe Asp Arg Arg Ile Asn Phe His
65 70 75 80

His Gly His Ser Leu Asn Ser Gln Val Thr Gly Leu Pro Leu Gly Thr
85 90 95

Thr Leu Phe Val Cys Lys Leu Ala Cys Ile Asn Ser Asp Glu Ile Gln
100 105 110

Ile Cys Gly Ala Glu Ile Phe Val Gly Val Ala Pro Glu Gln Pro Gln
115 120 125

Asn Leu Ser Cys Ile Gln Lys Gly Glu Gln Gly Thr Val Ala Cys Thr
130 135 140

Trp Glu Arg Gly Arg Asp Thr His Leu Tyr Thr Glu Tyr Thr Leu Gln

```
145                 150                 155                 160

Leu Ser Gly Pro Lys Asn Leu Thr Trp Gln Lys Gln Cys Lys Asp Ile
                165                 170                 175

Tyr Cys Asp Tyr Leu Asp Phe Gly Ile Asn Leu Thr Pro Glu Ser Pro
            180                 185                 190

Glu Ser Asn Phe Thr Ala Lys Val Thr Ala Val Asn Ser Leu Gly Ser
        195                 200                 205

Ser Ser Ser Leu Pro Ser Thr Phe Thr Phe Leu Asp Ile Val Arg Pro
    210                 215                 220

Leu Pro Pro Trp Asp Ile Arg Ile Lys Phe Gln Lys Ala Ser Val Ser
225                 230                 235                 240

Arg Cys Thr Leu Tyr Trp Arg Asp Glu Gly Leu Val Leu Leu Asn Arg
                245                 250                 255

Leu Arg Tyr Arg Pro Ser Asn Ser Arg Leu Trp Asn Met Val Asn Val
            260                 265                 270

Thr Lys Ala Lys Gly Arg His Asp Leu Leu Asp Leu Lys Pro Phe Thr
        275                 280                 285

Glu Tyr Glu Phe Gln Ile Ser Ser Lys Leu His Leu Tyr Lys Gly Ser
    290                 295                 300

Trp Ser Asp Trp Ser Glu Ser Leu Arg Ala Gln Thr Pro Glu Glu Glu
305                 310                 315                 320

Pro Thr Gly Met Leu Asp Val Trp Tyr Met Lys Arg His Ile Asp Tyr
                325                 330                 335

Ser Arg Gln Gln Ile Ser Leu Phe Trp Lys Asn Leu Ser Val Ser Glu
            340                 345                 350

Ala Arg Gly Lys Ile Leu His Tyr Gln Val Thr Leu Gln Glu Leu Thr
        355                 360                 365

Gly Gly Lys Ala Met Thr Gln Asn Ile Thr Gly His Thr Ser Trp Thr
    370                 375                 380

Thr Val Ile Pro Arg Thr Gly Asn Trp Ala Val Ala Val Ser Ala Ala
385                 390                 395                 400

Asn Ser Lys Gly Ser Ser Leu Pro Thr Arg Ile Asn Ile Met Asn Leu
                405                 410                 415

Cys Glu Ala Gly Leu Leu Ala Pro Arg Gln Val Ser Ala Asn Ser Glu
```

```
            420                 425                 430

Gly Met Asp Asn Ile Leu Val Thr Trp Gln Pro Pro Arg Lys Asp Pro
        435                 440                 445

Ser Ala Val Gln Glu Tyr Val Val Glu Trp Arg Glu Leu His Pro Gly
    450                 455                 460

Gly Asp Thr Gln Val Pro Leu Asn Trp Leu Arg Ser Arg Pro Tyr Asn
465                 470                 475                 480

Val Ser Ala Leu Ile Ser Glu Asn Ile Lys Ser Tyr Ile Cys Tyr Glu
                485                 490                 495

Ile Arg Val Tyr Ala Leu Ser Gly Asp Gln Gly Gly Cys Ser Ser Ile
            500                 505                 510

Leu Gly Asn Ser Lys His Lys Ala Pro Leu Ser Gly Pro His Ile Asn
        515                 520                 525

Ala Ile Thr Glu Glu Lys Gly Ser Ile Leu Ile Ser Trp Asn Ser Ile
    530                 535                 540

Pro Val Gln Glu Gln Met Gly Cys Leu Leu His Tyr Arg Ile Tyr Trp
545                 550                 555                 560

Lys Glu Arg Asp Ser Asn Ser Gln Pro Gln Leu Cys Glu Ile Pro Tyr
                565                 570                 575

Arg Val Ser Gln Asn Ser His Pro Ile Asn Ser Leu Gln Pro Arg Val
            580                 585                 590

Thr Tyr Val Leu Trp Met Thr Ala Leu Thr Ala Ala Gly Glu Ser Ser
        595                 600                 605

His Gly Asn Glu Arg Glu Phe Cys Leu Gln Gly Lys Ala Asn Trp Met
    610                 615                 620

Ala Phe Val Ala Pro Ser Ile Cys Ile Ala Ile Ile Met Val Gly Ile
625                 630                 635                 640

Phe Ser Thr His Tyr Phe Gln Gln Lys Val Phe Val Leu Leu Ala Ala
                645                 650                 655

Leu Arg Pro Gln Trp Cys Ser Arg Glu Ile Pro Asp Pro Ala Asn Ser
            660                 665                 670

Thr Cys Ala Lys Lys Tyr Pro Ile Ala Glu Glu Lys Thr Gln Leu Pro
        675                 680                 685

Leu Asp Arg Leu Leu Ile Asp Trp Pro Thr Pro Glu Asp Pro Glu Pro
```

690 695 700

Leu Val Ile Ser Glu Val Leu His Gln Val Thr Pro Val Phe Arg His
705 710 715 720

Pro Pro Cys Ser Asn Trp Pro Gln Arg Glu Lys Gly Ile Gln Gly His
725 730 735

Gln Ala Ser Glu Lys Asp Met Met His Ser Ala Ser Ser Pro Pro Pro
740 745 750

Pro Arg Ala Leu Gln Ala Glu Ser Arg Gln Leu Val Asp Leu Tyr Lys
755 760 765

Val Leu Glu Ser Arg Gly Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
770 775 780

Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
785 790 795 800

Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
805 810 815

Asp Ser Leu Glu Glu Leu Glu Pro Gln His Ile Ser Leu Ser Val Phe
820 825 830

Pro Ser Ser Ser Leu His Pro Leu Thr Phe Ser Cys Gly Asp Lys Leu
835 840 845

Thr Leu Asp Gln Leu Lys Met Arg Cys Asp Ser Leu Met Leu
850 855 860

<210> 395
<211> 396
<212> PRT
<213> Homo sapiens

<400> 395

Met Glu Phe Leu Lys Thr Cys Val Leu Arg Arg Asn Ala Cys Thr Ala
1 5 10 15

Val Cys Phe Trp Arg Ser Lys Val Val Gln Lys Pro Ser Val Arg Arg
20 25 30

Ile Ser Thr Thr Ser Pro Arg Ser Thr Val Met Pro Ala Trp Val Ile
35 40 45

Asp Lys Tyr Gly Lys Asn Glu Val Leu Arg Phe Thr Gln Asn Met Met
50 55 60

Met Pro Ile Ile His Tyr Pro Asn Glu Val Ile Val Lys Val His Ala
65 70 75 80

```
Ala Ser Val Asn Pro Ile Asp Val Asn Met Arg Ser Gly Tyr Gly Ala
                85                  90                  95

Thr Ala Leu Asn Met Lys Arg Asp Pro Leu His Val Lys Ile Lys Gly
            100                 105                 110

Glu Glu Phe Pro Leu Thr Leu Gly Arg Asp Val Ser Gly Val Val Met
        115                 120                 125

Glu Cys Gly Leu Asp Val Lys Tyr Phe Lys Pro Gly Asp Glu Val Trp
    130                 135                 140

Ala Ala Val Pro Pro Trp Lys Gln Gly Thr Leu Ser Glu Phe Val Val
145                 150                 155                 160

Val Ser Gly Asn Glu Val Ser His Lys Pro Lys Ser Leu Thr His Thr
                165                 170                 175

Gln Ala Ala Ser Leu Pro Tyr Val Ala Leu Thr Ala Trp Ser Ala Ile
            180                 185                 190

Asn Lys Val Gly Gly Leu Asn Asp Lys Asn Cys Thr Gly Lys Arg Val
        195                 200                 205

Leu Ile Leu Gly Ala Ser Gly Gly Val Gly Thr Phe Ala Ile Gln Val
    210                 215                 220

Met Lys Ala Trp Asp Ala His Val Thr Ala Val Cys Ser Gln Asp Ala
225                 230                 235                 240

Ser Glu Leu Val Arg Lys Leu Gly Ala Asp Asp Val Ile Asp Tyr Lys
                245                 250                 255

Ser Gly Ser Val Glu Glu Gln Leu Lys Ser Leu Lys Pro Phe Asp Phe
            260                 265                 270

Ile Leu Asp Asn Val Gly Gly Ser Thr Glu Thr Trp Ala Pro Asp Phe
        275                 280                 285

Leu Lys Lys Trp Ser Gly Ala Thr Tyr Val Thr Leu Val Thr Pro Phe
    290                 295                 300

Leu Leu Asn Met Asp Arg Leu Gly Ile Ala Asp Gly Met Leu Gln Thr
305                 310                 315                 320

Gly Val Thr Val Gly Ser Lys Ala Leu Lys His Phe Trp Lys Gly Val
                325                 330                 335

His Tyr Arg Trp Ala Phe Phe Met Ala Ser Gly Pro Cys Leu Asp Asp
            340                 345                 350
```

```
Ile Ala Glu Leu Val Asp Ala Gly Lys Ile Arg Pro Val Ile Glu Gln
        355                 360                 365

Thr Phe Pro Phe Ser Lys Val Pro Glu Ala Phe Leu Lys Val Glu Arg
    370                 375                 380

Gly His Ala Arg Gly Lys Thr Val Ile Asn Val Val
385                 390                 395


<210>  396
<211>  570
<212>  PRT
<213>  Homo sapiens

<400>  396

Met Thr Leu Leu Trp Cys Val Val Ser Leu Tyr Phe Tyr Gly Ile Leu
1               5                   10                  15

Gln Ser Asp Ala Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr Met
            20                  25                  30

Arg Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro
        35                  40                  45

Leu Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala
    50                  55                  60

Gly Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu
65                  70                  75                  80

Glu Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys
                85                  90                  95

Asp Val Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly Asn Tyr
            100                 105                 110

Thr Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro
        115                 120                 125

Leu Glu Val Val Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu
    130                 135                 140

Pro Val His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys
145                 150                 155                 160

Pro Asn Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr
                165                 170                 175

Trp Tyr Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro
            180                 185                 190
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```
Glu Gly Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly
        195                 200                 205

Asn Tyr Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His
    210                 215                 220

Leu Thr Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala
225                 230                 235                 240

Val Pro Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys
                245                 250                 255

Glu Pro Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe
            260                 265                 270

Leu Met Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys
        275                 280                 285

Pro Asp Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His
    290                 295                 300

Ser Arg Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys
305                 310                 315                 320

Val Thr Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser
                325                 330                 335

Ala Lys Gly Glu Val Ala Lys Ala Ala Lys Val Thr Gln Lys Val Pro
            340                 345                 350

Ala Pro Arg Tyr Thr Val Glu Leu Ala Cys Gly Phe Gly Ala Thr Val
        355                 360                 365

Leu Leu Val Val Ile Leu Ile Val Val Tyr His Val Tyr Trp Leu Glu
    370                 375                 380

Met Val Leu Phe Tyr Arg Ala His Phe Gly Thr Asp Glu Thr Ile Leu
385                 390                 395                 400

Asp Gly Lys Glu Tyr Asp Ile Tyr Val Ser Tyr Ala Arg Asn Ala Glu
                405                 410                 415

Glu Glu Glu Phe Val Leu Leu Thr Leu Arg Gly Val Leu Glu Asn Glu
            420                 425                 430

Phe Gly Tyr Lys Leu Cys Ile Phe Asp Arg Asp Ser Leu Pro Gly Gly
        435                 440                 445

Ile Val Thr Asp Glu Thr Leu Ser Phe Ile Gln Lys Ser Arg Arg Leu
    450                 455                 460
```

```
Leu Val Val Leu Ser Pro Asn Tyr Val Leu Gln Gly Thr Gln Ala Leu
465                 470                 475                 480


Leu Glu Leu Lys Ala Gly Leu Glu Asn Met Gly Ser Arg Gly Asn Ile
                485                 490                 495


Asn Val Ile Leu Val Gln Tyr Lys Ala Val Lys Glu Thr Lys Val Lys
            500                 505                 510


Glu Leu Lys Arg Ala Lys Thr Val Leu Thr Val Ile Lys Trp Lys Gly
        515                 520                 525


Glu Lys Ser Lys Tyr Pro Gln Gly Arg Phe Trp Lys Gln Leu Gln Val
    530                 535                 540


Ala Met Pro Val Lys Lys Ser Pro Arg Arg Ser Ser Ser Asp Glu Gln
545                 550                 555                 560


Gly Leu Ser Tyr Ser Ser Leu Lys Asn Val
                565                 570


<210>  397
<211>  357
<212>  PRT
<213>  Homo sapiens

<400>  397

Met Thr Leu Leu Trp Cys Trp Ser Leu Tyr Phe Tyr Gly Ile Leu Gln
1               5                   10                  15


Ser Asp Ala Ser Glu Arg Cys Asp Asp Trp Gly Leu Asp Thr His Arg
            20                  25                  30


Gln Ile Gln Val Phe Glu Asp Glu Pro Ala Arg Ile Lys Cys Pro Leu
        35                  40                  45


Phe Glu His Phe Leu Lys Phe Asn Tyr Ser Thr Ala His Ser Ala Gly
    50                  55                  60


Leu Thr Leu Ile Trp Tyr Trp Thr Arg Gln Asp Arg Asp Leu Glu Glu
65                  70                  75                  80


Pro Ile Asn Phe Arg Leu Pro Glu Asn Arg Ile Ser Lys Glu Lys Asp
                85                  90                  95


Val Leu Trp Phe Arg Pro Thr Leu Leu Asn Asp Thr Gly Asn Tyr Thr
            100                 105                 110


Cys Met Leu Arg Asn Thr Thr Tyr Cys Ser Lys Val Ala Phe Pro Leu
        115                 120                 125
```

```
Glu Trp Gln Lys Asp Ser Cys Phe Asn Ser Pro Met Lys Leu Pro Val
    130                 135                 140

His Lys Leu Tyr Ile Glu Tyr Gly Ile Gln Arg Ile Thr Cys Pro Asn
145                 150                 155                 160

Val Asp Gly Tyr Phe Pro Ser Ser Val Lys Pro Thr Ile Thr Asn Tyr
                165                 170                 175

Met Gly Cys Tyr Lys Ile Gln Asn Phe Asn Asn Val Ile Pro Glu Gly
            180                 185                 190

Met Asn Leu Ser Phe Leu Ile Ala Leu Ile Ser Asn Asn Gly Asn Tyr
        195                 200                 205

Thr Cys Val Val Thr Tyr Pro Glu Asn Gly Arg Thr Phe His Leu Thr
    210                 215                 220

Arg Thr Leu Thr Val Lys Val Val Gly Ser Pro Lys Asn Ala Val Pro
225                 230                 235                 240

Pro Val Ile His Ser Pro Asn Asp His Val Val Tyr Glu Lys Glu Pro
                245                 250                 255

Gly Glu Glu Leu Leu Ile Pro Cys Thr Val Tyr Phe Ser Phe Leu Met
            260                 265                 270

Asp Ser Arg Asn Glu Val Trp Trp Thr Ile Asp Gly Lys Lys Pro Asp
        275                 280                 285

Asp Ile Thr Ile Asp Val Thr Ile Asn Glu Ser Ile Ser His Ser Arg
    290                 295                 300

Thr Glu Asp Glu Thr Arg Thr Gln Ile Leu Ser Ile Lys Lys Val Thr
305                 310                 315                 320

Ser Glu Asp Leu Lys Arg Ser Tyr Val Cys His Ala Arg Ser Ala Lys
                325                 330                 335

Gly Glu Val Ala Lys Ala Ala Lys Val Thr Gln Lys Val Pro Ala Pro
            340                 345                 350

Arg Tyr Thr Val Glu
        355


<210>  398
<211>  562
<212>  PRT
<213>  Homo sapiens

<400>  398

Met Trp Ser Leu Leu Leu Cys Gly Leu Ser Ile Ala Leu Pro Leu Ser
```

```
1               5                   10                  15

Val Thr Ala Asp Gly Cys Lys Asp Ile Phe Met Lys Asn Glu Ile Leu
            20                  25                  30

Ser Ala Ser Gln Pro Phe Ala Phe Asn Cys Thr Phe Pro Pro Ile Thr
        35                  40                  45

Ser Gly Glu Val Ser Val Thr Trp Tyr Lys Asn Ser Ser Lys Ile Pro
    50                  55                  60

Val Ser Lys Ile Ile Gln Ser Arg Ile His Gln Asp Glu Thr Trp Ile
65                  70                  75                  80

Leu Phe Leu Pro Met Glu Trp Gly Asp Ser Gly Val Tyr Gln Cys Val
                85                  90                  95

Ile Lys Gly Arg Asp Ser Cys His Arg Ile His Val Asn Leu Thr Val
            100                 105                 110

Phe Glu Lys His Trp Cys Asp Thr Ser Ile Gly Gly Leu Pro Asn Leu
        115                 120                 125

Ser Asp Glu Tyr Lys Gln Ile Leu His Leu Gly Lys Asp Asp Ser Leu
    130                 135                 140

Thr Cys His Leu His Phe Pro Lys Ser Cys Val Leu Gly Pro Ile Lys
145                 150                 155                 160

Trp Tyr Lys Asp Cys Asn Glu Ile Lys Gly Glu Arg Phe Thr Val Leu
                165                 170                 175

Glu Thr Arg Leu Leu Val Ser Asn Val Ser Ala Glu Asp Arg Gly Asn
            180                 185                 190

Tyr Ala Cys Gln Ala Ile Leu Thr His Ser Gly Lys Gln Tyr Glu Val
        195                 200                 205

Leu Asn Gly Ile Thr Val Ser Ile Thr Glu Arg Ala Gly Tyr Gly Gly
    210                 215                 220

Ser Val Pro Lys Ile Ile Tyr Pro Lys Asn His Ser Ile Glu Val Gln
225                 230                 235                 240

Leu Gly Thr Thr Leu Ile Val Asp Cys Asn Val Thr Asp Thr Lys Asp
                245                 250                 255

Asn Thr Asn Leu Arg Cys Trp Arg Val Asn Asn Thr Leu Val Asp Asp
            260                 265                 270

Tyr Tyr Asp Glu Ser Lys Arg Ile Arg Glu Gly Val Glu Thr His Val
```

275 280 285

Ser Phe Arg Glu His Asn Leu Tyr Thr Val Asn Ile Thr Phe Leu Glu
290 295 300

Val Lys Met Glu Asp Tyr Gly Leu Pro Phe Met Cys His Ala Gly Val
305 310 315 320

Ser Thr Ala Tyr Ile Ile Leu Gln Leu Pro Ala Pro Asp Phe Arg Ala
325 330 335

Tyr Leu Ile Gly Gly Leu Ile Ala Leu Val Ala Val Ala Val Ser Val
340 345 350

Val Tyr Ile Tyr Asn Ile Phe Lys Ile Asp Ile Val Leu Trp Tyr Arg
355 360 365

Ser Ala Phe His Ser Thr Glu Thr Ile Val Asp Gly Lys Leu Tyr Asp
370 375 380

Ala Tyr Val Leu Tyr Pro Lys Pro His Lys Glu Ser Gln Arg His Ala
385 390 395 400

Val Asp Ala Leu Val Leu Asn Ile Leu Pro Glu Val Leu Glu Arg Gln
405 410 415

Cys Gly Tyr Lys Leu Phe Ile Phe Gly Arg Asp Glu Phe Pro Gly Gln
420 425 430

Ala Val Ala Asn Val Ile Asp Glu Asn Val Lys Leu Cys Arg Arg Leu
435 440 445

Ile Val Ile Val Val Pro Glu Ser Leu Gly Phe Gly Leu Leu Lys Asn
450 455 460

Leu Ser Glu Glu Gln Ile Ala Val Tyr Ser Ala Leu Ile Gln Asp Gly
465 470 475 480

Met Lys Val Ile Leu Ile Glu Leu Glu Lys Ile Glu Asp Tyr Thr Val
485 490 495

Met Pro Glu Ser Ile Gln Tyr Ile Lys Gln Lys His Gly Ala Ile Arg
500 505 510

Trp His Gly Asp Phe Thr Glu Gln Ser Gln Cys Met Lys Thr Lys Phe
515 520 525

Trp Lys Thr Val Arg Tyr His Met Pro Pro Arg Arg Cys Arg Pro Phe
530 535 540

Leu Arg Ser Thr Cys Arg Ser Thr His Leu Cys Thr Ala Pro Gln Ala

545 550 555 560

Gln Asn

<210> 399
<211> 561
<212> PRT
<213> Homo sapiens

<400> 399

Met Gly Met Pro Pro Leu Leu Phe Cys Trp Val Ser Phe Val Leu Pro
1 5 10 15

Leu Phe Val Ala Ala Gly Asn Cys Thr Asp Val Tyr Met His His Glu
20 25 30

Met Ile Ser Glu Gly Gln Pro Phe Pro Phe Asn Cys Thr Tyr Pro Pro
35 40 45

Val Thr Asn Gly Ala Val Asn Leu Thr Trp His Arg Thr Pro Ser Lys
50 55 60

Ser Pro Ile Ser Ile Asn Arg His Val Arg Ile His Gln Asp Gln Ser
65 70 75 80

Trp Ile Leu Phe Leu Pro Leu Ala Leu Glu Asp Ser Gly Ile Tyr Gln
85 90 95

Cys Val Ile Lys Asp Ala His Ser Cys Tyr Arg Ile Ala Ile Asn Leu
100 105 110

Thr Val Phe Arg Lys His Trp Cys Asp Ser Ser Asn Glu Glu Ser Ser
115 120 125

Ile Asn Ser Ser Asp Glu Tyr Gln Gln Trp Leu Pro Ile Gly Lys Ser
130 135 140

Gly Ser Leu Thr Cys His Leu Tyr Phe Pro Glu Ser Cys Val Leu Asp
145 150 155 160

Ser Ile Lys Trp Tyr Lys Gly Cys Glu Glu Ile Lys Val Ser Lys Lys
165 170 175

Phe Cys Pro Thr Gly Thr Lys Leu Leu Val Asn Asn Ile Asp Val Glu
180 185 190

Asp Ser Gly Ser Tyr Ala Cys Ser Ala Arg Leu Thr His Leu Gly Arg
195 200 205

Ile Phe Thr Val Arg Asn Tyr Ile Ala Val Asn Thr Lys Glu Val Gly
210 215 220

```
Ser Gly Gly Arg Ile Pro Asn Ile Thr Tyr Pro Lys Asn Asn Ser Ile
225                 230                 235                 240

Glu Val Gln Leu Gly Ser Thr Leu Ile Val Asp Cys Asn Ile Thr Asp
                245                 250                 255

Thr Lys Glu Asn Thr Asn Leu Arg Cys Trp Arg Val Asn Asn Thr Leu
            260                 265                 270

Val Asp Asp Tyr Tyr Asn Asp Phe Lys Arg Ile Gln Glu Gly Ile Glu
        275                 280                 285

Thr Asn Leu Ser Leu Arg Asn His Ile Leu Tyr Thr Val Asn Ile Thr
    290                 295                 300

Phe Leu Glu Val Lys Met Glu Asp Tyr Gly His Pro Phe Thr Cys His
305                 310                 315                 320

Ala Ala Val Ser Ala Ala Tyr Ile Ile Leu Lys Arg Pro Ala Pro Asp
                325                 330                 335

Phe Arg Ala Tyr Leu Ile Gly Gly Leu Met Ala Phe Leu Leu Leu Ala
            340                 345                 350

Val Ser Ile Leu Tyr Ile Tyr Asn Thr Phe Lys Val Asp Ile Val Leu
        355                 360                 365

Trp Tyr Arg Ser Thr Phe His Thr Ala Gln Ala Pro Asp Asp Glu Lys
    370                 375                 380

Leu Tyr Asp Ala Tyr Val Leu Tyr Pro Lys Tyr Pro Arg Glu Ser Gln
385                 390                 395                 400

Gly His Asp Val Asp Thr Leu Val Leu Lys Ile Leu Pro Glu Val Leu
                405                 410                 415

Glu Lys Gln Cys Gly Tyr Lys Leu Phe Ile Phe Gly Arg Asp Glu Phe
            420                 425                 430

Pro Gly Gln Ala Val Ala Ser Val Ile Asp Glu Asn Ile Lys Leu Cys
        435                 440                 445

Arg Arg Leu Met Val Leu Val Ala Pro Glu Thr Ser Ser Phe Ser Phe
    450                 455                 460

Leu Lys Asn Leu Thr Glu Glu Gln Ile Ala Val Tyr Asn Ala Leu Val
465                 470                 475                 480

Gln Asp Gly Met Lys Val Ile Leu Ile Glu Leu Glu Arg Val Lys Asp
                485                 490                 495
```

```
Tyr Ser Thr Met Pro Glu Ser Ile Gln Tyr Ile Arg Gln Lys His Gly
            500                 505                 510

Ala Ile Gln Trp Asp Gly Asp Phe Thr Glu Gln Ala Gln Cys Ala Lys
        515                 520                 525

Thr Lys Phe Trp Lys Lys Val Arg Tyr His Met Pro Pro Arg Arg Tyr
    530                 535                 540

Pro Ala Ser Pro Pro Val Gln Leu Leu Gly His Thr Pro Arg Ile Pro
545                 550                 555                 560

Gly
```

<210> 400
<211> 380
<212> PRT
<213> Homo sapiens

<400> 400

```
Met Ala Phe Val Cys Leu Ala Ile Gly Cys Leu Tyr Thr Phe Leu Ile
1               5                   10                  15

Ser Thr Thr Phe Gly Cys Thr Ser Ser Ser Asp Thr Glu Ile Lys Val
            20                  25                  30

Asn Pro Pro Gln Asp Phe Glu Ile Val Asp Pro Gly Tyr Leu Gly Tyr
        35                  40                  45

Leu Tyr Leu Gln Trp Gln Pro Pro Leu Ser Leu Asp His Phe Lys Glu
    50                  55                  60

Cys Thr Val Glu Tyr Glu Leu Lys Tyr Arg Asn Ile Gly Ser Glu Thr
65                  70                  75                  80

Trp Lys Thr Ile Ile Thr Lys Asn Leu His Tyr Lys Asp Gly Phe Asp
                85                  90                  95

Leu Asn Lys Gly Ile Glu Ala Lys Ile His Thr Leu Leu Pro Trp Gln
            100                 105                 110

Cys Thr Asn Gly Ser Glu Val Gln Ser Ser Trp Ala Glu Thr Thr Tyr
        115                 120                 125

Trp Ile Ser Pro Gln Gly Ile Pro Glu Thr Lys Val Gln Asp Met Asp
    130                 135                 140

Cys Val Tyr Tyr Asn Trp Gln Tyr Leu Leu Cys Ser Trp Lys Pro Gly
145                 150                 155                 160
```

```
Ile Gly Val Leu Leu Asp Thr Asn Tyr Asn Leu Phe Tyr Trp Tyr Glu
                165                 170                 175

Gly Leu Asp His Ala Leu Gln Cys Val Asp Tyr Ile Lys Ala Asp Gly
            180                 185                 190

Gln Asn Ile Gly Cys Arg Phe Pro Tyr Leu Glu Ala Ser Asp Tyr Lys
        195                 200                 205

Asp Phe Tyr Ile Cys Val Asn Gly Ser Ser Glu Asn Lys Pro Ile Arg
    210                 215                 220

Ser Ser Tyr Phe Thr Phe Gln Leu Gln Asn Ile Val Lys Pro Leu Pro
225                 230                 235                 240

Pro Val Tyr Leu Thr Phe Thr Arg Glu Ser Ser Cys Glu Ile Lys Leu
                245                 250                 255

Lys Trp Ser Ile Pro Leu Gly Pro Ile Pro Ala Arg Cys Phe Asp Tyr
            260                 265                 270

Glu Ile Glu Ile Arg Glu Asp Asp Thr Thr Leu Val Thr Ala Thr Val
        275                 280                 285

Glu Asn Glu Thr Tyr Thr Leu Lys Thr Thr Asn Glu Thr Arg Gln Leu
    290                 295                 300

Cys Phe Val Val Arg Ser Lys Val Asn Ile Tyr Cys Ser Asp Asp Gly
305                 310                 315                 320

Ile Trp Ser Glu Trp Ser Asp Lys Gln Cys Trp Glu Gly Glu Asp Leu
                325                 330                 335

Ser Lys Lys Thr Leu Leu Arg Phe Trp Leu Pro Phe Gly Phe Ile Leu
            340                 345                 350

Ile Leu Val Ile Phe Val Thr Gly Leu Leu Leu Arg Lys Pro Asn Thr
        355                 360                 365

Tyr Pro Lys Met Ile Pro Glu Phe Phe Cys Asp Thr
    370                 375                 380


<210>  401
<211>  137
<212>  PRT
<213>  Homo sapiens

<400>  401

Met Lys Val Ser Val Ala Ala Leu Ser Cys Leu Met Leu Val Thr Ala
1               5                   10                  15
```

Leu Gly Ser Gln Ala Arg Val Thr Lys Asp Ala Glu Thr Glu Phe Met
            20   25   30

Met Ser Lys Leu Pro Leu Glu Asn Pro Val Leu Leu Asp Met Leu Trp
        35   40   45

Arg Arg Lys Ile Gly Pro Gln Met Thr Leu Ser His Ala Ala Gly Phe
    50   55   60

His Ala Thr Ser Ala Asp Cys Cys Ile Ser Tyr Thr Pro Arg Ser Ile
65   70   75   80

Pro Cys Ser Leu Leu Glu Ser Tyr Phe Glu Thr Asn Ser Glu Cys Ser
                85   90   95

Lys Pro Gly Val Ile Phe Leu Thr Lys Lys Gly Arg Arg Phe Cys Ala
            100   105   110

Asn Pro Ser Asp Lys Gln Val Gln Val Cys Met Arg Met Leu Lys Leu
        115   120   125

Asp Thr Arg Ile Lys Thr Arg Lys Asn
    130   135

<210> 402
<211> 101
<212> PRT
<213> Homo sapiens

<400> 402

Met Ser Ser Ala Ala Gly Phe Cys Ala Ser Arg Pro Gly Leu Leu Phe
1   5   10   15

Leu Gly Leu Leu Leu Leu Pro Leu Val Val Ala Phe Ala Ser Ala Glu
            20   25   30

Ala Glu Glu Asp Gly Asp Leu Gln Cys Leu Cys Val Lys Thr Thr Ser
        35   40   45

Gln Val Arg Pro Arg His Ile Thr Ser Leu Glu Val Ile Lys Ala Gly
    50   55   60

Pro His Cys Pro Thr Ala Gln Leu Ile Ala Thr Leu Lys Lys Gly Arg
65   70   75   80

Lys Ala Cys Leu Asn Pro Ala Ser Pro Ile Val Lys Lys Ile Ile Lys
                85   90   95

Lys Leu Leu Glu Ser
            100

<210> 403

<211> 73
<212> PRT
<213> Homo sapiens

<400> 403

Met Ser Ala Lys Asp Leu Gln Cys Gln Cys Ile Lys Thr Tyr Ser Lys
1 5 10 15

Pro Phe His Pro Lys Phe Ile Lys Glu Leu Arg Val Ile Glu Ser Gly
20 25 30

Pro His Cys Ala Asn Thr Glu Ile Ile Val Lys Leu Ser Asp Gly Arg
35 40 45

Glu Leu Cys Leu Asp Pro Lys Glu Asn Trp Val Gln Arg Val Val Glu
50 55 60

Lys Phe Leu Lys Arg Ala Glu Asn Ser
65 70

<210> 404
<211> 73
<212> PRT
<213> Homo sapiens

<400> 404

Met Ser Ala Lys Glu Leu Gln Cys Gln Cys Ile Lys Thr Tyr Ser Lys
1 5 10 15

Pro Phe His Pro Lys Phe Ile Lys Glu Leu Arg Val Ile Glu Ser Gly
20 25 30

Pro His Cys Ala Asn Thr Glu Ile Ile Val Lys Leu Ser Asp Gly Arg
35 40 45

Glu Leu Cys Leu Asp Pro Lys Glu Asn Trp Val Gln Arg Val Val Glu
50 55 60

Lys Phe Leu Lys Arg Ala Glu Asn Ser
65 70

<210> 405
<211> 98
<212> PRT
<213> Homo sapiens

<400> 405

Met Ala Leu Leu Leu Ala Leu Ser Leu Leu Val Leu Trp Thr Ser Pro
1 5 10 15

Ala Pro Thr Leu Ser Gly Thr Asn Asp Ala Glu Asp Cys Cys Leu Ser
20 25 30

Val Thr Gln Lys Pro Ile Pro Gly Tyr Ile Val Arg Asn Phe His Tyr
        35   40   45

Leu Leu Ile Lys Asp Gly Cys Arg Val Pro Ala Val Val Phe Thr Thr
    50   55   60

Leu Arg Gly Arg Gln Leu Cys Ala Pro Pro Asp Gln Pro Trp Val Glu
65   70   75   80

Arg Ile Ile Gln Arg Leu Gln Arg Thr Ser Ala Lys Met Lys Arg Arg
                85   90   95

Ser Ser

<210> 406
<211> 120
<212> PRT
<213> Homo sapiens

<400> 406

Met Lys Val Ser Glu Ala Ala Leu Ser Leu Leu Val Leu Ile Leu Ile
1   5   10   15

Ile Thr Ser Ala Ser Arg Ser Gln Pro Lys Val Pro Glu Trp Val Asn
            20   25   30

Thr Pro Ser Thr Cys Cys Leu Lys Tyr Tyr Glu Lys Val Leu Pro Arg
        35   40   45

Arg Leu Val Val Gly Tyr Arg Lys Ala Leu Asn Cys His Leu Pro Ala
    50   55   60

Ile Ile Phe Val Thr Lys Arg Asn Arg Glu Val Cys Thr Asn Pro Asn
65   70   75   80

Asp Asp Trp Val Gln Glu Tyr Ile Lys Asp Pro Asn Leu Pro Leu Leu
                85   90   95

Pro Thr Arg Asn Leu Ser Thr Val Lys Ile Ile Thr Ala Lys Asn Gly
            100   105   110

Gln Pro Gln Leu Leu Asn Ser Gln
        115   120

<210> 407
<211> 96
<212> PRT
<213> Homo sapiens

<400> 407

Met Cys Cys Thr Lys Ser Leu Leu Leu Ala Ala Leu Met Ser Val Leu
1   5   10   15

```
Leu Leu His Leu Cys Gly Glu Ser Glu Ala Ala Ser Asn Phe Asp Cys
            20                  25                  30

Cys Leu Gly Tyr Thr Asp Arg Ile Leu His Pro Lys Phe Ile Val Gly
        35                  40                  45

Phe Thr Arg Gln Leu Ala Asn Glu Gly Cys Asp Ile Asn Ala Ile Ile
    50                  55                  60

Phe His Thr Lys Lys Lys Leu Ser Val Cys Ala Asn Pro Lys Gln Thr
65                  70                  75                  80

Trp Val Lys Tyr Ile Val Arg Leu Leu Ser Lys Lys Val Lys Asn Met
                85                  90                  95


<210>  408
<211>  93
<212>  PRT
<213>  Homo sapiens

<400>  408

Met Lys Ile Ser Val Ala Ala Ile Pro Phe Phe Leu Leu Ile Thr Ile
1               5                   10                  15

Ala Leu Gly Thr Lys Thr Glu Ser Ser Ser Arg Gly Pro Tyr His Pro
            20                  25                  30

Ser Glu Cys Cys Phe Thr Tyr Thr Thr Tyr Lys Ile Pro Arg Gln Arg
        35                  40                  45

Ile Met Asp Tyr Tyr Glu Thr Asn Ser Gln Cys Ser Lys Pro Gly Ile
    50                  55                  60

Val Phe Ile Thr Lys Arg Gly His Ser Val Cys Thr Asn Pro Ser Asp
65                  70                  75                  80

Lys Trp Val Gln Asp Tyr Ile Lys Asp Met Lys Glu Asn
                85                  90


<210>  409
<211>  109
<212>  PRT
<213>  Homo sapiens

<400>  409

Met Lys Phe Ile Ser Thr Ser Leu Leu Leu Met Leu Leu Val Ser Ser
1               5                   10                  15

Leu Ser Pro Val Gln Gly Val Leu Glu Val Tyr Tyr Thr Ser Leu Arg
            20                  25                  30
```

Cys Arg Cys Val Gln Glu Ser Ser Val Phe Ile Pro Arg Arg Phe Ile
35 40 45

Asp Arg Ile Gln Ile Leu Pro Arg Gly Asn Gly Cys Pro Arg Lys Glu
50 55 60

Ile Ile Val Trp Lys Lys Asn Lys Ser Ile Val Cys Val Asp Pro Gln
65 70 75 80

Ala Glu Trp Ile Gln Arg Met Met Glu Val Leu Arg Lys Arg Ser Ser
85 90 95

Ser Thr Leu Pro Val Pro Val Phe Lys Arg Lys Ile Pro
100 105

<210> 410
<211> 93
<212> PRT
<213> Homo sapiens

<400> 410

Met Gly Leu Ser Leu Ala Ser Ala Val Leu Leu Ala Ser Leu Leu Ser
1 5 10 15

Leu His Leu Gly Thr Ala Thr Arg Gly Ser Asp Ile Ser Lys Thr Cys
20 25 30

Cys Phe Gln Tyr Leu Gly Thr Ala Thr Arg Gly Ser Asp Ile Ser Lys
35 40 45

Thr Cys Cys Phe Gln Tyr Ser Cys Ser Gln Arg Ala Val Ile Phe Thr
50 55 60

Thr Lys Arg Gly Lys Lys Val Cys Thr His Pro Arg Lys Lys Trp Val
65 70 75 80

Gln Lys Tyr Ile Ser Leu Leu Lys Thr Pro Lys Gln Leu
85 90

<210> 411
<211> 111
<212> PRT
<213> Homo sapiens

<400> 411

Met Ala Pro Ile Ser Leu Ser Trp Leu Leu Arg Leu Ala Thr Phe Cys
1 5 10 15

His Leu Thr Val Leu Leu Ala Gly Gln His His Gly Val Thr Lys Cys
20 25 30

Asn Ile Thr Cys Ser Lys Met Thr Ser Lys Ile Pro Val Ala Leu Leu
35 40 45

```
Ile His Tyr Gln Gln Asn Gln Ala Ser Cys Gly Lys Arg Ala Ile Ile
    50                  55                  60

Leu Glu Thr Arg Gln His Arg Leu Phe Cys Ala Asp Pro Lys Glu Gln
65                  70                  75                  80

Trp Val Lys Asp Ala Met Gln His Leu Asp Arg Gln Ala Ala Ala Leu
                85                  90                  95

Thr Pro Lys Trp Arg His Leu Pro Lys Lys Pro Asp Arg Arg Gly
            100                 105                 110
```

<210> 412
<211> 113
<212> PRT
<213> Homo sapiens

<400> 412

```
Met Lys Val Ser Val Ala Ala Leu Ser Cys Leu Met Leu Val Ala Val
1               5                   10                  15

Leu Gly Ser Gln Ala Gln Phe Ile Asn Asp Ala Glu Thr Glu Leu Met
            20                  25                  30

Met Ser Lys Leu Pro Leu Glu Asn Pro Val Val Leu Asn Ser Phe His
        35                  40                  45

Phe Ala Ala Asp Cys Cys Thr Ser Tyr Ile Ser Gln Ser Ile Pro Cys
    50                  55                  60

Ser Leu Met Lys Ser Tyr Phe Glu Thr Ser Ser Glu Cys Ser Lys Pro
65                  70                  75                  80

Gly Val Ile Phe Leu Thr Lys Lys Gly Arg Gln Val Cys Ala Lys Pro
                85                  90                  95

Ser Gly Pro Gly Val Gln Asp Cys Met Lys Lys Leu Lys Pro Tyr Ser
            100                 105                 110

Ile
```

<210> 413
<211> 150
<212> PRT
<213> Homo sapiens

<400> 413

```
Met Asn Leu Trp Leu Leu Ala Cys Leu Val Ala Gly Phe Leu Gly Ala
1               5                   10                  15
```

Trp Ala Pro Ala Val His Thr Gln Gly Val Phe Glu Asp Cys Cys Leu
20 25 30

Ala Tyr His Tyr Pro Ile Gly Trp Ala Val Leu Arg Arg Ala Trp Thr
35 40 45

Tyr Arg Ile Gln Glu Val Ser Gly Ser Cys Asn Leu Pro Ala Ala Ile
50 55 60

Phe Tyr Leu Pro Lys Arg His Arg Lys Val Cys Gly Asn Pro Lys Ser
65 70 75 80

Arg Glu Val Gln Arg Ala Met Lys Leu Leu Asp Ala Arg Asn Lys Val
85 90 95

Phe Ala Lys Leu Arg His Asn Thr Gln Thr Phe Gln Ala Gly Pro His
100 105 110

Ala Val Lys Lys Leu Ser Ser Gly Asn Ser Lys Leu Ser Ser Ser Lys
115 120 125

Phe Ser Asn Pro Ile Ser Ser Ser Lys Arg Asn Val Ser Leu Leu Ile
130 135 140

Ser Ala Asn Ser Gly Leu
145 150

<210> 414
<211> 120
<212> PRT
<213> Homo sapiens

<400> 414

Met Lys Val Ser Glu Ala Ala Leu Ser Leu Leu Val Leu Ile Leu Ile
1 5 10 15

Ile Thr Ser Ala Ser Arg Ser Gln Pro Lys Val Pro Glu Trp Val Asn
20 25 30

Thr Pro Ser Thr Cys Cys Leu Lys Tyr Tyr Glu Lys Val Leu Pro Arg
35 40 45

Arg Leu Val Val Gly Tyr Arg Lys Ala Leu Asn Cys His Leu Pro Ala
50 55 60

Ile Ile Phe Val Thr Lys Arg Asn Arg Glu Val Cys Thr Asn Pro Asn
65 70 75 80

Asp Asp Trp Val Gln Glu Tyr Ile Lys Asp Pro Asn Leu Pro Leu Leu
85 90 95

Pro Thr Arg Asn Leu Ser Thr Val Lys Ile Ile Thr Ala Lys Asn Gly

100 105 110

Gln Pro Gln Leu Leu Asn Ser Gln
115 120

<210> 415
<211> 95
<212> PRT
<213> Homo sapiens

<400> 415

Met Ser Val Lys Gly Met Ala Ile Ala Leu Ala Val Ile Leu Cys Ala
1 5 10 15

Thr Val Val Gln Gly Phe Pro Met Phe Lys Arg Gly Arg Cys Leu Cys
20 25 30

Ile Gly Pro Gly Val Lys Ala Val Lys Val Ala Asp Ile Glu Lys Ala
35 40 45

Ser Ile Met Tyr Pro Ser Asn Asn Cys Asp Lys Ile Glu Val Ile Ile
50 55 60

Thr Leu Lys Glu Ile Arg Lys Arg Cys Leu Thr Pro Asn Arg Ala Ser
65 70 75 80

Lys Gln Ala Arg Leu Ile Ile Lys Lys Ala Glu Arg Lys Asn Phe
85 90 95

<210> 416
<211> 127
<212> PRT
<213> Homo sapiens

<400> 416

Met Gln Gln Arg Gly Leu Ala Ile Val Ala Leu Ala Val Cys Ala Ala
1 5 10 15

Leu His Ala Ser Glu Ala Ile Leu Pro Ile Ala Ser Ser Cys Cys Thr
20 25 30

Glu Val Ser His His Ile Ser Arg Arg Leu Leu Glu Arg Val Asn Met
35 40 45

Cys Arg Ile Gln Arg Ala Asp Gly Asp Cys Asp Leu Ala Ala Val Ile
50 55 60

Leu His Val Lys Arg Arg Arg Ile Cys Val Ser Pro His Asn His Thr
65 70 75 80

Val Lys Gln Trp Met Lys Val Gln Ala Ala Lys Lys Asn Gly Lys Gly
85 90 95

```
Asn Val Cys His Arg Lys Lys His His Gly Lys Arg Asn Ser Asn Arg
            100                 105                 110


Ala His Gln Gly Lys His Glu Thr Tyr Gly His Lys Thr Pro Tyr
        115                 120                 125


<210>  417
<211>  112
<212>  PRT
<213>  Homo sapiens

<400>  417

Met Lys Gly Pro Pro Thr Phe Cys Ser Leu Leu Leu Leu Ser Leu Leu
1               5                   10                  15


Leu Ser Pro Asp Pro Thr Ala Ala Phe Leu Leu Pro Pro Ser Thr Ala
            20                  25                  30


Cys Cys Thr Gln Leu Tyr Arg Lys Pro Leu Ser Asp Lys Leu Leu Arg
        35                  40                  45


Lys Val Ile Gln Val Glu Leu Gln Glu Ala Asp Gly Asp Cys His Leu
    50                  55                  60


Gln Ala Phe Val Leu His Leu Ala Gln Arg Ser Ile Cys Ile His Pro
65                  70                  75                  80


Gln Asn Pro Ser Leu Ser Gln Trp Phe Glu His Gln Glu Arg Lys Leu
                85                  90                  95


His Gly Thr Leu Pro Lys Leu Asn Phe Gly Met Leu Arg Lys Met Gly
            100                 105                 110


<210>  418
<211>  42
<212>  PRT
<213>  Homo sapiens

<400>  418

Arg Phe Glu Gly Tyr Arg Pro Asn Leu Ala Glu Ser Cys Pro Cys Arg
1               5                   10                  15


Gln Tyr Arg Ala Tyr Val Leu Thr His Ser Gly Glu Leu Tyr Glu Arg
            20                  25                  30


Pro Glu Arg Ser Asp Arg Gln Ile Cys Val
        35                  40


<210>  419
<211>  134
<212>  PRT
<213>  Homo sapiens
```

<400> 419

Met Ala Gln Ser Leu Ala Leu Ser Leu Leu Ile Leu Val Leu Ala Phe
1 5 10 15

Gly Ile Pro Arg Thr Gln Gly Ser Asp Gly Gly Ala Gln Asp Cys Cys
20 25 30

Leu Lys Tyr Ser Gln Arg Lys Ile Pro Ala Lys Val Val Arg Ser Tyr
35 40 45

Arg Lys Gln Glu Pro Ser Leu Gly Cys Ser Ile Pro Ala Ile Leu Phe
50 55 60

Leu Pro Arg Lys Arg Ser Gln Ala Glu Leu Cys Ala Asp Pro Lys Glu
65 70 75 80

Leu Trp Val Gln Gln Leu Met Gln His Leu Asp Lys Thr Pro Ser Pro
85 90 95

Gln Lys Pro Ala Gln Gly Cys Arg Lys Asp Arg Gly Ala Ser Lys Thr
100 105 110

Gly Lys Lys Gly Lys Gly Ser Lys Gly Cys Lys Arg Thr Glu Arg Ser
115 120 125

Gln Thr Pro Lys Gly Pro
130

<210> 420
<211> 93
<212> PRT
<213> Homo sapiens

<400> 420

Met Ala Arg Leu Gln Thr Ala Leu Leu Val Val Leu Val Leu Leu Ala
1 5 10 15

Val Ala Leu Gln Ala Thr Glu Ala Gly Pro Tyr Gly Ala Asn Met Glu
20 25 30

Asp Ser Val Cys Cys Arg Asp Tyr Val Arg Tyr Arg Leu Pro Leu Arg
35 40 45

Val Val Lys His Phe Tyr Trp Thr Ser Asp Ser Cys Pro Arg Pro Gly
50 55 60

Val Val Leu Leu Thr Phe Arg Asp Lys Glu Ile Cys Ala Asp Pro Arg
65 70 75 80

Val Pro Trp Val Lys Met Ile Leu Asn Lys Leu Ser Gln
85 90

<210> 421
<211> 109
<212> PRT
<213> Homo sapiens

<400> 421

Met Lys Phe Ile Ser Thr Ser Leu Leu Leu Met Leu Leu Val Ser Ser
1 5 10 15

Leu Ser Pro Val Gln Gly Val Leu Glu Val Tyr Tyr Thr Ser Leu Arg
20 25 30

Cys Arg Cys Val Gln Glu Ser Ser Val Phe Ile Pro Arg Arg Phe Ile
35 40 45

Asp Arg Ile Gln Ile Leu Pro Arg Gly Asn Gly Cys Pro Arg Lys Glu
50 55 60

Ile Ile Val Trp Lys Lys Asn Lys Ser Ile Val Cys Val Asp Pro Gln
65 70 75 80

Ala Glu Trp Ile Gln Arg Met Met Glu Val Leu Arg Lys Arg Ser Ser
85 90 95

Ser Thr Leu Pro Val Pro Val Phe Lys Arg Lys Ile Pro
100 105

<210> 422
<211> 93
<212> PRT
<213> Homo sapiens

<400> 422

Met Ala Arg Leu Gln Thr Ala Leu Leu Val Val Leu Val Leu Leu Ala
1 5 10 15

Val Ala Leu Gln Ala Thr Glu Ala Gly Pro Tyr Gly Ala Asn Met Glu
20 25 30

Asp Ser Val Cys Cys Arg Asp Tyr Val Arg Tyr Arg Leu Pro Leu Arg
35 40 45

Val Val Lys His Phe Tyr Trp Thr Ser Asp Ser Cys Pro Arg Pro Gly
50 55 60

Val Val Leu Leu Thr Phe Arg Asp Lys Glu Ile Cys Ala Asp Pro Arg
65 70 75 80

Val Pro Trp Val Lys Met Ile Leu Asn Lys Leu Ser Gln
85 90

<210> 423

<211> 127
<212> PRT
<213> Homo sapiens

<220>
<221> MOD_RES
<222> (70)..(70)
<223> Any naturally occurring amino acid

<220>
<221> MOD_RES
<222> (91)..(91)
<223> Any naturally occurring amino acid

<400> 423

Met Gln Gln Arg Gly Leu Ala Ile Val Ala Leu Ala Val Cys Ala Ala
1 5 10 15

Leu His Ala Ser Glu Ala Ile Leu Pro Ile Ala Ser Ser Cys Cys Thr
20 25 30

Glu Val Ser His His Ile Ser Arg Arg Leu Leu Glu Arg Val Asn Met
35 40 45

Cys Arg Ile Gln Arg Ala Asp Gly Asp Cys Asp Leu Ala Ala Val Ile
50 55 60

Leu His Val Lys Arg Xaa Arg Ile Cys Val Ser Pro His Asn His Thr
65 70 75 80

Val Lys Gln Trp Met Lys Val Gln Ala Ala Xaa Lys Asn Gly Lys Gly
85 90 95

Asn Val Cys His Arg Lys Lys His His Gly Lys Arg Asn Ser Asn Arg
100 105 110

Ala His Gln Gly Lys His Glu Thr Tyr Gly His Lys Thr Pro Tyr
115 120 125

<210> 424
<211> 104
<212> PRT
<213> Homo sapiens

<220>
<221> MOD_RES
<222> (47)..(47)
<223> Any naturally occurring amino acid

<220>
<221> MOD_RES
<222> (68)..(68)
<223> Any naturally occurring amino acid

<400> 424

Leu Pro Ile Ala Ser Ser Cys Cys Thr Glu Val Ser His His Ile Ser

1 5 10 15

Arg Arg Leu Leu Glu Arg Val Asn Met Cys Arg Ile Gln Arg Ala Asp
20 25 30

Gly Asp Cys Asp Leu Ala Ala Val Ile Leu His Val Lys Arg Xaa Arg
35 40 45

Ile Cys Val Ser Pro His Asn His Thr Val Lys Gln Trp Met Lys Val
50 55 60

Gln Ala Ala Xaa Lys Asn Gly Lys Gly Asn Val Cys His Arg Lys Lys
65 70 75 80

His His Gly Lys Arg Asn Ser Asn Arg Ala His Gln Gly Lys His Glu
85 90 95

Thr Tyr Gly His Lys Thr Pro Tyr
100

<210> 425
<211> 69
<212> PRT
<213> Homo sapiens

<400> 425

Met Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu
1 5 10 15

Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys Ile Leu Asn Thr
20 25 30

Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys Asn Asn Asn Arg
35 40 45

Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln Glu Tyr Leu Glu
50 55 60

Lys Ala Leu Asn Lys
65

<210> 426
<211> 73
<212> PRT
<213> Homo sapiens

<400> 426

Met Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro Cys Arg Phe Phe Glu
1 5 10 15

Ser His Val Ala Arg Ala Asn Val Lys His Leu Lys Ile Leu Asn Thr
20 25 30

```
Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu Lys Asn Asn Asn Arg
        35                  40                  45


Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile Gln Glu Tyr Leu Glu
    50                  55                  60


Lys Ala Leu Asn Lys Arg Phe Lys Met
65                  70


<210>  427
<211>  90
<212>  PRT
<213>  Homo sapiens

<400>  427

Met Ala Ala Lys Asp Val Lys His His His His His His Gly Ser Gly
1               5                   10                  15


Ser Asp Asp Asp Asp Lys Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro
            20                  25                  30


Cys Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu
        35                  40                  45


Lys Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu
    50                  55                  60


Lys Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile
65                  70                  75                  80


Gln Glu Tyr Leu Glu Lys Ala Leu Asn Lys
                85                  90


<210>  428
<211>  94
<212>  PRT
<213>  Homo sapiens

<400>  428

Met Ala Ala Lys Asp Val Lys His His His His His His Gly Ser Gly
1               5                   10                  15


Ser Asp Asp Asp Asp Lys Lys Pro Val Ser Leu Ser Tyr Arg Cys Pro
            20                  25                  30


Cys Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys His Leu
        35                  40                  45


Lys Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val Ala Arg Leu
    50                  55                  60


Lys Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys Leu Lys Trp Ile
```

65 70 75 80

Gln Glu Tyr Leu Glu Lys Ala Leu Asn Lys Arg Phe Lys Met
85 90

<210> 429
<211> 71
<212> PRT
<213> Homo sapiens

<400> 429

Ser Ile Pro Ile Thr Cys Cys Phe Asn Val Ile Asn Arg Lys Ile Pro
1 5 10 15

Ile Gln Arg Leu Glu Ser Tyr Thr Arg Ile Thr Asn Ile Gln Cys Pro
20 25 30

Lys Glu Ala Val Ile Phe Lys Thr Lys Arg Gly Lys Glu Val Cys Ala
35 40 45

Asp Pro Lys Glu Arg Trp Val Arg Asp Ser Met Lys His Leu Asp Gln
50 55 60

Ile Phe Gln Asn Leu Lys Pro
65 70

<210> 430
<211> 66
<212> PRT
<213> Homo sapiens

<400> 430

Tyr Ser Ser Asp Thr Thr Pro Cys Cys Phe Ala Tyr Ile Ala Arg Pro
1 5 10 15

Leu Pro Arg Ala His Ile Lys Glu Tyr Phe Tyr Thr Ser Gly Lys Cys
20 25 30

Ser Asn Pro Ala Val Val Phe Val Thr Arg Lys Asn Arg Gln Val Cys
35 40 45

Ala Asn Pro Glu Lys Lys Trp Val Arg Glu Tyr Ile Asn Ser Leu Glu
50 55 60

Met Ser
65

<210> 431
<211> 356
<212> PRT
<213> Homo sapiens

<400> 431

```
Met Ser Ile Pro Leu Pro Leu Leu Gln Ile Tyr Thr Ser Asp Asn Tyr
1               5                  10                  15

Thr Glu Glu Met Gly Ser Gly Asp Tyr Asp Ser Met Lys Glu Pro Cys
            20                  25                  30

Phe Arg Glu Glu Asn Ala Asn Phe Asn Lys Ile Phe Leu Pro Thr Ile
        35                  40                  45

Tyr Ser Ile Ile Phe Leu Thr Gly Ile Val Gly Asn Gly Leu Val Ile
    50                  55                  60

Leu Val Met Gly Tyr Gln Lys Lys Leu Arg Ser Met Thr Asp Lys Tyr
65                  70                  75                  80

Arg Leu His Leu Ser Val Ala Asp Leu Leu Phe Val Ile Thr Leu Pro
                85                  90                  95

Phe Trp Ala Val Asp Ala Val Ala Asn Trp Tyr Phe Gly Asn Phe Leu
            100                 105                 110

Cys Lys Ala Val His Val Ile Tyr Thr Val Asn Leu Tyr Ser Ser Val
        115                 120                 125

Leu Ile Leu Ala Phe Ile Ser Leu Asp Arg Tyr Leu Ala Ile Val His
    130                 135                 140

Ala Thr Asn Ser Gln Arg Pro Arg Lys Leu Leu Ala Glu Lys Val Val
145                 150                 155                 160

Tyr Val Gly Val Trp Ile Pro Ala Leu Leu Leu Thr Ile Pro Asp Phe
                165                 170                 175

Ile Phe Ala Asn Val Ser Glu Ala Asp Asp Arg Tyr Ile Cys Asp Arg
            180                 185                 190

Phe Tyr Pro Asn Asp Leu Trp Val Val Val Phe Gln Phe Gln His Ile
        195                 200                 205

Met Val Gly Leu Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys
    210                 215                 220

Ile Ile Ile Ser Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys
225                 230                 235                 240

Ala Leu Lys Thr Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp
                245                 250                 255

Leu Pro Tyr Tyr Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu
            260                 265                 270
```

```
Ile Ile Lys Gln Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile
        275                 280                 285


Ser Ile Thr Glu Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile
    290                 295                 300


Leu Tyr Ala Phe Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala
305                 310                 315                 320


Leu Thr Ser Val Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly
                325                 330                 335


Lys Arg Gly Gly His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser
            340                 345                 350


Phe His Ser Ser
        355


<210>  432
<211>  94
<212>  PRT
<213>  Homo sapiens

<400>  432

Met Met Gly Leu Ser Leu Ala Ser Ala Val Leu Leu Ala Ser Leu Leu
1               5                   10                  15


Ser Leu His Leu Gly Thr Ala Thr Arg Gly Ser Asp Ile Ser Lys Thr
            20                  25                  30


Cys Cys Phe Gln Tyr Ser His Lys Pro Leu Pro Trp Thr Trp Val Arg
        35                  40                  45


Ser Tyr Glu Phe Thr Ser Asn Ser Cys Ser Gln Arg Ala Val Ile Phe
    50                  55                  60


Thr Thr Lys Arg Gly Lys Lys Val Cys Thr His Pro Arg Lys Lys Trp
65                  70                  75                  80


Val Gln Lys Tyr Ile Ser Leu Leu Lys Thr Pro Lys Gln Leu
                85                  90


<210>  433
<211>  93
<212>  PRT
<213>  Homo sapiens

<400>  433

Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
1               5                   10                  15


Leu Cys Asn Gln Val Leu Ser Ala Pro Leu Ala Ala Asp Thr Pro Thr
            20                  25                  30
```

```
Ala Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile
        35                  40                  45


Ala Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Ser Val Ile
    50                  55                  60


Phe Leu Thr Lys Arg Gly Arg Gln Val Cys Ala Asp Pro Ser Glu Glu
65                  70                  75                  80


Trp Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
                85                  90


<210>  434
<211>  92
<212>  PRT
<213>  Homo sapiens

<400>  434

Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
1               5                   10                  15


Leu Cys Asn Gln Phe Ser Ala Ser Leu Ala Ala Asp Thr Pro Thr Ala
            20                  25                  30


Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile Ala
        35                  40                  45


Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Gly Val Ile Phe
    50                  55                  60


Leu Thr Lys Arg Ser Arg Gln Val Cys Ala Asp Pro Ser Glu Glu Trp
65                  70                  75                  80


Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
                85                  90


<210>  435
<211>  109
<212>  PRT
<213>  Homo sapiens

<400>  435

Met Lys Ile Ser Val Ala Ala Ile Pro Phe Phe Leu Leu Ile Thr Ile
1               5                   10                  15


Ala Leu Gly Thr Lys Thr Glu Ser Ser Ser Gln Thr Gly Gly Lys Pro
            20                  25                  30


Lys Val Val Lys Ile Gln Leu Lys Leu Val Gly Gly Pro Tyr His Pro
        35                  40                  45
```

Ser Glu Cys Cys Phe Thr Tyr Thr Thr Tyr Lys Ile Pro Arg Gln Arg
50 55 60

Ile Met Asp Tyr Tyr Glu Thr Asn Ser Gln Cys Ser Lys Pro Gly Ile
65 70 75 80

Val Phe Ile Thr Lys Arg Gly His Ser Val Cys Thr Asn Pro Ser Asp
85 90 95

Lys Trp Val Gln Asp Tyr Ile Lys Asp Met Lys Glu Asn
100 105

<210> 436
<211> 134
<212> PRT
<213> Homo sapiens

<400> 436

Met Ala Gln Ser Leu Ala Leu Ser Leu Leu Ile Leu Val Leu Ala Phe
1 5 10 15

Gly Ile Pro Arg Thr Gln Gly Ser Asp Gly Gly Ala Gln Asp Cys Cys
20 25 30

Leu Lys Tyr Ser Gln Arg Lys Ile Pro Ala Lys Val Val Arg Ser Tyr
35 40 45

Arg Lys Gln Glu Pro Ser Leu Gly Cys Ser Ile Pro Ala Ile Leu Phe
50 55 60

Leu Pro Arg Lys Arg Ser Gln Ala Glu Leu Cys Ala Asp Pro Lys Glu
65 70 75 80

Leu Trp Val Gln Gln Leu Met Gln His Leu Asp Lys Thr Pro Ser Pro
85 90 95

Gln Lys Pro Ala Gln Gly Cys Arg Lys Asp Arg Gly Ala Ser Lys Thr
100 105 110

Gly Lys Lys Gly Lys Gly Ser Lys Gly Cys Lys Arg Thr Glu Arg Ser
115 120 125

Gln Thr Pro Lys Gly Pro
130

<210> 437
<211> 145
<212> PRT
<213> Homo sapiens

<400> 437

Met Ala Gln Ser Leu Ala Leu Ser Leu Leu Ile Leu Val Leu Ala Phe
1 5 10 15

Gly Ile Pro Arg Thr Gln Gly Ser Asp Gly Gly Ala Gln Asp Cys Cys
            20   25   30

Leu Lys Tyr Ser Gln Arg Lys Ile Pro Ala Lys Val Val Arg Ser Tyr
        35   40   45

Arg Lys Gln Glu Pro Ser Leu Gly Cys Ser Ile Pro Ala Ile Leu Phe
    50   55   60

Leu Pro Arg Lys Arg Ser Gln Ala Glu Leu Cys Ala Asp Pro Lys Glu
65   70   75   80

Leu Trp Val Gln Gln Leu Met Gln His Leu Asp Lys Thr Pro Ser Pro
                85   90   95

Gln Lys Pro Ala Gln Gly Cys Arg Lys Asp Arg Gly Ala Ser Lys Thr
            100   105   110

Gly Lys Lys Gly Lys Gly Ser Lys Gly Cys Lys Ser Gln Pro Leu Thr
        115   120   125

Pro Leu Phe Cys Pro His Arg Thr Glu Arg Ser Gln Thr Pro Lys Gly
    130   135   140

Pro
145

<210> 438
<211> 93
<212> PRT
<213> Homo sapiens

<400> 438

Met Gln Val Ser Thr Ala Ala Leu Ala Val Leu Leu Cys Thr Met Ala
1   5   10   15

Leu Cys Asn Gln Val Leu Ser Ala Pro Leu Ala Ala Asp Thr Pro Thr
            20   25   30

Ala Cys Cys Phe Ser Tyr Thr Ser Arg Gln Ile Pro Gln Asn Phe Ile
        35   40   45

Ala Asp Tyr Phe Glu Thr Ser Ser Gln Cys Ser Lys Pro Ser Val Ile
    50   55   60

Phe Leu Thr Lys Arg Gly Arg Gln Val Cys Ala Asp Pro Ser Glu Glu
65   70   75   80

Trp Val Gln Lys Tyr Val Ser Asp Leu Glu Leu Ser Ala
                85   90

<210> 439
<211> 89
<212> PRT
<213> Homo sapiens

<400> 439

Met Lys Gly Leu Ala Ala Ala Leu Leu Val Leu Val Cys Thr Met Ala
1 5 10 15

Leu Cys Ser Cys Ala Gln Val Gly Thr Asn Lys Glu Leu Cys Cys Leu
20 25 30

Val Tyr Thr Ser Trp Gln Ile Pro Gln Lys Phe Ile Val Asp Tyr Ser
35 40 45

Glu Thr Ser Pro Gln Cys Pro Lys Pro Gly Val Ile Leu Leu Thr Lys
50 55 60

Arg Gly Arg Gln Ile Cys Ala Asp Pro Asn Lys Lys Trp Val Gln Lys
65 70 75 80

Tyr Ile Ser Asp Leu Lys Leu Asn Ala
85

<210> 440
<211> 69
<212> PRT
<213> Homo sapiens

<400> 440

Ala Gln Val Gly Thr Asn Lys Glu Leu Cys Cys Leu Val Tyr Thr Ser
1 5 10 15

Trp Gln Ile Pro Gln Lys Phe Ile Val Asp Tyr Ser Glu Thr Ser Pro
20 25 30

Gln Cys Pro Lys Pro Gly Val Ile Leu Leu Thr Lys Arg Gly Arg Gln
35 40 45

Ile Cys Ala Asp Pro Asn Lys Lys Trp Val Gln Lys Tyr Ile Ser Asp
50 55 60

Leu Lys Leu Asn Ala
65

<210> 441
<211> 264
<212> PRT
<213> Homo sapiens

<400> 441

Met Lys Lys Thr Ala Ile Ala Ile Ala Val Ala Leu Ala Gly Phe Ala
1 5 10 15

```
Thr Val Ala Asn Ala Asp Glu Pro Pro Gln Ser Pro Trp Asp Arg Val
            20                  25                  30

Lys Asp Leu Ala Thr Val Tyr Val Asp Val Leu Lys Asp Ser Gly Arg
        35                  40                  45

Asp Tyr Val Ser Gln Phe Glu Gly Ser Ala Leu Gly Lys Gln Leu Asn
    50                  55                  60

Leu Lys Leu Leu Asp Asn Trp Asp Ser Val Thr Ser Thr Phe Ser Lys
65                  70                  75                  80

Leu Arg Glu Gln Leu Gly Pro Val Thr Gln Glu Phe Trp Asp Asn Leu
                85                  90                  95

Glu Lys Glu Thr Glu Gly Leu Arg Gln Glu Met Ser Lys Asp Leu Glu
            100                 105                 110

Glu Val Lys Ala Lys Val Gln Pro Tyr Leu Asp Asp Phe Gln Lys Lys
        115                 120                 125

Trp Gln Glu Glu Met Glu Leu Tyr Arg Gln Lys Val Glu Pro Leu Arg
    130                 135                 140

Ala Glu Leu Gln Glu Gly Ala Arg Gln Lys Leu His Glu Leu Gln Glu
145                 150                 155                 160

Lys Leu Ser Pro Leu Gly Glu Glu Met Arg Asp Arg Ala Arg Ala His
                165                 170                 175

Val Asp Ala Leu Arg Thr His Leu Ala Pro Tyr Ser Asp Glu Leu Arg
            180                 185                 190

Gln Cys Leu Ala Ala Arg Leu Glu Ala Leu Lys Glu Asn Gly Gly Ala
        195                 200                 205

Arg Leu Ala Glu Tyr His Ala Lys Ala Thr Glu His Leu Ser Thr Leu
    210                 215                 220

Ser Glu Lys Ala Lys Pro Ala Leu Glu Asp Leu Arg Gln Gly Leu Leu
225                 230                 235                 240

Pro Val Leu Glu Ser Phe Lys Val Ser Phe Leu Ser Ala Leu Glu Glu
                245                 250                 255

Tyr Thr Lys Lys Leu Asn Thr Gln
            260
```

<210> 442
<211> 687

<212> PRT
<213> Homo sapiens

<400> 442

```
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                  10                  15

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30

Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45

Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60

Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80

Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95

Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110

Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125

Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195                 200                 205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240

Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255
```

```
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260                 265                 270

Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285

Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290                 295                 300

Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320

Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
                325                 330                 335

Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
            340                 345                 350

Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
        355                 360                 365

Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
    370                 375                 380

Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385                 390                 395                 400

Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
                405                 410                 415

Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
            420                 425                 430

Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
        435                 440                 445

Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
    450                 455                 460

Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys
465                 470                 475                 480

Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser
                485                 490                 495

Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile
            500                 505                 510

Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp Ser Arg
        515                 520                 525
```

```
Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val
    530                 535                 540

Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly Phe His
545                 550                 555                 560

Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu Asp Leu Lys Leu Ser
                565                 570                 575

Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr Trp Ile Leu Leu
            580                 585                 590

Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys
        595                 600                 605

Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu Asn Leu Thr Ile Met
    610                 615                 620

Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr Ala Cys Arg Ala Arg Asn
625                 630                 635                 640

Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys Lys Glu Ile Thr Ile Arg
                645                 650                 655

Gly Glu His Cys Asn Lys Lys Ala Val Phe Ser Arg Ile Ser Lys Phe
            660                 665                 670

Lys Ser Thr Arg Asn Asp Cys Thr Thr Gln Ser Asn Val Lys His
        675                 680                 685


<210>  443
<211>  668
<212>  PRT
<213>  Homo sapiens

<400>  443

Ser Glu Gln Asn Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp
1               5                   10                  15

Leu Cys Val Glu Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser
            20                  25                  30

Leu Asp Leu Pro Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys
        35                  40                  45

Ala Asn Thr Thr Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp
    50                  55                  60

Trp Leu Trp Pro Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val
65                  70                  75                  80
```

```
Thr Glu Cys Ser Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys
                85                  90                  95

Val Ile Gly Asn Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr
            100                 105                 110

Asp Leu Ala Ser Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro
        115                 120                 125

Phe Ile Ala Ser Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu
    130                 135                 140

Asn Lys Asn Lys Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn
145                 150                 155                 160

Leu Asn Val Ser Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro
                165                 170                 175

Asp Gly Asn Arg Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro
            180                 185                 190

Ser Tyr Met Ile Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile
        195                 200                 205

Asn Asp Glu Ser Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly
    210                 215                 220

Tyr Arg Ile Tyr Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu
225                 230                 235                 240

Ser Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu
                245                 250                 255

Asn Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln
            260                 265                 270

His Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu
        275                 280                 285

Met Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser
    290                 295                 300

Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys
305                 310                 315                 320

Lys Asn Ser Thr Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe
                325                 330                 335

Gly Ser Gly Met Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val
            340                 345                 350
```

```
Arg Ile Pro Ala Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp
        355                 360                 365

Tyr Lys Asn Gly Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly
    370                 375                 380

His Val Leu Thr Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr
385                 390                 395                 400

Thr Val Ile Leu Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val
                405                 410                 415

Val Ser Leu Val Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu
            420                 425                 430

Ile Ser Pro Val Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr
        435                 440                 445

Cys Thr Val Tyr Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp
    450                 455                 460

Gln Leu Glu Glu Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val
465                 470                 475                 480

Thr Asn Pro Tyr Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln
                485                 490                 495

Gly Gly Asn Lys Ile Ala Val Asn Lys Asn Gln Phe Ala Leu Ile Glu
            500                 505                 510

Gly Lys Asn Lys Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val
        515                 520                 525

Ser Ala Leu Tyr Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu
    530                 535                 540

Arg Val Ile Ser Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln
545                 550                 555                 560

Pro Asp Met Gln Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr
                565                 570                 575

Ala Asp Arg Ser Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro
            580                 585                 590

Gln Pro Leu Pro Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys
        595                 600                 605

Asn Leu Asp Thr Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser
    610                 615                 620
```

```
Thr Asn Asp Ile Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp
625                 630                 635                 640


Gln Gly Asp Tyr Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg
                645                 650                 655


His Cys Val Val Arg Gln Leu Thr Val Leu Glu Arg
            660                 665


<210>  444
<211>  780
<212>  PRT
<213>  Homo sapiens

<400>  444

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                   10                  15


Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30


Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45


Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60


Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80


Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95


Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100                 105                 110


Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115                 120                 125


Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140


Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160


Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175


Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190


Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
```

195 200 205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
210 215 220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225 230 235 240

Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
245 250 255

Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
260 265 270

Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
275 280 285

Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
290 295 300

Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305 310 315 320

Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Phe Ile Thr Val
325 330 335

Lys His Arg Lys Gln Gln Val Leu Glu Thr Val Ala Gly Lys Arg Ser
340 345 350

Tyr Arg Leu Ser Met Lys Val Lys Ala Phe Pro Ser Pro Glu Val Val
355 360 365

Trp Leu Lys Asp Gly Leu Pro Ala Thr Glu Lys Ser Ala Arg Tyr Leu
370 375 380

Thr Arg Gly Tyr Ser Leu Ile Ile Lys Asp Val Thr Glu Glu Asp Ala
385 390 395 400

Gly Asn Tyr Thr Ile Leu Leu Ser Ile Lys Gln Ser Asn Val Phe Lys
405 410 415

Asn Leu Thr Ala Thr Leu Ile Val Asn Val Lys Pro Gln Ile Tyr Glu
420 425 430

Lys Ala Val Ser Ser Phe Pro Asp Pro Ala Leu Tyr Pro Leu Gly Ser
435 440 445

Arg Gln Ile Leu Thr Cys Thr Ala Tyr Gly Ile Pro Gln Pro Thr Ile
450 455 460

Lys Trp Phe Trp His Pro Cys Asn His Asn His Ser Glu Ala Arg Cys

```
465                 470                 475                 480

Asp Phe Cys Ser Asn Asn Glu Glu Ser Phe Ile Leu Asp Ala Asp Ser
                485                 490                 495

Asn Met Gly Asn Arg Ile Glu Ser Ile Thr Gln Arg Met Ala Ile Ile
            500                 505                 510

Glu Gly Lys Asn Lys Met Ala Ser Thr Leu Val Val Ala Asp Ser Arg
        515                 520                 525

Ile Ser Gly Ile Tyr Ile Cys Ile Ala Ser Asn Lys Val Gly Thr Val
    530                 535                 540

Gly Arg Asn Ile Ser Phe Tyr Ile Thr Asp Val Pro Asn Gly Phe His
545                 550                 555                 560

Val Asn Leu Glu Lys Met Pro Thr Glu Gly Glu Asp Leu Lys Leu Ser
                565                 570                 575

Cys Thr Val Asn Lys Phe Leu Tyr Arg Asp Val Thr Trp Ile Leu Leu
            580                 585                 590

Arg Thr Val Asn Asn Arg Thr Met His Tyr Ser Ile Ser Lys Gln Lys
        595                 600                 605

Met Ala Ile Thr Lys Glu His Ser Ile Thr Leu Asn Leu Thr Ile Met
    610                 615                 620

Asn Val Ser Leu Gln Asp Ser Gly Thr Tyr Ala Cys Arg Ala Arg Asn
625                 630                 635                 640

Val Tyr Thr Gly Glu Glu Ile Leu Gln Lys Lys Glu Ile Thr Ile Arg
                645                 650                 655

Asp Gln Glu Ala Pro Tyr Leu Leu Arg Asn Leu Ser Asp His Thr Val
            660                 665                 670

Ala Ile Ser Ser Ser Thr Thr Leu Asp Cys His Ala Asn Gly Val Pro
        675                 680                 685

Glu Pro Gln Ile Thr Trp Phe Lys Asn Asn His Lys Ile Gln Gln Glu
    690                 695                 700

Pro Gly Ile Ile Leu Gly Pro Gly Ser Ser Thr Leu Phe Ile Glu Arg
705                 710                 715                 720

Val Thr Glu Glu Asp Glu Gly Val Tyr His Cys Lys Ala Thr Asn Gln
                725                 730                 735

Lys Gly Ser Val Glu Ser Ser Ala Tyr Leu Thr Val Gln Gly Thr Ser
```

740 745 750

Asp Lys Ser Asn Leu Glu Leu Ile Thr Leu Thr Cys Thr Cys Val Ala
755 760 765

Ala Thr Leu Phe Trp Leu Leu Leu Thr Leu Leu Ile
770 775 780

<210> 445
<211> 788
<212> PRT
<213> Homo sapiens

<400> 445

Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
1 5 10 15

Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
20 25 30

Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
35 40 45

Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
50 55 60

Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
65 70 75 80

Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
85 90 95

Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
100 105 110

Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
115 120 125

Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
130 135 140

Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
145 150 155 160

Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
165 170 175

Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
180 185 190

Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
195 200 205

```
Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
    210                 215                 220

Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
225                 230                 235                 240

Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
                245                 250                 255

Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
            260                 265                 270

Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
        275                 280                 285

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
    290                 295                 300

Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
305                 310                 315                 320

Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
                325                 330                 335

Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
            340                 345                 350

Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
        355                 360                 365

Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
    370                 375                 380

Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
385                 390                 395                 400

Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
                405                 410                 415

Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
            420                 425                 430

Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
        435                 440                 445

Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
    450                 455                 460

Glu Cys Ala Asn Glu Pro Ser Gln Ala Val Ser Val Thr Asn Pro Tyr
465                 470                 475                 480
```

```
Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
                485                 490                 495

Ile Ala Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
            500                 505                 510

Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
        515                 520                 525

Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
    530                 535                 540

Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
545                 550                 555                 560

Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
                565                 570                 575

Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
            580                 585                 590

Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
        595                 600                 605

Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
    610                 615                 620

Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
625                 630                 635                 640

Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
                645                 650                 655

Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
            660                 665                 670

Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
        675                 680                 685

Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
    690                 695                 700

Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705                 710                 715                 720

Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Cys
                725                 730                 735

Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe Ile
            740                 745                 750
```

Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu Ile Ile Ile Leu Val
        755   760   765

Gly Thr Thr Val Ile Ala Met Phe Phe Trp Leu Leu Leu Val Ile Ile
    770   775   780

Leu Gly Thr Val
785

<210> 446
<211> 374
<212> PRT
<213> Homo sapiens

<400> 446

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
1   5   10   15

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
            20   25   30

His Lys Phe Asp Val Lys Gln Ile Gly Ala Gln Leu Leu Pro Pro Leu
        35   40   45

Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn Met Leu Val Val
    50   55   60

Leu Ile Leu Ile Asn Cys Lys Lys Leu Lys Cys Leu Thr Asp Ile Tyr
65   70   75   80

Leu Leu Asn Leu Ala Ile Ser Asp Leu Leu Phe Leu Ile Thr Leu Pro
                85   90   95

Leu Trp Ala His Ser Ala Ala Asn Glu Trp Val Phe Gly Asn Ala Met
            100   105   110

Cys Lys Leu Phe Thr Gly Leu Tyr His Ile Gly Tyr Phe Gly Gly Ile
        115   120   125

Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu Ala Ile Val His
    130   135   140

Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe Gly Val Val Thr
145   150   155   160

Ser Val Ile Thr Trp Leu Val Ala Val Phe Ala Ser Val Pro Gly Ile
                165   170   175

Ile Phe Thr Lys Cys Gln Lys Glu Asp Ser Val Tyr Val Cys Gly Pro
            180   185   190

```
Tyr Phe Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg Asn Ile
        195                 200                 205

Leu Gly Leu Val Leu Pro Leu Leu Ile Met Val Ile Cys Tyr Ser Gly
    210                 215                 220

Ile Leu Lys Thr Leu Leu Arg Cys Arg Asn Glu Lys Lys Arg His Arg
225                 230                 235                 240

Ala Val Arg Val Ile Phe Thr Ile Met Ile Val Tyr Phe Leu Phe Trp
                245                 250                 255

Thr Pro Tyr Asn Ile Val Ile Leu Leu Asn Thr Phe Gln Glu Phe Phe
            260                 265                 270

Gly Leu Ser Asn Cys Glu Ser Thr Ser Gln Leu Asp Gln Ala Thr Gln
        275                 280                 285

Val Thr Glu Thr Leu Gly Met Thr His Cys Cys Ile Asn Pro Ile Ile
    290                 295                 300

Tyr Ala Phe Val Gly Glu Lys Phe Arg Ser Leu Phe His Ile Ala Leu
305                 310                 315                 320

Gly Cys Arg Ile Ala Pro Leu Gln Lys Pro Val Cys Gly Gly Pro Gly
                325                 330                 335

Val Arg Pro Gly Lys Asn Val Lys Val Thr Thr Gln Gly Leu Leu Asp
            340                 345                 350

Gly Arg Gly Lys Gly Lys Ser Ile Gly Arg Ala Pro Glu Ala Ser Leu
        355                 360                 365

Gln Asp Lys Glu Gly Ala
    370


<210>  447
<211>  360
<212>  PRT
<213>  Homo sapiens

<400>  447

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
1               5                   10                  15

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
            20                  25                  30

His Lys Phe Asp Val Lys Gln Ile Gly Ala Gln Leu Leu Pro Pro Leu
        35                  40                  45
```

```
Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn Met Leu Val Val
    50                  55                  60

Leu Ile Leu Ile Asn Cys Lys Lys Leu Lys Cys Leu Thr Asp Ile Tyr
65                  70                  75                  80

Leu Leu Asn Leu Ala Ile Ser Asp Leu Leu Phe Leu Ile Thr Leu Pro
                85                  90                  95

Leu Trp Ala His Ser Ala Ala Asn Glu Trp Val Phe Gly Asn Ala Met
            100                 105                 110

Cys Lys Leu Phe Thr Gly Leu Tyr His Ile Gly Tyr Phe Gly Gly Ile
        115                 120                 125

Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu Ala Ile Val His
    130                 135                 140

Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe Gly Val Val Thr
145                 150                 155                 160

Ser Val Ile Thr Trp Leu Val Ala Val Phe Ala Ser Val Pro Gly Ile
                165                 170                 175

Ile Phe Thr Lys Cys Gln Lys Glu Asp Ser Val Tyr Val Cys Gly Pro
            180                 185                 190

Tyr Phe Pro Arg Gly Trp Asn Asn Phe His Thr Ile Met Arg Asn Ile
        195                 200                 205

Leu Gly Leu Val Leu Pro Leu Leu Ile Met Val Ile Cys Tyr Ser Gly
    210                 215                 220

Ile Leu Lys Thr Leu Leu Arg Cys Arg Asn Glu Lys Lys Arg His Arg
225                 230                 235                 240

Ala Val Arg Val Ile Phe Thr Ile Met Ile Val Tyr Phe Leu Phe Trp
                245                 250                 255

Thr Pro Tyr Asn Ile Val Ile Leu Leu Asn Thr Phe Gln Glu Phe Phe
            260                 265                 270

Gly Leu Ser Asn Cys Glu Ser Thr Ser Gln Leu Asp Gln Ala Thr Gln
        275                 280                 285

Val Thr Glu Thr Leu Gly Met Thr His Cys Cys Ile Asn Pro Ile Ile
    290                 295                 300

Tyr Ala Phe Val Gly Glu Lys Phe Arg Arg Tyr Leu Ser Val Phe Phe
305                 310                 315                 320
```

```
Arg Lys His Ile Thr Lys Arg Phe Cys Lys Gln Cys Pro Val Phe Tyr
                325                 330                 335

Arg Glu Thr Val Asp Gly Val Thr Ser Thr Asn Thr Pro Ser Thr Gly
            340                 345                 350

Glu Gln Glu Val Ser Ala Gly Leu
        355                 360


<210>  448
<211>  352
<212>  PRT
<213>  Homo sapiens

<400>  448

Met Asp Tyr Gln Val Ser Ser Pro Ile Tyr Asp Ile Asn Tyr Tyr Thr
1               5                   10                  15

Ser Glu Pro Cys Gln Lys Ile Asn Val Lys Gln Ile Ala Ala Arg Leu
            20                  25                  30

Leu Pro Pro Leu Tyr Ser Leu Val Phe Ile Phe Gly Phe Val Gly Asn
        35                  40                  45

Met Leu Val Ile Leu Ile Leu Ile Asn Cys Lys Arg Leu Lys Ser Met
    50                  55                  60

Thr Asp Ile Tyr Leu Leu Asn Leu Ala Ile Ser Asp Leu Phe Phe Leu
65                  70                  75                  80

Leu Thr Val Pro Phe Trp Ala His Tyr Ala Ala Ala Gln Trp Asp Phe
                85                  90                  95

Gly Asn Thr Met Cys Gln Leu Leu Thr Gly Leu Tyr Phe Ile Gly Phe
            100                 105                 110

Phe Ser Gly Ile Phe Phe Ile Ile Leu Leu Thr Ile Asp Arg Tyr Leu
        115                 120                 125

Ala Val Val His Ala Val Phe Ala Leu Lys Ala Arg Thr Val Thr Phe
    130                 135                 140

Gly Val Val Thr Ser Val Ile Thr Trp Val Val Ala Val Phe Ala Ser
145                 150                 155                 160

Leu Pro Gly Ile Ile Phe Thr Arg Ser Gln Lys Glu Gly Leu His Tyr
                165                 170                 175

Thr Cys Ser Ser His Phe Pro Tyr Ser Gln Tyr Gln Phe Trp Lys Asn
            180                 185                 190

Phe Gln Thr Leu Lys Ile Val Ile Leu Gly Leu Val Leu Pro Leu Leu
```

195 200 205

Val Met Val Ile Cys Tyr Ser Gly Ile Leu Lys Thr Leu Leu Arg Cys
210 215 220

Arg Asn Glu Lys Lys Arg His Arg Ala Val Arg Leu Ile Phe Thr Ile
225 230 235 240

Met Ile Val Tyr Phe Leu Phe Trp Ala Pro Tyr Asn Ile Val Leu Leu
245 250 255

Leu Asn Thr Phe Gln Glu Phe Phe Gly Leu Asn Asn Cys Ser Ser Ser
260 265 270

Asn Arg Leu Asp Gln Ala Met Gln Val Thr Glu Thr Leu Gly Met Thr
275 280 285

His Cys Cys Ile Asn Pro Ile Ile Tyr Ala Phe Val Gly Glu Lys Phe
290 295 300

Arg Asn Tyr Leu Leu Val Phe Phe Gln Lys His Ile Ala Lys Arg Phe
305 310 315 320

Cys Lys Cys Cys Ser Ile Phe Gln Gln Glu Ala Pro Glu Arg Ala Ser
325 330 335

Ser Val Tyr Thr Arg Ser Thr Gly Glu Gln Glu Ile Ser Val Gly Leu
340 345 350

<210> 449
<211> 152
<212> PRT
<213> Homo sapiens

<400> 449

Met Ser Arg Leu Pro Val Leu Leu Leu Leu Gln Leu Leu Val Arg Pro
1 5 10 15

Gly Leu Gln Ala Pro Met Thr Gln Thr Thr Pro Leu Lys Thr Ser Trp
20 25 30

Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln
35 40 45

Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln
50 55 60

Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe
65 70 75 80

Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile
85 90 95

Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr
100 105 110

Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg
115 120 125

Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln
130 135 140

Thr Thr Leu Ser Leu Ala Ile Phe
145 150

<210> 450
<211> 195
<212> PRT
<213> Homo sapiens

<400> 450

Asp Ser Gln Gly Val Leu Ser Ser Phe Pro Ala Pro Gln Ala Val Gln
1 5 10 15

Asp Asn Pro Ala Met Pro Thr Ser Ser Gly Ser Glu Gly Asn Val Lys
20 25 30

Leu Cys Ser Leu Glu Glu Ala Gln Arg Ile Trp Lys Gln Lys Ser Ala
35 40 45

Glu Ile Tyr Pro Ile Met Asp Lys Ser Ser Arg Thr Arg Leu Ala Leu
50 55 60

Ile Ile Cys Asn Glu Glu Phe Asp Ser Ile Pro Arg Arg Thr Gly Ala
65 70 75 80

Glu Val Asp Ile Thr Gly Met Thr Met Leu Leu Gln Asn Leu Gly Tyr
85 90 95

Ser Val Asp Val Lys Lys Asn Leu Thr Ala Ser Asp Met Thr Thr Glu
100 105 110

Leu Glu Ala Phe Ala His Arg Pro Glu His Lys Thr Ser Asp Ser Thr
115 120 125

Phe Leu Val Phe Met Ser His Gly Ile Arg Glu Gly Ile Cys Gly Lys
130 135 140

Lys His Ser Glu Gln Val Pro Asp Ile Leu Gln Leu Asn Ala Ile Phe
145 150 155 160

Asn Met Leu Asn Thr Lys Asn Cys Pro Ser Leu Lys Asp Lys Pro Lys
165 170 175

```
Val Ile Ile Ile Gln Ala Cys Arg Gly Asp Ser Pro Gly Val Val Trp
            180                 185                 190


Phe Lys Asp
        195


<210>  451
<211>  178
<212>  PRT
<213>  Homo sapiens


<220>
<221>  MOD_RES
<222>  (1)..(1)
<223>  Asp or Asn

<400>  451

Xaa Pro Ala Met Pro Thr Ser Ser Gly Ser Glu Gly Asn Val Lys Leu
1               5                   10                  15


Cys Ser Leu Glu Glu Ala Gln Arg Ile Trp Lys Gln Lys Ser Ala Glu
            20                  25                  30


Ile Tyr Pro Ile Met Asp Lys Ser Ser Arg Thr Arg Leu Ala Leu Ile
        35                  40                  45


Ile Cys Asn Glu Glu Phe Asp Ser Ile Pro Arg Arg Thr Gly Ala Glu
    50                  55                  60


Val Asp Ile Thr Gly Met Thr Met Leu Leu Gln Asn Leu Gly Tyr Ser
65                  70                  75                  80


Val Asp Val Lys Lys Asn Leu Thr Ala Ser Asp Met Thr Thr Glu Leu
                85                  90                  95


Glu Ala Phe Ala His Arg Pro Glu His Lys Thr Ser Asp Ser Thr Phe
            100                 105                 110


Leu Val Phe Met Ser His Gly Ile Arg Glu Gly Ile Cys Gly Lys Lys
        115                 120                 125


His Ser Glu Gln Val Pro Asp Ile Leu Gln Leu Asn Ala Ile Phe Asn
    130                 135                 140


Met Leu Asn Thr Lys Asn Cys Pro Ser Leu Lys Asp Lys Pro Lys Val
145                 150                 155                 160


Ile Ile Ile Gln Ala Cys Arg Gly Asp Ser Pro Gly Val Val Trp Phe
                165                 170                 175


Lys Asp
```

<210> 452
<211> 86
<212> PRT
<213> Homo sapiens

<400> 452

Ala Ile Lys Lys Ala His Ile Glu Lys Asp Phe Ile Ala Phe Cys Ser
1 5 10 15

Ser Thr Pro Asp Asn Val Ser Trp Arg His Pro Thr Met Gly Ser Val
20 25 30

Phe Ile Gly Arg Leu Ile Glu His Met Gln Glu Tyr Ala Cys Ser Cys
35 40 45

Asp Val Glu Glu Ile Phe Arg Lys Val Arg Phe Ser Phe Glu Gln Pro
50 55 60

Gly Arg Ala Gln Met Pro Thr Thr Glu Arg Val Thr Thr Arg Cys Phe
65 70 75 80

Tyr Leu Phe Pro Gly His
85

<210> 453
<211> 267
<212> PRT
<213> Homo sapiens

<400> 453

Met Ala Pro Arg Arg Ala Arg Gly Cys Arg Thr Leu Gly Leu Pro Ala
1 5 10 15

Leu Leu Leu Leu Leu Leu Leu Arg Pro Pro Ala Thr Arg Gly Ile Thr
20 25 30

Cys Pro Pro Pro Met Ser Val Glu His Ala Asp Ile Trp Val Lys Ser
35 40 45

Tyr Ser Leu Tyr Ser Arg Glu Arg Tyr Ile Cys Asn Ser Gly Phe Lys
50 55 60

Arg Lys Ala Gly Thr Ser Ser Leu Thr Glu Cys Val Leu Asn Lys Ala
65 70 75 80

Thr Asn Val Ala His Trp Thr Thr Pro Ser Leu Lys Cys Ile Arg Asp
85 90 95

Pro Ala Leu Val His Gln Arg Pro Ala Pro Pro Ser Thr Val Thr Thr
100 105 110

```
Ala Gly Val Thr Pro Gln Pro Glu Ser Leu Ser Pro Ser Gly Lys Glu
        115                 120                 125


Pro Ala Ala Ser Ser Pro Ser Ser Asn Asn Thr Ala Ala Thr Thr Ala
    130                 135                 140


Ala Ile Val Pro Gly Ser Gln Leu Met Pro Ser Lys Ser Pro Ser Thr
145                 150                 155                 160


Gly Thr Thr Glu Ile Ser Ser His Glu Ser Ser His Gly Thr Pro Ser
                165                 170                 175


Gln Thr Thr Ala Lys Asn Trp Glu Leu Thr Ala Ser Ala Ser His Gln
            180                 185                 190


Pro Pro Gly Val Tyr Pro Gln Gly His Ser Asp Thr Thr Val Ala Ile
        195                 200                 205


Ser Thr Ser Thr Val Leu Leu Cys Gly Leu Ser Ala Val Ser Leu Leu
    210                 215                 220


Ala Cys Tyr Leu Lys Ser Arg Gln Thr Pro Pro Leu Ala Ser Val Glu
225                 230                 235                 240


Met Glu Ala Met Glu Ala Leu Pro Val Thr Trp Gly Thr Ser Ser Arg
                245                 250                 255


Asp Glu Asp Leu Glu Asn Cys Ser His His Leu
            260                 265


<210>  454
<211>  208
<212>  PRT
<213>  Homo sapiens

<400>  454

Met Thr His Leu Ser Leu Leu Gly Pro Leu Pro Cys Val Arg Thr Ser
1               5                   10                  15


Gln Gln Leu Pro Glu Thr Gln Gln Val Thr Thr Pro Gly Lys Lys Pro
            20                  25                  30


Val Ser Val Gly Arg Arg Glu Val Arg Val Pro Gly Thr Ala Leu Val
        35                  40                  45


Pro Ser Leu Leu Ser Val Ser Val Ser Pro Ala Ala Pro Gln Tyr Gln
    50                  55                  60


Gly Ser Pro Phe Ser Asp Pro Gly Phe Ser Ala Pro Glu Leu Gln Leu
65                  70                  75                  80


Ser Ser Leu Pro Pro Ala Thr Ala Phe Phe Lys Thr Trp His Ala Leu
```

85 90 95

Asp Asp Gly Glu Arg Leu Ser Pro Arg Gly Pro Leu Thr Gln His Leu
100 105 110

Gln Leu Val Glu Asp Asp Gln Ser Asp Leu Asn Pro Gly Ser Pro Ile
115 120 125

Leu Pro Ala Gln Leu Gly Ala Ala Arg Leu Arg Ala Gln Gly Pro Leu
130 135 140

Gly Asn Met Ala Ala Ile Met Thr Ala Leu Gly Leu Pro Ile Pro Pro
145 150 155 160

Glu Glu Asp Thr Pro Gly Leu Ala Ala Phe Gly Ala Ser Ala Phe Glu
165 170 175

Arg Lys Cys Arg Gly Tyr Val Val Thr Arg Glu Tyr Gly His Trp Thr
180 185 190

Asp Arg Ala Val Arg Asp Leu Ala Leu Leu Lys Ala Lys Tyr Ser Ala
195 200 205

<210> 455
<211> 208
<212> PRT
<213> Homo sapiens

<400> 455

Met Thr His Leu Ser Leu Leu Gly Pro Leu Pro Cys Val Arg Thr Ser
1 5 10 15

Gln Gln Leu Pro Glu Thr Gln Gln Val Thr Thr Pro Gly Lys Lys Pro
20 25 30

Val Ser Val Gly Arg Arg Glu Val Arg Val Pro Gly Thr Ala Leu Val
35 40 45

Pro Ser Leu Leu Ser Val Ser Val Leu Leu Gln Leu Gln Tyr Gln Gly
50 55 60

Ser Pro Phe Ser Asp Pro Gly Phe Ser Ala Pro Glu Leu Gln Leu Ser
65 70 75 80

Ser Leu Pro Pro Ala Thr Ala Phe Phe Lys Thr Trp His Ala Leu Asp
85 90 95

Asp Gly Glu Arg Leu Ser Leu Ala Gln Arg Ala Ile Asp Pro His Leu
100 105 110

Gln Leu Val Glu Asp Asp Gln Ser Asp Leu Asn Pro Gly Ser Pro Ile
115 120 125

```
Leu Pro Ala Gln Leu Gly Ala Ala Arg Leu Arg Ala Gln Gly Pro Leu
    130                 135                 140

Gly Asn Met Ala Ala Ile Met Thr Ala Leu Gly Leu Pro Ile Pro Pro
145                 150                 155                 160

Glu Glu Asp Thr Pro Gly Leu Ala Ala Phe Gly Ala Ser Ala Phe Glu
                165                 170                 175

Arg Lys Cys Arg Gly Tyr Val Val Thr Arg Glu Tyr Gly His Trp Thr
            180                 185                 190

Asp Arg Ala Val Arg Asp Leu Ala Leu Leu Lys Ala Lys Tyr Ser Ala
        195                 200                 205


<210>  456
<211>  109
<212>  PRT
<213>  Homo sapiens

<400>  456

Met Leu Lys Leu Thr Pro Leu Pro Ser Lys Met Lys Val Ser Ala Ala
1               5                   10                  15

Leu Leu Cys Leu Leu Leu Met Ala Ala Thr Phe Ser Pro Gln Gly Leu
            20                  25                  30

Ala Gln Pro Asp Ser Val Ser Ile Pro Ile Thr Cys Cys Phe Asn Val
        35                  40                  45

Ile Asn Arg Lys Ile Pro Ile Gln Arg Leu Glu Ser Tyr Thr Arg Ile
    50                  55                  60

Thr Asn Ile Gln Cys Pro Lys Glu Ala Val Ile Phe Lys Thr Lys Arg
65                  70                  75                  80

Gly Lys Glu Val Cys Ala Asp Pro Lys Glu Arg Trp Val Arg Asp Ser
                85                  90                  95

Met Lys His Leu Asp Gln Ile Phe Gln Asn Leu Lys Pro
            100                 105


<210>  457
<211>  122
<212>  PRT
<213>  Homo sapiens

<400>  457

Met Lys Pro Phe His Thr Ala Leu Ser Phe Leu Ile Leu Thr Thr Ala
1               5                   10                  15
```

```
Leu Gly Ile Trp Ala Gln Ile Thr His Ala Thr Glu Thr Lys Glu Val
            20                  25                  30

Gln Ser Ser Leu Lys Ala Gln Gln Gly Leu Glu Ile Glu Met Phe His
        35                  40                  45

Met Gly Phe Gln Asp Ser Ser Asp Cys Cys Leu Ser Tyr Asn Ser Arg
    50                  55                  60

Ile Gln Cys Ser Arg Phe Ile Gly Tyr Phe Pro Thr Ser Gly Gly Cys
65                  70                  75                  80

Thr Arg Pro Gly Ile Ile Phe Ile Ser Lys Arg Gly Phe Gln Val Cys
                85                  90                  95

Ala Asn Pro Ser Asp Arg Arg Val Gln Arg Cys Ile Glu Arg Leu Glu
            100                 105                 110

Gln Asn Ser Gln Pro Arg Thr Tyr Lys Gln
        115                 120


<210>  458
<211>  131
<212>  PRT
<213>  Homo sapiens

<400>  458

Met Ala Arg Ser Leu Val Cys Leu Gly Val Ile Ile Leu Leu Ser Ala
1               5                   10                  15

Phe Ser Gly Pro Gly Val Arg Gly Gly Pro Met Pro Lys Leu Ala Asp
            20                  25                  30

Arg Lys Leu Cys Ala Asp Gln Glu Cys Ser His Pro Ile Ser Met Ala
        35                  40                  45

Val Ala Leu Gln Asp Tyr Met Ala Pro Asp Cys Arg Phe Leu Thr Ile
    50                  55                  60

His Arg Gly Gln Val Val Tyr Val Phe Ser Lys Leu Lys Gly Arg Gly
65                  70                  75                  80

Arg Leu Phe Trp Gly Gly Ser Val Gln Gly Asp Tyr Tyr Gly Asp Leu
                85                  90                  95

Ala Ala Arg Leu Gly Tyr Phe Pro Ser Ser Ile Val Arg Glu Asp Gln
            100                 105                 110

Thr Leu Lys Pro Gly Lys Val Asp Val Lys Thr Asp Lys Trp Asp Phe
        115                 120                 125

Tyr Cys Gln
```

130

<210> 459
<211> 120
<212> PRT
<213> Homo sapiens

<400> 459

Met Lys Val Ser Val Ala Ala Leu Ser Cys Leu Met Leu Val Thr Ala
1 5 10 15

Leu Gly Ser Gln Ala Arg Val Thr Lys Asp Ala Glu Thr Glu Phe Met
20 25 30

Met Ser Lys Leu Pro Leu Glu Asn Pro Val Leu Leu Asp Arg Phe His
35 40 45

Ala Thr Ser Ala Asp Cys Cys Ile Ser Tyr Thr Pro Arg Ser Ile Pro
50 55 60

Cys Ser Leu Leu Glu Ser Tyr Phe Glu Thr Asn Ser Glu Cys Ser Lys
65 70 75 80

Pro Gly Val Ile Phe Leu Thr Lys Lys Gly Arg Arg Phe Cys Ala Asn
85 90 95

Pro Ser Asp Lys Gln Val Gln Val Cys Val Arg Met Leu Lys Leu Asp
100 105 110

Thr Arg Ile Lys Thr Arg Lys Asn
115 120

<210> 460
<211> 114
<212> PRT
<213> Homo sapiens

<400> 460

Met Arg Leu Leu Ile Leu Ala Leu Leu Gly Ile Cys Ser Leu Thr Ala
1 5 10 15

Tyr Ile Val Glu Gly Val Gly Ser Glu Val Ser His Arg Arg Thr Cys
20 25 30

Val Ser Leu Thr Thr Gln Arg Leu Pro Val Ser Arg Ile Lys Thr Tyr
35 40 45

Thr Ile Thr Glu Gly Ser Leu Arg Ala Val Ile Phe Ile Thr Lys Arg
50 55 60

Gly Leu Lys Val Cys Ala Asp Pro Gln Ala Thr Trp Val Arg Asp Val
65 70 75 80

Val Arg Ser Met Asp Arg Lys Ser Asn Thr Arg Asn Asn Met Ile Gln
85 90 95

Thr Lys Pro Thr Gly Thr Gln Gln Ser Thr Asn Thr Ala Val Thr Leu
100 105 110

Thr Gly

<210> 461
<211> 1255
<212> PRT
<213> Homo sapiens

<400> 461

Met Thr Pro Gly Thr Gln Ser Pro Phe Phe Leu Leu Leu Leu Leu Thr
1 5 10 15

Val Leu Thr Val Val Thr Gly Ser Gly His Ala Ser Ser Thr Pro Gly
20 25 30

Gly Glu Lys Glu Thr Ser Ala Thr Gln Arg Ser Ser Val Pro Ser Ser
35 40 45

Thr Glu Lys Asn Ala Val Ser Met Thr Ser Ser Val Leu Ser Ser His
50 55 60

Ser Pro Gly Ser Gly Ser Ser Thr Thr Gln Gly Gln Asp Val Thr Leu
65 70 75 80

Ala Pro Ala Thr Glu Pro Ala Ser Gly Ser Ala Ala Thr Trp Gly Gln
85 90 95

Asp Val Thr Ser Val Pro Val Thr Arg Pro Ala Leu Gly Ser Thr Thr
100 105 110

Pro Pro Ala His Asp Val Thr Ser Ala Pro Asp Asn Lys Pro Ala Pro
115 120 125

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
130 135 140

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
145 150 155 160

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
165 170 175

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
180 185 190

```
Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        195                 200                 205

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    210                 215                 220

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
225                 230                 235                 240

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                245                 250                 255

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            260                 265                 270

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        275                 280                 285

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    290                 295                 300

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
305                 310                 315                 320

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                325                 330                 335

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            340                 345                 350

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        355                 360                 365

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    370                 375                 380

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
385                 390                 395                 400

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                405                 410                 415

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            420                 425                 430

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        435                 440                 445

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    450                 455                 460
```

```
Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
465                 470                 475                 480

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                485                 490                 495

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            500                 505                 510

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        515                 520                 525

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    530                 535                 540

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
545                 550                 555                 560

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                565                 570                 575

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            580                 585                 590

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        595                 600                 605

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    610                 615                 620

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
625                 630                 635                 640

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                645                 650                 655

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            660                 665                 670

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        675                 680                 685

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    690                 695                 700

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
705                 710                 715                 720

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                725                 730                 735
```

```
Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            740                 745                 750

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        755                 760                 765

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    770                 775                 780

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
785                 790                 795                 800

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                805                 810                 815

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            820                 825                 830

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        835                 840                 845

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr
    850                 855                 860

Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser
865                 870                 875                 880

Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His
                885                 890                 895

Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala
            900                 905                 910

Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Thr Arg Pro Ala Pro
        915                 920                 925

Gly Ser Thr Ala Pro Pro Ala His Gly Val Thr Ser Ala Pro Asp Asn
    930                 935                 940

Arg Pro Ala Leu Gly Ser Thr Ala Pro Pro Val His Asn Val Thr Ser
945                 950                 955                 960

Ala Ser Gly Ser Ala Ser Gly Ser Ala Ser Thr Leu Val His Asn Gly
                965                 970                 975

Thr Ser Ala Arg Ala Thr Thr Thr Pro Ala Ser Lys Ser Thr Pro Phe
            980                 985                 990

Ser Ile Pro Ser His His Ser Asp  Thr Pro Thr Thr Leu  Ala Ser His
        995                 1000                1005
```

```
Ser Thr  Lys Thr Asp Ala Ser  Ser Thr His His Ser  Ser Val Pro
    1010                1015                1020

Pro Leu  Thr Ser Ser Asn His  Ser Thr Ser Pro Gln  Leu Ser Thr
    1025                1030                1035

Gly Val  Ser Phe Phe Phe Leu  Ser Phe His Ile Ser  Asn Leu Gln
    1040                1045                1050

Phe Asn  Ser Ser Leu Glu Asp  Pro Ser Thr Asp Tyr  Tyr Gln Glu
    1055                1060                1065

Leu Gln  Arg Asp Ile Ser Glu  Met Phe Leu Gln Ile  Tyr Lys Gln
    1070                1075                1080

Gly Gly  Phe Leu Gly Leu Ser  Asn Ile Lys Phe Arg  Pro Gly Ser
    1085                1090                1095

Val Val  Val Gln Leu Thr Leu  Ala Phe Arg Glu Gly  Thr Ile Asn
    1100                1105                1110

Val His  Asp Val Glu Thr Gln  Phe Asn Gln Tyr Lys  Thr Glu Ala
    1115                1120                1125

Ala Ser  Arg Tyr Asn Leu Thr  Ile Ser Asp Val Ser  Val Ser Asp
    1130                1135                1140

Val Pro  Phe Pro Phe Ser Ala  Gln Ser Gly Ala Gly  Val Pro Gly
    1145                1150                1155

Trp Gly  Ile Ala Leu Leu Val  Leu Val Cys Val Leu  Val Ala Leu
    1160                1165                1170

Ala Ile  Val Tyr Leu Ile Ala  Leu Ala Val Cys Gln  Cys Arg Arg
    1175                1180                1185

Lys Asn  Tyr Gly Gln Leu Asp  Ile Phe Pro Ala Arg  Asp Thr Tyr
    1190                1195                1200

His Pro  Met Ser Glu Tyr Pro  Thr Tyr His Thr His  Gly Arg Tyr
    1205                1210                1215

Val Pro  Pro Ser Ser Thr Asp  Arg Ser Pro Tyr Glu  Lys Val Ser
    1220                1225                1230

Ala Gly  Asn Gly Gly Ser Ser  Leu Ser Tyr Thr Asn  Pro Ala Val
    1235                1240                1245

Ala Ala  Thr Ser Ala Asn Leu
    1250                1255
```

<210> 462
<211> 478
<212> PRT
<213> Human immunodeficiency virus

<400> 462

```
Lys Leu Trp Val Thr Val Tyr Tyr Gly Val Pro Val Trp Lys Glu Ala
1               5                   10                  15

Thr Thr Thr Leu Phe Cys Ala Ser Asp Ala Arg Ala Tyr Asp Thr Glu
            20                  25                  30

Val His Asn Val Trp Ala Thr His Ala Cys Val Pro Thr Asp Pro Asn
        35                  40                  45

Pro Gln Glu Val Val Leu Gly Asn Val Thr Glu Asn Phe Asn Met Trp
    50                  55                  60

Lys Asn Asn Met Val Glu Gln Met Gln Glu Asp Ile Ile Ser Leu Trp
65                  70                  75                  80

Asp Gln Ser Leu Lys Pro Cys Val Lys Leu Thr Pro Leu Cys Val Thr
                85                  90                  95

Leu Asn Cys Thr Asp Leu Gly Lys Ala Thr Asn Thr Asn Ser Ser Asn
            100                 105                 110

Trp Lys Glu Glu Ile Lys Gly Glu Ile Lys Asn Cys Ser Phe Asn Ile
        115                 120                 125

Thr Thr Ser Ile Arg Asp Lys Ile Gln Lys Glu Asn Ala Leu Phe Arg
    130                 135                 140

Asn Leu Asp Val Val Pro Ile Asp Asn Ala Ser Thr Thr Thr Asn Tyr
145                 150                 155                 160

Thr Asn Tyr Arg Leu Ile His Cys Asn Arg Ser Val Ile Thr Gln Ala
                165                 170                 175

Cys Pro Lys Val Ser Phe Glu Pro Ile Pro Ile His Tyr Cys Thr Pro
            180                 185                 190

Ala Gly Phe Ala Ile Leu Lys Cys Asn Asn Lys Thr Phe Asn Gly Lys
        195                 200                 205

Gly Pro Cys Thr Asn Val Ser Thr Val Gln Cys Thr His Gly Ile Arg
    210                 215                 220

Pro Ile Val Ser Thr Gln Leu Leu Leu Asn Gly Ser Leu Ala Glu Glu
225                 230                 235                 240

Glu Val Val Ile Arg Ser Asp Asn Phe Thr Asn Asn Ala Lys Thr Ile
```

245 250 255

Ile Val Gln Leu Asn Glu Ser Val Ala Ile Asn Cys Thr Arg Pro Asn
260 265 270

Asn Asn Thr Arg Lys Ser Ile Tyr Ile Gly Pro Gly Arg Ala Phe His
275 280 285

Thr Thr Gly Arg Ile Ile Gly Asp Ile Arg Lys Ala His Cys Asn Ile
290 295 300

Ser Arg Ala Gln Trp Asn Asn Thr Leu Glu Gln Ile Val Lys Lys Leu
305 310 315 320

Arg Glu Gln Phe Gly Asn Asn Lys Thr Ile Val Phe Asn Gln Ser Ser
325 330 335

Gly Gly Asp Pro Glu Ile Val Met His Ser Phe Asn Cys Arg Gly Glu
340 345 350

Phe Phe Tyr Cys Asn Thr Thr Gln Leu Phe Asn Asn Thr Trp Arg Leu
355 360 365

Asn His Thr Glu Gly Thr Lys Gly Asn Asp Thr Ile Ile Leu Pro Cys
370 375 380

Arg Ile Lys Gln Ile Ile Asn Met Trp Gln Glu Val Gly Lys Ala Met
385 390 395 400

Tyr Ala Pro Pro Ile Gly Gly Gln Ile Ser Cys Ser Ser Asn Ile Thr
405 410 415

Gly Leu Leu Leu Thr Arg Asp Gly Gly Thr Asn Val Thr Asn Asp Thr
420 425 430

Glu Val Phe Arg Pro Gly Gly Gly Asp Met Arg Asp Asn Trp Arg Ser
435 440 445

Glu Leu Tyr Lys Tyr Lys Val Ile Lys Ile Glu Pro Leu Gly Ile Ala
450 455 460

Pro Thr Lys Ala Lys Arg Arg Val Val Gln Arg Glu Lys Arg
465 470 475

<210> 463
<211> 94
<212> PRT
<213> Homo sapiens

<400> 463

Met Ser Val Lys Gly Met Ala Ile Ala Leu Ala Val Ile Leu Cys Ala
1 5 10 15

Thr Val Val Gln Gly Phe Pro Met Phe Lys Arg Gly Arg Cys Leu Cys
            20   25   30

Ile Gly Pro Gly Val Lys Ala Val Lys Val Ala Asp Ile Glu Lys Ala
        35   40   45

Ser Ile Met Tyr Pro Ser Asn Asn Cys Asp Lys Ile Glu Val Ile Ile
    50   55   60

Thr Leu Lys Glu Asn Lys Gly Gln Arg Cys Leu Asn Pro Lys Ser Lys
65   70   75   80

Gln Ala Arg Leu Ile Ile Lys Lys Val Glu Arg Lys Asn Phe
                85   90

<210> 464
<211> 477
<212> PRT
<213> Homo sapiens

<400> 464

Leu Glu His Asp Asn Pro Glu Asp Asp Lys Val Tyr Phe Phe Phe Arg
1   5   10   15

Glu Asn Ala Ile Asp Gly Glu His Ser Gly Lys Ala Thr His Ala Arg
            20   25   30

Ile Gly Gln Ile Cys Lys Asn Asp Phe Gly Gly His Arg Ser Leu Val
        35   40   45

Asn Lys Trp Thr Thr Phe Leu Lys Ala Arg Leu Ile Cys Ser Val Pro
    50   55   60

Gly Pro Asn Gly Ile Asp Thr His Phe Asp Glu Leu Gln Asp Val Phe
65   70   75   80

Leu Met Asn Phe Lys Asp Pro Lys Asn Pro Val Val Tyr Gly Val Phe
                85   90   95

Thr Thr Ser Ser Asn Ile Phe Lys Gly Ser Ala Val Cys Met Tyr Ser
            100   105   110

Met Ser Asp Val Arg Arg Val Phe Leu Gly Pro Tyr Ala His Arg Asp
        115   120   125

Gly Pro Asn Tyr Gln Trp Val Pro Tyr Gln Gly Arg Val Pro Tyr Pro
    130   135   140

Arg Pro Gly Thr Cys Pro Ser Lys Thr Phe Gly Gly Phe Asp Ser Thr
145   150   155   160

```
Lys Asp Leu Pro Asp Asp Val Ile Thr Phe Ala Arg Ser His Pro Ala
                165                 170                 175

Met Tyr Asn Pro Val Phe Pro Met Asn Asn Arg Pro Ile Val Ile Lys
            180                 185                 190

Thr Asp Val Asn Tyr Gln Phe Thr Gln Ile Val Val Asp Arg Val Asp
        195                 200                 205

Ala Glu Asp Gly Gln Tyr Asp Val Met Phe Ile Gly Thr Asp Val Gly
    210                 215                 220

Thr Val Leu Lys Val Val Ser Ile Pro Lys Glu Thr Trp Tyr Asp Leu
225                 230                 235                 240

Glu Glu Val Leu Leu Glu Glu Met Thr Val Phe Arg Glu Pro Thr Ala
                245                 250                 255

Ile Ser Ala Met Glu Leu Ser Thr Lys Gln Gln Gln Leu Tyr Ile Gly
            260                 265                 270

Ser Thr Ala Gly Val Ala Gln Leu Pro Leu His Arg Cys Asp Ile Tyr
        275                 280                 285

Gly Lys Ala Cys Ala Glu Cys Cys Leu Ala Arg Asp Pro Tyr Cys Ala
    290                 295                 300

Trp Asp Gly Ser Ala Cys Ser Arg Tyr Phe Pro Thr Ala Lys Arg Arg
305                 310                 315                 320

Thr Arg Arg Gln Asp Ile Arg Asn Gly Asp Pro Leu Thr His Cys Ser
                325                 330                 335

Asp Leu His His Asp Asn His His Gly His Ser Pro Glu Glu Arg Ile
            340                 345                 350

Ile Tyr Gly Val Glu Asn Ser Ser Thr Phe Leu Glu Cys Ser Pro Lys
        355                 360                 365

Ser Gln Arg Ala Leu Val Tyr Trp Gln Phe Gln Arg Arg Asn Glu Glu
    370                 375                 380

Arg Lys Glu Glu Ile Arg Val Asp Asp His Ile Ile Arg Thr Asp Gln
385                 390                 395                 400

Gly Leu Leu Leu Arg Ser Leu Gln Gln Lys Asp Ser Gly Asn Tyr Leu
                405                 410                 415

Cys His Ala Val Glu His Gly Phe Ile Gln Thr Leu Leu Lys Val Thr
            420                 425                 430
```

```
Leu Glu Val Ile Asp Asn Glu His Leu Glu Glu Leu Leu His Lys Asp
        435                 440                 445


Asp Asp Gly His Gly Ser Lys Thr Lys Glu Met Ser Asn Ser Met Thr
    450                 455                 460


Pro Ser Gln Lys Val Trp Tyr Arg Asp Phe Met Gln Pro
465                 470                 475


<210>  465
<211>  241
<212>  PRT
<213>  Homo sapiens

<400>  465

Met Ser Met Leu Phe Tyr Thr Leu Ile Thr Ala Phe Leu Ile Gly Ile
1               5                   10                  15


Gln Ala Glu Pro His Ser Glu Ser Asn Val Pro Ala Gly His Thr Ile
            20                  25                  30


Pro Gln Ala His Trp Thr Lys Leu Gln His Ser Leu Asp Thr Ala Leu
        35                  40                  45


Arg Arg Ala Arg Ser Ala Pro Ala Ala Ala Ile Ala Ala Arg Val Ala
    50                  55                  60


Gly Gln Thr Arg Asn Ile Thr Val Asp Pro Arg Leu Phe Lys Lys Arg
65                  70                  75                  80


Arg Leu Arg Ser Pro Arg Val Leu Phe Ser Thr Gln Pro Pro Arg Glu
                85                  90                  95


Ala Ala Asp Thr Gln Asp Leu Asp Phe Glu Val Gly Gly Ala Ala Pro
            100                 105                 110


Phe Asn Arg Thr His Arg Ser Lys Arg Ser Ser Ser His Pro Ile Phe
        115                 120                 125


His Arg Gly Glu Phe Ser Val Cys Asp Ser Val Ser Val Trp Val Gly
    130                 135                 140


Asp Lys Thr Thr Ala Thr Asp Ile Lys Gly Lys Glu Val Met Val Leu
145                 150                 155                 160


Gly Glu Val Asn Ile Asn Asn Ser Val Phe Lys Gln Tyr Phe Phe Glu
                165                 170                 175


Thr Lys Cys Arg Asp Pro Asn Pro Val Asp Ser Gly Cys Arg Gly Ile
            180                 185                 190
```

```
Asp Ser Lys His Trp Asn Ser Tyr Cys Thr Thr Thr His Thr Phe Val
        195                 200                 205

Lys Ala Leu Thr Met Asp Gly Lys Gln Ala Ala Trp Arg Phe Ile Arg
    210                 215                 220

Ile Asp Thr Ala Cys Val Cys Val Leu Ser Arg Lys Ala Val Arg Arg
225                 230                 235                 240

Ala
```

<210> 466
<211> 267
<212> PRT
<213> Homo sapiens

<400> 466

```
Met Lys Ala Ala Val Leu Thr Leu Ala Val Leu Phe Leu Thr Gly Ser
1               5                   10                  15

Gln Ala Arg His Phe Trp Gln Gln Asp Glu Pro Pro Gln Ser Pro Trp
            20                  25                  30

Asp Arg Val Lys Asp Leu Ala Thr Val Tyr Val Asp Val Leu Lys Asp
        35                  40                  45

Ser Gly Arg Asp Tyr Val Ser Gln Phe Glu Gly Ser Ala Leu Gly Lys
    50                  55                  60

Gln Leu Asn Leu Lys Leu Leu Asp Asn Trp Asp Ser Val Thr Ser Thr
65                  70                  75                  80

Phe Ser Lys Leu Arg Glu Gln Leu Gly Pro Val Thr Gln Glu Phe Trp
                85                  90                  95

Asp Asn Leu Glu Lys Glu Thr Glu Gly Leu Arg Gln Glu Met Ser Lys
            100                 105                 110

Asp Leu Glu Glu Val Lys Ala Lys Val Gln Pro Tyr Leu Asp Asp Phe
        115                 120                 125

Gln Lys Lys Trp Gln Glu Glu Met Glu Leu Tyr Arg Gln Lys Val Glu
    130                 135                 140

Pro Leu Arg Ala Glu Leu Gln Glu Gly Ala Arg Gln Lys Leu His Glu
145                 150                 155                 160

Leu Gln Glu Lys Leu Ser Pro Leu Gly Glu Glu Met Arg Asp Arg Ala
                165                 170                 175

Arg Ala His Val Asp Ala Leu Arg Thr His Leu Ala Pro Tyr Ser Asp
```

180 185 190

Glu Leu Arg Gln Arg Leu Ala Ala Arg Leu Glu Ala Leu Lys Glu Asn
195 200 205

Gly Gly Ala Arg Leu Ala Glu Tyr His Ala Lys Ala Thr Glu His Leu
210 215 220

Ser Thr Leu Ser Glu Lys Ala Lys Pro Ala Leu Glu Asp Leu Arg Gln
225 230 235 240

Gly Leu Leu Pro Val Leu Glu Ser Phe Lys Val Ser Phe Leu Ser Ala
245 250 255

Leu Glu Glu Tyr Thr Lys Lys Leu Asn Thr Gln
260 265

<210> 467
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 467
tgagcagaag tggctcagtg 20

<210> 468
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 468
tggctgtaca gctacacccc 20

<210> 469
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 469
ttccactcct gcagggcccc 20

<210> 470
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 470

tcgcccttca gcccgcgttc 20

<210> 471
<211> 7
<212> PRT
<213> Homo sapiens

<400> 471

Pro Lys Lys Lys Arg Lys Val
1 5

<210> 472
<211> 16
<212> PRT
<213> Homo sapiens

<400> 472

Leu Gly Arg Val Ile Pro Arg Lys Ile Ala Ser Arg Ala Ser Leu Met
1 5 10 15

<210> 473
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 473
tgagcagaag tggctcagtg 20

<210> 474
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 474
tcggccgccg ccaagctcgt 20

<210> 475
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 475
tgcgcgcagc ctggtaggag 20

<210> 476
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 476
taactcaaga ctgcctcccg cttt 24

<210> 477
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 477
agcccaaggt ttcagaggtg atga 24

<210> 478
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 478
gcatctgccc tgcgggagat c 21

<210> 479
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 479
ccacgttctc ctttctctcc ccgttc 26

<210> 480

<400> 480
000

<210> 481
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 481
gcatctgccc tgcgggagat c 21

<210> 482
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 482
ccacgttctc ctttctctcc ccgttc 26

<210> 483
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 483
aaaaaaaccg gttcattttc tcttccggcc ac 32

<210> 484
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 484
aaaaaagcta gcatggcggg tctgacg 27

<210> 485
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 485
aaaaaaaccg gttcattttc tcttccggcc ac 32

<210> 486
<211> 786
<212> PRT
<213> Homo sapiens

<400> 486

Met Ala Gly Leu Thr Ala Ala Ala Pro Arg Pro Gly Val Leu Leu Leu
1 5 10 15

Leu Leu Ser Ile Leu His Pro Ser Arg Pro Gly Gly Val Pro Gly Ala
20 25 30

Ile Pro Gly Gly Val Pro Gly Gly Val Phe Tyr Pro Gly Ala Gly Leu
35 40 45

Gly Ala Leu Gly Gly Gly Ala Leu Gly Pro Gly Gly Lys Pro Leu Lys
50 55 60

Pro Val Pro Gly Gly Leu Ala Gly Ala Gly Leu Gly Ala Gly Leu Gly
65 70 75 80

Ala Phe Pro Ala Val Thr Phe Pro Gly Ala Leu Val Pro Gly Gly Val
85 90 95

```
Ala Asp Ala Ala Ala Ala Tyr Lys Ala Ala Lys Ala Gly Ala Gly Leu
            100                 105                 110

Gly Gly Val Pro Gly Val Gly Gly Leu Gly Val Ser Ala Gly Ala Val
        115                 120                 125

Val Pro Gln Pro Gly Ala Gly Val Lys Pro Gly Lys Val Pro Gly Val
    130                 135                 140

Gly Leu Pro Gly Val Tyr Pro Gly Gly Val Leu Pro Gly Ala Arg Phe
145                 150                 155                 160

Pro Gly Val Gly Val Leu Pro Gly Val Pro Thr Gly Ala Gly Val Lys
                165                 170                 175

Pro Lys Ala Pro Gly Val Gly Gly Ala Phe Ala Gly Ile Pro Gly Val
            180                 185                 190

Gly Pro Phe Gly Gly Pro Gln Pro Gly Val Pro Leu Gly Tyr Pro Ile
        195                 200                 205

Lys Ala Pro Lys Leu Pro Gly Gly Tyr Gly Leu Pro Tyr Thr Thr Gly
    210                 215                 220

Lys Leu Pro Tyr Gly Tyr Gly Pro Gly Gly Val Ala Gly Ala Ala Gly
225                 230                 235                 240

Lys Ala Gly Tyr Pro Thr Gly Thr Gly Val Gly Pro Gln Ala Ala Ala
                245                 250                 255

Ala Ala Ala Ala Lys Ala Ala Ala Lys Phe Gly Ala Gly Ala Ala Gly
            260                 265                 270

Val Leu Pro Gly Val Gly Gly Ala Gly Val Pro Gly Val Pro Gly Ala
        275                 280                 285

Ile Pro Gly Ile Gly Gly Ile Ala Gly Val Gly Thr Pro Ala Ala Ala
    290                 295                 300

Ala Ala Ala Ala Ala Ala Ala Lys Ala Ala Lys Tyr Gly Ala Ala Ala
305                 310                 315                 320

Gly Leu Val Pro Gly Gly Pro Gly Phe Gly Pro Gly Val Val Gly Val
                325                 330                 335

Pro Gly Ala Gly Val Pro Gly Val Gly Val Pro Gly Ala Gly Ile Pro
            340                 345                 350

Val Val Pro Gly Ala Gly Ile Pro Gly Ala Ala Val Pro Gly Val Val
        355                 360                 365
```

```
Ser Pro Glu Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Lys Tyr Gly
    370                 375                 380

Ala Arg Pro Gly Val Gly Val Gly Gly Ile Pro Thr Tyr Gly Val Gly
385                 390                 395                 400

Ala Gly Gly Phe Pro Gly Phe Gly Val Gly Val Gly Gly Ile Pro Gly
                405                 410                 415

Val Ala Gly Val Pro Gly Val Gly Gly Val Pro Gly Val Gly Gly Val
            420                 425                 430

Pro Gly Val Gly Ile Ser Pro Glu Ala Gln Ala Ala Ala Ala Ala Lys
        435                 440                 445

Ala Ala Lys Tyr Gly Ala Ala Gly Ala Gly Val Leu Gly Gly Leu Val
    450                 455                 460

Pro Gly Pro Gln Ala Ala Val Pro Gly Val Pro Gly Thr Gly Gly Val
465                 470                 475                 480

Pro Gly Val Gly Thr Pro Ala Ala Ala Ala Ala Lys Ala Ala Ala Lys
                485                 490                 495

Ala Ala Gln Phe Gly Leu Val Pro Gly Val Gly Val Ala Pro Gly Val
            500                 505                 510

Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Leu Ala Pro
        515                 520                 525

Gly Val Gly Val Ala Pro Gly Val Gly Val Ala Pro Gly Val Gly Val
    530                 535                 540

Ala Pro Gly Ile Gly Pro Gly Gly Val Ala Ala Ala Ala Lys Ser Ala
545                 550                 555                 560

Ala Lys Val Ala Ala Lys Ala Gln Leu Arg Ala Ala Ala Gly Leu Gly
                565                 570                 575

Ala Gly Ile Pro Gly Leu Gly Val Gly Val Gly Val Pro Gly Leu Gly
            580                 585                 590

Val Gly Ala Gly Val Pro Gly Leu Gly Val Gly Ala Gly Val Pro Gly
        595                 600                 605

Phe Gly Ala Gly Ala Asp Glu Gly Val Arg Arg Ser Leu Ser Pro Glu
    610                 615                 620

Leu Arg Glu Gly Asp Pro Ser Ser Ser Gln His Leu Pro Ser Thr Pro
625                 630                 635                 640
```

```
Ser Ser Pro Arg Val Pro Gly Ala Leu Ala Ala Ala Lys Ala Ala Lys
                645                 650                 655

Tyr Gly Ala Ala Val Pro Gly Val Leu Gly Gly Leu Gly Ala Leu Gly
            660                 665                 670

Gly Val Gly Ile Pro Gly Gly Val Val Gly Ala Gly Pro Ala Ala Ala
        675                 680                 685

Ala Ala Ala Ala Lys Ala Ala Ala Lys Ala Ala Gln Phe Gly Leu Val
    690                 695                 700

Gly Ala Ala Gly Leu Gly Gly Leu Gly Val Gly Gly Leu Gly Val Pro
705                 710                 715                 720

Gly Val Gly Gly Leu Gly Gly Ile Pro Pro Ala Ala Ala Ala Lys Ala
                725                 730                 735

Ala Lys Tyr Gly Ala Ala Gly Leu Gly Gly Val Leu Gly Gly Ala Gly
            740                 745                 750

Gln Phe Pro Leu Gly Gly Val Ala Ala Arg Pro Gly Phe Gly Leu Ser
        755                 760                 765

Pro Ile Phe Pro Gly Gly Ala Cys Leu Gly Lys Ala Cys Gly Arg Lys
    770                 775                 780

Arg Lys
785


<210>  487
<211>  1464
<212>  PRT
<213>  Homo sapiens

<400>  487

Met Phe Ser Phe Val Asp Leu Arg Leu Leu Leu Leu Leu Ala Ala Thr
1               5                   10                  15

Ala Leu Leu Thr His Gly Gln Glu Glu Gly Gln Val Glu Gly Gln Asp
            20                  25                  30

Glu Asp Ile Pro Pro Ile Thr Cys Val Gln Asn Gly Leu Arg Tyr His
        35                  40                  45

Asp Arg Asp Val Trp Lys Pro Glu Pro Cys Arg Ile Cys Val Cys Asp
    50                  55                  60

Asn Gly Lys Val Leu Cys Asp Asp Val Ile Cys Asp Glu Thr Lys Asn
65                  70                  75                  80
```

```
Cys Pro Gly Ala Glu Val Pro Glu Gly Glu Cys Cys Pro Val Cys Pro
                85                  90                  95

Asp Gly Ser Glu Ser Pro Thr Asp Gln Glu Thr Thr Gly Val Glu Gly
            100                 105                 110

Pro Lys Gly Asp Thr Gly Pro Arg Gly Pro Arg Gly Pro Ala Gly Pro
        115                 120                 125

Pro Gly Arg Asp Gly Ile Pro Gly Gln Pro Gly Leu Pro Gly Pro Pro
    130                 135                 140

Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly Gly Asn Phe Ala
145                 150                 155                 160

Pro Gln Leu Ser Tyr Gly Tyr Asp Glu Lys Ser Thr Gly Gly Ile Ser
                165                 170                 175

Val Pro Gly Pro Met Gly Pro Ser Gly Pro Arg Gly Leu Pro Gly Pro
            180                 185                 190

Pro Gly Ala Pro Gly Pro Gln Gly Phe Gln Gly Pro Pro Gly Glu Pro
        195                 200                 205

Gly Glu Pro Gly Ala Ser Gly Pro Met Gly Pro Arg Gly Pro Pro Gly
    210                 215                 220

Pro Pro Gly Lys Asn Gly Asp Asp Gly Glu Ala Gly Lys Pro Gly Arg
225                 230                 235                 240

Pro Gly Glu Arg Gly Pro Pro Gly Pro Gln Gly Ala Arg Gly Leu Pro
                245                 250                 255

Gly Thr Ala Gly Leu Pro Gly Met Lys Gly His Arg Gly Phe Ser Gly
            260                 265                 270

Leu Asp Gly Ala Lys Gly Asp Ala Gly Pro Ala Gly Pro Lys Gly Glu
        275                 280                 285

Pro Gly Ser Pro Gly Glu Asn Gly Ala Pro Gly Gln Met Gly Pro Arg
    290                 295                 300

Gly Leu Pro Gly Glu Arg Gly Arg Pro Gly Ala Pro Gly Pro Ala Gly
305                 310                 315                 320

Ala Arg Gly Asn Asp Gly Ala Thr Gly Ala Ala Gly Pro Pro Gly Pro
                325                 330                 335

Thr Gly Pro Ala Gly Pro Pro Gly Phe Pro Gly Ala Val Gly Ala Lys
            340                 345                 350
```

```
Gly Glu Ala Gly Pro Gln Gly Pro Arg Gly Ser Glu Gly Pro Gln Gly
        355                 360                 365

Val Arg Gly Glu Pro Gly Pro Pro Gly Pro Ala Gly Ala Ala Gly Pro
    370                 375                 380

Ala Gly Asn Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys Gly Ala Asn
385                 390                 395                 400

Gly Ala Pro Gly Ile Ala Gly Ala Pro Gly Phe Pro Gly Ala Arg Gly
                405                 410                 415

Pro Ser Gly Pro Gln Gly Pro Gly Gly Pro Pro Gly Pro Lys Gly Asn
            420                 425                 430

Ser Gly Glu Pro Gly Ala Pro Gly Ser Lys Gly Asp Thr Gly Ala Lys
        435                 440                 445

Gly Glu Pro Gly Pro Val Gly Val Gln Gly Pro Pro Gly Pro Ala Gly
    450                 455                 460

Glu Glu Gly Lys Arg Gly Ala Arg Gly Glu Pro Gly Pro Thr Gly Leu
465                 470                 475                 480

Pro Gly Pro Pro Gly Glu Arg Gly Gly Pro Gly Ser Arg Gly Phe Pro
                485                 490                 495

Gly Ala Asp Gly Val Ala Gly Pro Lys Gly Pro Ala Gly Glu Arg Gly
            500                 505                 510

Ser Pro Gly Pro Ala Gly Pro Lys Gly Ser Pro Gly Glu Ala Gly Arg
        515                 520                 525

Pro Gly Glu Ala Gly Leu Pro Gly Ala Lys Gly Leu Thr Gly Ser Pro
    530                 535                 540

Gly Ser Pro Gly Pro Asp Gly Lys Thr Gly Pro Pro Gly Pro Ala Gly
545                 550                 555                 560

Gln Asp Gly Arg Pro Gly Pro Pro Gly Pro Pro Gly Ala Arg Gly Gln
                565                 570                 575

Ala Gly Val Met Gly Phe Pro Gly Pro Lys Gly Ala Ala Gly Glu Pro
            580                 585                 590

Gly Lys Ala Gly Glu Arg Gly Val Pro Gly Pro Pro Gly Ala Val Gly
        595                 600                 605

Pro Ala Gly Lys Asp Gly Glu Ala Gly Ala Gln Gly Pro Pro Gly Pro
    610                 615                 620
```

```
Ala Gly Pro Ala Gly Glu Arg Gly Glu Gln Gly Pro Ala Gly Ser Pro
625                 630                 635                 640

Gly Phe Gln Gly Leu Pro Gly Pro Ala Gly Pro Pro Gly Glu Ala Gly
                645                 650                 655

Lys Pro Gly Glu Gln Gly Val Pro Gly Asp Leu Gly Ala Pro Gly Pro
            660                 665                 670

Ser Gly Ala Arg Gly Glu Arg Gly Phe Pro Gly Glu Arg Gly Val Gln
        675                 680                 685

Gly Pro Pro Gly Pro Ala Gly Pro Arg Gly Ala Asn Gly Ala Pro Gly
    690                 695                 700

Asn Asp Gly Ala Lys Gly Asp Ala Gly Ala Pro Gly Ala Pro Gly Ser
705                 710                 715                 720

Gln Gly Ala Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Ala Ala
                725                 730                 735

Gly Leu Pro Gly Pro Lys Gly Asp Arg Gly Asp Ala Gly Pro Lys Gly
            740                 745                 750

Ala Asp Gly Ser Pro Gly Lys Asp Gly Val Arg Gly Leu Thr Gly Pro
        755                 760                 765

Ile Gly Pro Pro Gly Pro Ala Gly Ala Pro Gly Asp Lys Gly Glu Ser
    770                 775                 780

Gly Pro Ser Gly Pro Ala Gly Pro Thr Gly Ala Arg Gly Ala Pro Gly
785                 790                 795                 800

Asp Arg Gly Glu Pro Gly Pro Pro Gly Pro Ala Gly Phe Ala Gly Pro
                805                 810                 815

Pro Gly Ala Asp Gly Gln Pro Gly Ala Lys Gly Glu Pro Gly Asp Ala
            820                 825                 830

Gly Ala Lys Gly Asp Ala Gly Pro Pro Gly Pro Ala Gly Pro Ala Gly
        835                 840                 845

Pro Pro Gly Pro Ile Gly Asn Val Gly Ala Pro Gly Ala Lys Gly Ala
    850                 855                 860

Arg Gly Ser Ala Gly Pro Pro Gly Ala Thr Gly Phe Pro Gly Ala Ala
865                 870                 875                 880

Gly Arg Val Gly Pro Pro Gly Pro Ser Gly Asn Ala Gly Pro Pro Gly
                885                 890                 895
```

```
Pro Pro Gly Pro Ala Gly Lys Glu Gly Gly Lys Gly Pro Arg Gly Glu
            900                 905                 910

Thr Gly Pro Ala Gly Arg Pro Gly Glu Val Gly Pro Pro Gly Pro Pro
        915                 920                 925

Gly Pro Ala Gly Glu Lys Gly Ser Pro Gly Ala Asp Gly Pro Ala Gly
    930                 935                 940

Ala Pro Gly Thr Pro Gly Pro Gln Gly Ile Ala Gly Gln Arg Gly Val
945                 950                 955                 960

Val Gly Leu Pro Gly Gln Arg Gly Glu Arg Gly Phe Pro Gly Leu Pro
                965                 970                 975

Gly Pro Ser Gly Glu Pro Gly Lys Gln Gly Pro Ser Gly Ala Ser Gly
            980                 985                 990

Glu Arg Gly Pro Pro Gly Pro Met  Gly Pro Pro Gly Leu  Ala Gly Pro
        995                 1000                1005

Pro Gly  Glu Ser Gly Arg Glu  Gly Ala Pro Gly Ala  Glu Gly Ser
    1010                1015                1020

Pro Gly  Arg Asp Gly Ser Pro  Gly Ala Lys Gly Asp  Arg Gly Glu
    1025                1030                1035

Thr Gly  Pro Ala Gly Pro Pro  Gly Ala Pro Gly Ala  Pro Gly Ala
    1040                1045                1050

Pro Gly  Pro Val Gly Pro Ala  Gly Lys Ser Gly Asp  Arg Gly Glu
    1055                1060                1065

Thr Gly  Pro Ala Gly Pro Thr  Gly Pro Val Gly Pro  Val Gly Ala
    1070                1075                1080

Arg Gly  Pro Ala Gly Pro Gln  Gly Pro Arg Gly Asp  Lys Gly Glu
    1085                1090                1095

Thr Gly  Glu Gln Gly Asp Arg  Gly Ile Lys Gly His  Arg Gly Phe
    1100                1105                1110

Ser Gly  Leu Gln Gly Pro Pro  Gly Pro Pro Gly Ser  Pro Gly Glu
    1115                1120                1125

Gln Gly  Pro Ser Gly Ala Ser  Gly Pro Ala Gly Pro  Arg Gly Pro
    1130                1135                1140

Pro Gly  Ser Ala Gly Ala Pro  Gly Lys Asp Gly Leu  Asn Gly Leu
    1145                1150                1155
```

```
Pro Gly  Pro Ile Gly Pro Pro  Gly Pro Arg Gly Arg  Thr Gly Asp
    1160                1165                1170

Ala Gly  Pro Val Gly Pro Pro  Gly Pro Pro Gly Pro  Pro Gly Pro
    1175                1180                1185

Pro Gly  Pro Pro Ser Ala Gly  Phe Asp Phe Ser Phe  Leu Pro Gln
    1190                1195                1200

Pro Pro  Gln Glu Lys Ala His  Asp Gly Gly Arg Tyr  Tyr Arg Ala
    1205                1210                1215

Asp Asp  Ala Asn Val Val Arg  Asp Arg Asp Leu Glu  Val Asp Thr
    1220                1225                1230

Thr Leu  Lys Ser Leu Ser Gln  Gln Ile Glu Asn Ile  Arg Ser Pro
    1235                1240                1245

Glu Gly  Ser Arg Lys Asn Pro  Ala Arg Thr Cys Arg  Asp Leu Lys
    1250                1255                1260

Met Cys  His Ser Asp Trp Lys  Ser Gly Glu Tyr Trp  Ile Asp Pro
    1265                1270                1275

Asn Gln  Gly Cys Asn Leu Asp  Ala Ile Lys Val Phe  Cys Asn Met
    1280                1285                1290

Glu Thr  Gly Glu Thr Cys Val  Tyr Pro Thr Gln Pro  Ser Val Ala
    1295                1300                1305

Gln Lys  Asn Trp Tyr Ile Ser  Lys Asn Pro Lys Asp  Lys Arg His
    1310                1315                1320

Val Trp  Phe Gly Glu Ser Met  Thr Asp Gly Phe Gln  Phe Glu Tyr
    1325                1330                1335

Gly Gly  Gln Gly Ser Asp Pro  Ala Asp Val Ala Ile  Gln Leu Thr
    1340                1345                1350

Phe Leu  Arg Leu Met Ser Thr  Glu Ala Ser Gln Asn  Ile Thr Tyr
    1355                1360                1365

His Cys  Lys Asn Ser Val Ala  Tyr Met Asp Gln Gln  Thr Gly Asn
    1370                1375                1380

Leu Lys  Lys Ala Leu Leu Leu  Gln Gly Ser Asn Glu  Ile Glu Ile
    1385                1390                1395

Arg Ala  Glu Gly Asn Ser Arg  Phe Thr Tyr Ser Val  Thr Val Asp
    1400                1405                1410
```

Gly Cys Thr Ser His Thr Gly Ala Trp Gly Lys Thr Val Ile Glu
1415 1420 1425

Tyr Lys Thr Thr Lys Thr Ser Arg Leu Pro Ile Ile Asp Val Ala
1430 1435 1440

Pro Leu Asp Val Gly Ala Pro Asp Gln Glu Phe Gly Phe Asp Val
1445 1450 1455

Gly Pro Val Cys Phe Leu
1460

<210> 488
<211> 1366
<212> PRT
<213> Homo sapiens

<400> 488

Met Leu Ser Phe Val Asp Thr Arg Thr Leu Leu Leu Leu Ala Val Thr
1 5 10 15

Leu Cys Leu Ala Thr Cys Gln Ser Leu Gln Glu Glu Thr Val Arg Lys
20 25 30

Gly Pro Ala Gly Asp Arg Gly Pro Arg Gly Glu Arg Gly Pro Pro Gly
35 40 45

Pro Pro Gly Arg Asp Gly Glu Asp Gly Pro Thr Gly Pro Pro Gly Pro
50 55 60

Pro Gly Pro Pro Gly Pro Pro Gly Leu Gly Gly Asn Phe Ala Ala Gln
65 70 75 80

Tyr Asp Gly Lys Gly Val Gly Leu Gly Pro Gly Pro Met Gly Leu Met
85 90 95

Gly Pro Arg Gly Pro Pro Gly Ala Ala Gly Ala Pro Gly Pro Gln Gly
100 105 110

Phe Gln Gly Pro Ala Gly Glu Pro Gly Glu Pro Gly Gln Thr Gly Pro
115 120 125

Ala Gly Ala Arg Gly Pro Ala Gly Pro Pro Gly Lys Ala Gly Glu Asp
130 135 140

Gly His Pro Gly Lys Pro Gly Arg Pro Gly Glu Arg Gly Val Val Gly
145 150 155 160

Pro Gln Gly Ala Arg Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Phe
165 170 175

Lys Gly Ile Arg Gly His Asn Gly Leu Asp Gly Leu Lys Gly Gln Pro

180 185 190

Gly Ala Pro Gly Val Lys Gly Glu Pro Gly Ala Pro Gly Glu Asn Gly
195 200 205

Thr Pro Gly Gln Thr Gly Ala Arg Gly Leu Pro Gly Glu Arg Gly Arg
210 215 220

Val Gly Ala Pro Gly Pro Ala Gly Ala Arg Gly Ser Asp Gly Ser Val
225 230 235 240

Gly Pro Val Gly Pro Ala Gly Pro Ile Gly Ser Ala Gly Pro Pro Gly
245 250 255

Phe Pro Gly Ala Pro Gly Pro Lys Gly Glu Ile Gly Ala Val Gly Asn
260 265 270

Ala Gly Pro Ala Gly Pro Ala Gly Pro Arg Gly Glu Val Gly Leu Pro
275 280 285

Gly Leu Ser Gly Pro Val Gly Pro Pro Gly Asn Pro Gly Ala Asn Gly
290 295 300

Leu Thr Gly Ala Lys Gly Ala Ala Gly Leu Pro Gly Val Ala Gly Ala
305 310 315 320

Pro Gly Leu Pro Gly Pro Arg Gly Ile Pro Gly Pro Val Gly Ala Ala
325 330 335

Gly Ala Thr Gly Ala Arg Gly Leu Val Gly Glu Pro Gly Pro Ala Gly
340 345 350

Ser Lys Gly Glu Ser Gly Asn Lys Gly Glu Pro Gly Ser Ala Gly Pro
355 360 365

Gln Gly Pro Pro Gly Pro Ser Gly Glu Glu Gly Lys Arg Gly Pro Asn
370 375 380

Gly Glu Ala Gly Ser Ala Gly Pro Pro Gly Pro Pro Gly Leu Arg Gly
385 390 395 400

Ser Pro Gly Ser Arg Gly Leu Pro Gly Ala Asp Gly Arg Ala Gly Val
405 410 415

Met Gly Pro Pro Gly Ser Arg Gly Ala Ser Gly Pro Ala Gly Val Arg
420 425 430

Gly Pro Asn Gly Asp Ala Gly Arg Pro Gly Glu Pro Gly Leu Met Gly
435 440 445

Pro Arg Gly Leu Pro Gly Ser Pro Gly Asn Ile Gly Pro Ala Gly Lys

```
    450                 455                 460

Glu Gly Pro Val Gly Leu Pro Gly Ile Asp Gly Arg Pro Gly Pro Ile
465                 470                 475                 480

Gly Pro Ala Gly Ala Arg Gly Glu Pro Gly Asn Ile Gly Phe Pro Gly
                485                 490                 495

Pro Lys Gly Pro Thr Gly Asp Pro Gly Lys Asn Gly Asp Lys Gly His
            500                 505                 510

Ala Gly Leu Ala Gly Ala Arg Gly Ala Pro Gly Pro Asp Gly Asn Asn
        515                 520                 525

Gly Ala Gln Gly Pro Pro Gly Pro Gln Gly Val Gln Gly Gly Lys Gly
    530                 535                 540

Glu Gln Gly Pro Pro Gly Pro Pro Gly Phe Gln Gly Leu Pro Gly Pro
545                 550                 555                 560

Ser Gly Pro Ala Gly Glu Val Gly Lys Pro Gly Glu Arg Gly Leu His
                565                 570                 575

Gly Glu Phe Gly Leu Pro Gly Pro Ala Gly Pro Arg Gly Glu Arg Gly
            580                 585                 590

Pro Pro Gly Glu Ser Gly Ala Ala Gly Pro Thr Gly Pro Ile Gly Ser
        595                 600                 605

Arg Gly Pro Ser Gly Pro Pro Gly Pro Asp Gly Asn Lys Gly Glu Pro
    610                 615                 620

Gly Val Val Gly Ala Val Gly Thr Ala Gly Pro Ser Gly Pro Ser Gly
625                 630                 635                 640

Leu Pro Gly Glu Arg Gly Ala Ala Gly Ile Pro Gly Gly Lys Gly Glu
                645                 650                 655

Lys Gly Glu Pro Gly Leu Arg Gly Glu Ile Gly Asn Pro Gly Arg Asp
            660                 665                 670

Gly Ala Arg Gly Ala Pro Gly Ala Val Gly Ala Pro Gly Pro Ala Gly
        675                 680                 685

Ala Thr Gly Asp Arg Gly Glu Ala Gly Ala Ala Gly Pro Ala Gly Pro
    690                 695                 700

Ala Gly Pro Arg Gly Ser Pro Gly Glu Arg Gly Glu Val Gly Pro Ala
705                 710                 715                 720

Gly Pro Asn Gly Phe Ala Gly Pro Ala Gly Ala Ala Gly Gln Pro Gly
```

```
                725                 730                 735

Ala Lys Gly Glu Arg Gly Ala Lys Gly Pro Lys Gly Glu Asn Gly Val
            740                 745                 750

Val Gly Pro Thr Gly Pro Val Gly Ala Ala Gly Pro Ala Gly Pro Asn
        755                 760                 765

Gly Pro Pro Gly Pro Ala Gly Ser Arg Gly Asp Gly Gly Pro Pro Gly
    770                 775                 780

Met Thr Gly Phe Pro Gly Ala Ala Gly Arg Thr Gly Pro Pro Gly Pro
785                 790                 795                 800

Ser Gly Ile Ser Gly Pro Pro Gly Pro Pro Gly Pro Ala Gly Lys Glu
                805                 810                 815

Gly Leu Arg Gly Pro Arg Gly Asp Gln Gly Pro Val Gly Arg Thr Gly
            820                 825                 830

Glu Val Gly Ala Val Gly Pro Pro Gly Phe Ala Gly Glu Lys Gly Pro
        835                 840                 845

Ser Gly Glu Ala Gly Thr Ala Gly Pro Pro Gly Thr Pro Gly Pro Gln
    850                 855                 860

Gly Leu Leu Gly Ala Pro Gly Ile Leu Gly Leu Pro Gly Ser Arg Gly
865                 870                 875                 880

Glu Arg Gly Leu Pro Gly Val Ala Gly Ala Val Gly Glu Pro Gly Pro
                885                 890                 895

Leu Gly Ile Ala Gly Pro Pro Gly Ala Arg Gly Pro Pro Gly Ala Val
            900                 905                 910

Gly Ser Pro Gly Val Asn Gly Ala Pro Gly Glu Ala Gly Arg Asp Gly
        915                 920                 925

Asn Pro Gly Asn Asp Gly Pro Pro Gly Arg Asp Gly Gln Pro Gly His
    930                 935                 940

Lys Gly Glu Arg Gly Tyr Pro Gly Asn Ile Gly Pro Val Gly Ala Ala
945                 950                 955                 960

Gly Ala Pro Gly Pro His Gly Pro Val Gly Pro Ala Gly Lys His Gly
                965                 970                 975

Asn Arg Gly Glu Thr Gly Pro Ser Gly Pro Val Gly Pro Ala Gly Ala
            980                 985                 990

Val Gly Pro Arg Gly Pro Ser Gly  Pro Gln Gly Ile Arg  Gly Asp Lys
```

995 1000 1005

Gly Glu Pro Gly Glu Lys Gly Pro Arg Gly Leu Pro Gly Leu Lys
1010 1015 1020

Gly His Asn Gly Leu Gln Gly Leu Pro Gly Ile Ala Gly His His
1025 1030 1035

Gly Asp Gln Gly Ala Pro Gly Ser Val Gly Pro Ala Gly Pro Arg
1040 1045 1050

Gly Pro Ala Gly Pro Ser Gly Pro Ala Gly Lys Asp Gly Arg Thr
1055 1060 1065

Gly His Pro Gly Thr Val Gly Pro Ala Gly Ile Arg Gly Pro Gln
1070 1075 1080

Gly His Gln Gly Pro Ala Gly Pro Pro Gly Pro Pro Gly Pro Pro
1085 1090 1095

Gly Pro Pro Gly Val Ser Gly Gly Gly Tyr Asp Phe Gly Tyr Asp
1100 1105 1110

Gly Asp Phe Tyr Arg Ala Asp Gln Pro Arg Ser Ala Pro Ser Leu
1115 1120 1125

Arg Pro Lys Asp Tyr Glu Val Asp Ala Thr Leu Lys Ser Leu Asn
1130 1135 1140

Asn Gln Ile Glu Thr Leu Leu Thr Pro Glu Gly Ser Arg Lys Asn
1145 1150 1155

Pro Ala Arg Thr Cys Arg Asp Leu Arg Leu Ser His Pro Glu Trp
1160 1165 1170

Ser Ser Gly Tyr Tyr Trp Ile Asp Pro Asn Gln Gly Cys Thr Met
1175 1180 1185

Asp Ala Ile Lys Val Tyr Cys Asp Phe Ser Thr Gly Glu Thr Cys
1190 1195 1200

Ile Arg Ala Gln Pro Glu Asn Ile Pro Ala Lys Asn Trp Tyr Arg
1205 1210 1215

Ser Ser Lys Asp Lys Lys His Val Trp Leu Gly Glu Thr Ile Asn
1220 1225 1230

Ala Gly Ser Gln Phe Glu Tyr Asn Val Glu Gly Val Thr Ser Lys
1235 1240 1245

Glu Met Ala Thr Gln Leu Ala Phe Met Arg Leu Leu Ala Asn Tyr

1250 1255 1260

Ala Ser Gln Asn Ile Thr Tyr His Cys Lys Asn Ser Ile Ala Tyr
1265 1270 1275

Met Asp Glu Glu Thr Gly Asn Leu Lys Lys Ala Val Ile Leu Gln
1280 1285 1290

Gly Ser Asn Asp Val Glu Leu Val Ala Glu Gly Asn Ser Arg Phe
1295 1300 1305

Thr Tyr Thr Val Leu Val Asp Gly Cys Ser Lys Lys Thr Asn Glu
1310 1315 1320

Trp Gly Lys Thr Ile Ile Glu Tyr Lys Thr Asn Lys Pro Ser Arg
1325 1330 1335

Leu Pro Phe Leu Asp Ile Ala Pro Leu Asp Ile Gly Gly Ala Asp
1340 1345 1350

Gln Glu Phe Phe Val Asp Ile Gly Pro Val Cys Phe Lys
1355 1360 1365

<210> 489
<211> 1466
<212> PRT
<213> Homo sapiens

<400> 489

Met Met Ser Phe Val Gln Lys Gly Ser Trp Leu Leu Leu Ala Leu Leu
1 5 10 15

His Pro Thr Ile Ile Leu Ala Gln Gln Glu Ala Val Glu Gly Gly Cys
20 25 30

Ser His Leu Gly Gln Ser Tyr Ala Asp Arg Asp Val Trp Lys Pro Glu
35 40 45

Pro Cys Gln Ile Cys Val Cys Asp Ser Gly Ser Val Leu Cys Asp Asp
50 55 60

Ile Ile Cys Asp Asp Gln Glu Leu Asp Cys Pro Asn Pro Glu Ile Pro
65 70 75 80

Phe Gly Glu Cys Cys Ala Val Cys Pro Gln Pro Pro Thr Ala Pro Thr
85 90 95

Arg Pro Pro Asn Gly Gln Gly Pro Gln Gly Pro Lys Gly Asp Pro Gly
100 105 110

Pro Pro Gly Ile Pro Gly Arg Asn Gly Asp Pro Gly Ile Pro Gly Gln
115 120 125

```
Pro Gly Ser Pro Gly Ser Pro Gly Pro Pro Gly Ile Cys Glu Ser Cys
    130                 135                 140

Pro Thr Gly Pro Gln Asn Tyr Ser Pro Gln Tyr Asp Ser Tyr Asp Val
145                 150                 155                 160

Lys Ser Gly Val Ala Val Gly Gly Leu Ala Gly Tyr Pro Gly Pro Ala
                165                 170                 175

Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly Thr Ser Gly His Pro Gly
            180                 185                 190

Ser Pro Gly Ser Pro Gly Tyr Gln Gly Pro Pro Gly Glu Pro Gly Gln
        195                 200                 205

Ala Gly Pro Ser Gly Pro Pro Gly Pro Pro Gly Ala Ile Gly Pro Ser
    210                 215                 220

Gly Pro Ala Gly Lys Asp Gly Glu Ser Gly Arg Pro Gly Arg Pro Gly
225                 230                 235                 240

Glu Arg Gly Leu Pro Gly Pro Pro Gly Ile Lys Gly Pro Ala Gly Ile
                245                 250                 255

Pro Gly Phe Pro Gly Met Lys Gly His Arg Gly Phe Asp Gly Arg Asn
            260                 265                 270

Gly Glu Lys Gly Glu Thr Gly Ala Pro Gly Leu Lys Gly Glu Asn Gly
        275                 280                 285

Leu Pro Gly Glu Asn Gly Ala Pro Gly Pro Met Gly Pro Arg Gly Ala
    290                 295                 300

Pro Gly Glu Arg Gly Arg Pro Gly Leu Pro Gly Ala Ala Gly Ala Arg
305                 310                 315                 320

Gly Asn Asp Gly Ala Arg Gly Ser Asp Gly Gln Pro Gly Pro Pro Gly
                325                 330                 335

Pro Pro Gly Thr Ala Gly Phe Pro Gly Ser Pro Gly Ala Lys Gly Glu
            340                 345                 350

Val Gly Pro Ala Gly Ser Pro Gly Ser Asn Gly Ala Pro Gly Gln Arg
        355                 360                 365

Gly Glu Pro Gly Pro Gln Gly His Ala Gly Ala Gln Gly Pro Pro Gly
    370                 375                 380

Pro Pro Gly Ile Asn Gly Ser Pro Gly Gly Lys Gly Glu Met Gly Pro
385                 390                 395                 400
```

```
Ala Gly Ile Pro Gly Ala Pro Gly Leu Met Gly Ala Arg Gly Pro Pro
                405                 410                 415

Gly Pro Ala Gly Ala Asn Gly Ala Pro Gly Leu Arg Gly Gly Ala Gly
            420                 425                 430

Glu Pro Gly Lys Asn Gly Ala Lys Gly Glu Pro Gly Pro Arg Gly Glu
        435                 440                 445

Arg Gly Glu Ala Gly Ile Pro Gly Val Pro Gly Ala Lys Gly Glu Asp
    450                 455                 460

Gly Lys Asp Gly Ser Pro Gly Glu Pro Gly Ala Asn Gly Leu Pro Gly
465                 470                 475                 480

Ala Ala Gly Glu Arg Gly Ala Pro Gly Phe Arg Gly Pro Ala Gly Pro
                485                 490                 495

Asn Gly Ile Pro Gly Glu Lys Gly Pro Ala Gly Glu Arg Gly Ala Pro
            500                 505                 510

Gly Pro Ala Gly Pro Arg Gly Ala Ala Gly Glu Pro Gly Arg Asp Gly
        515                 520                 525

Val Pro Gly Gly Pro Gly Met Arg Gly Met Pro Gly Ser Pro Gly Gly
    530                 535                 540

Pro Gly Ser Asp Gly Lys Pro Gly Pro Pro Gly Ser Gln Gly Glu Ser
545                 550                 555                 560

Gly Arg Pro Gly Pro Pro Gly Pro Ser Gly Pro Arg Gly Gln Pro Gly
                565                 570                 575

Val Met Gly Phe Pro Gly Pro Lys Gly Asn Asp Gly Ala Pro Gly Lys
            580                 585                 590

Asn Gly Glu Arg Gly Gly Pro Gly Gly Pro Gly Pro Gln Gly Pro Pro
        595                 600                 605

Gly Lys Asn Gly Glu Thr Gly Pro Gln Gly Pro Pro Gly Pro Thr Gly
    610                 615                 620

Pro Gly Gly Asp Lys Gly Asp Thr Gly Pro Pro Gly Pro Gln Gly Leu
625                 630                 635                 640

Gln Gly Leu Pro Gly Thr Gly Gly Pro Pro Gly Glu Asn Gly Lys Pro
                645                 650                 655

Gly Glu Pro Gly Pro Lys Gly Asp Ala Gly Ala Pro Gly Ala Pro Gly
            660                 665                 670
```

```
Gly Lys Gly Asp Ala Gly Ala Pro Gly Glu Arg Gly Pro Pro Gly Leu
        675                 680                 685

Ala Gly Ala Pro Gly Leu Arg Gly Gly Ala Gly Pro Pro Gly Pro Glu
    690                 695                 700

Gly Gly Lys Gly Ala Ala Gly Pro Pro Gly Pro Pro Gly Ala Ala Gly
705                 710                 715                 720

Thr Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly Gly Leu Gly Ser
                725                 730                 735

Pro Gly Pro Lys Gly Asp Lys Gly Glu Pro Gly Gly Pro Gly Ala Asp
            740                 745                 750

Gly Val Pro Gly Lys Asp Gly Pro Arg Gly Pro Thr Gly Pro Ile Gly
        755                 760                 765

Pro Pro Gly Pro Ala Gly Gln Pro Gly Asp Lys Gly Glu Gly Gly Ala
    770                 775                 780

Pro Gly Leu Pro Gly Ile Ala Gly Pro Arg Gly Ser Pro Gly Glu Arg
785                 790                 795                 800

Gly Glu Thr Gly Pro Pro Gly Pro Ala Gly Phe Pro Gly Ala Pro Gly
                805                 810                 815

Gln Asn Gly Glu Pro Gly Gly Lys Gly Glu Arg Gly Ala Pro Gly Glu
            820                 825                 830

Lys Gly Glu Gly Gly Pro Pro Gly Val Ala Gly Pro Pro Gly Gly Ser
        835                 840                 845

Gly Pro Ala Gly Pro Pro Gly Pro Gln Gly Val Lys Gly Glu Arg Gly
    850                 855                 860

Ser Pro Gly Gly Pro Gly Ala Ala Gly Phe Pro Gly Ala Arg Gly Leu
865                 870                 875                 880

Pro Gly Pro Pro Gly Ser Asn Gly Asn Pro Gly Pro Pro Gly Pro Ser
                885                 890                 895

Gly Ser Pro Gly Lys Asp Gly Pro Pro Gly Pro Ala Gly Asn Thr Gly
            900                 905                 910

Ala Pro Gly Ser Pro Gly Val Ser Gly Pro Lys Gly Asp Ala Gly Gln
        915                 920                 925

Pro Gly Glu Lys Gly Ser Pro Gly Ala Gln Gly Pro Pro Gly Ala Pro
    930                 935                 940
```

```
Gly Pro Leu Gly Ile Ala Gly Ile Thr Gly Ala Arg Gly Leu Ala Gly
945                 950                 955                 960

Pro Pro Gly Met Pro Gly Pro Arg Gly Ser Pro Gly Pro Gln Gly Val
                965                 970                 975

Lys Gly Glu Ser Gly Lys Pro Gly Ala Asn Gly Leu Ser Gly Glu Arg
            980                 985                 990

Gly Pro Pro Gly Pro Gln Gly Leu  Pro Gly Leu Ala Gly  Thr Ala Gly
        995                 1000                1005

Glu Pro  Gly Arg Asp Gly Asn  Pro Gly Ser Asp Gly  Leu Pro Gly
    1010                1015                1020

Arg Asp  Gly Ser Pro Gly Gly  Lys Gly Asp Arg Gly  Glu Asn Gly
    1025                1030                1035

Ser Pro  Gly Ala Pro Gly Ala  Pro Gly His Pro Gly  Pro Pro Gly
    1040                1045                1050

Pro Val  Gly Pro Ala Gly Lys  Ser Gly Asp Arg Gly  Glu Ser Gly
    1055                1060                1065

Pro Ala  Gly Pro Ala Gly Ala  Pro Gly Pro Ala Gly  Ser Arg Gly
    1070                1075                1080

Ala Pro  Gly Pro Gln Gly Pro  Arg Gly Asp Lys Gly  Glu Thr Gly
    1085                1090                1095

Glu Arg  Gly Ala Ala Gly Ile  Lys Gly His Arg Gly  Phe Pro Gly
    1100                1105                1110

Asn Pro  Gly Ala Pro Gly Ser  Pro Gly Pro Ala Gly  Gln Gln Gly
    1115                1120                1125

Ala Ile  Gly Ser Pro Gly Pro  Ala Gly Pro Arg Gly  Pro Val Gly
    1130                1135                1140

Pro Ser  Gly Pro Pro Gly Lys  Asp Gly Thr Ser Gly  His Pro Gly
    1145                1150                1155

Pro Ile  Gly Pro Pro Gly Pro  Arg Gly Asn Arg Gly  Glu Arg Gly
    1160                1165                1170

Ser Glu  Gly Ser Pro Gly His  Pro Gly Gln Pro Gly  Pro Pro Gly
    1175                1180                1185

Pro Pro  Gly Ala Pro Gly Pro  Cys Cys Gly Gly Val  Gly Ala Ala
    1190                1195                1200
```

```
Ala Ile  Ala Gly Ile Gly Gly  Glu Lys Ala Gly Gly  Phe Ala Pro
    1205                 1210                 1215

Tyr Tyr  Gly Asp Glu Pro Met  Asp Phe Lys Ile Asn  Thr Asp Glu
    1220                 1225                 1230

Ile Met  Thr Ser Leu Lys Ser  Val Asn Gly Gln Ile  Glu Ser Leu
    1235                 1240                 1245

Ile Ser  Pro Asp Gly Ser Arg  Lys Asn Pro Ala Arg  Asn Cys Arg
    1250                 1255                 1260

Asp Leu  Lys Phe Cys His Pro  Glu Leu Lys Ser Gly  Glu Tyr Trp
    1265                 1270                 1275

Val Asp  Pro Asn Gln Gly Cys  Lys Leu Asp Ala Ile  Lys Val Phe
    1280                 1285                 1290

Cys Asn  Met Glu Thr Gly Glu  Thr Cys Ile Ser Ala  Asn Pro Leu
    1295                 1300                 1305

Asn Val  Pro Arg Lys His Trp  Trp Thr Asp Ser Ser  Ala Glu Lys
    1310                 1315                 1320

Lys His  Val Trp Phe Gly Glu  Ser Met Asp Gly Gly  Phe Gln Phe
    1325                 1330                 1335

Ser Tyr  Gly Asn Pro Glu Leu  Pro Glu Asp Val Leu  Asp Val His
    1340                 1345                 1350

Leu Ala  Phe Leu Arg Leu Leu  Ser Ser Arg Ala Ser  Gln Asn Ile
    1355                 1360                 1365

Thr Tyr  His Cys Lys Asn Ser  Ile Ala Tyr Met Asp  Gln Ala Ser
    1370                 1375                 1380

Gly Asn  Val Lys Lys Ala Leu  Lys Leu Met Gly Ser  Asn Glu Gly
    1385                 1390                 1395

Glu Phe  Lys Ala Glu Gly Asn  Ser Lys Phe Thr Tyr  Thr Val Leu
    1400                 1405                 1410

Glu Asp  Gly Cys Thr Lys His  Thr Gly Glu Trp Ser  Lys Thr Val
    1415                 1420                 1425

Phe Glu  Tyr Arg Thr Arg Lys  Ala Val Arg Leu Pro  Ile Val Asp
    1430                 1435                 1440

Ile Ala  Pro Tyr Asp Ile Gly  Gly Pro Asp Gln Glu  Phe Gly Val
    1445                 1450                 1455
```

```
Asp Val  Gly Pro Val Cys Phe  Leu
    1460                1465


<210>  490
<211>  2944
<212>  PRT
<213>  Homo sapiens

<400>  490

Met Thr Leu Arg Leu Leu Val Ala Ala Leu Cys Ala Gly Ile Leu Ala
1               5                  10                  15


Glu Ala Pro Arg Val Arg Ala Gln His Arg Glu Arg Val Thr Cys Thr
            20                  25                  30


Arg Leu Tyr Ala Ala Asp Ile Val Phe Leu Leu Asp Gly Ser Ser Ser
        35                  40                  45


Ile Gly Arg Ser Asn Phe Arg Glu Val Arg Ser Phe Leu Glu Gly Leu
    50                  55                  60


Val Leu Pro Phe Ser Gly Ala Ala Ser Ala Gln Gly Val Arg Phe Ala
65                  70                  75                  80


Thr Val Gln Tyr Ser Asp Asp Pro Arg Thr Glu Phe Gly Leu Asp Ala
                85                  90                  95


Leu Gly Ser Gly Gly Asp Val Ile Arg Ala Ile Arg Glu Leu Ser Tyr
            100                 105                 110


Lys Gly Gly Asn Thr Arg Thr Gly Ala Ala Ile Leu His Val Ala Asp
        115                 120                 125


His Val Phe Leu Pro Gln Leu Ala Arg Pro Gly Val Pro Lys Val Cys
    130                 135                 140


Ile Leu Ile Thr Asp Gly Lys Ser Gln Asp Leu Val Asp Thr Ala Ala
145                 150                 155                 160


Gln Arg Leu Lys Gly Gln Gly Val Lys Leu Phe Ala Val Gly Ile Lys
                165                 170                 175


Asn Ala Asp Pro Glu Glu Leu Lys Arg Val Ala Ser Gln Pro Thr Ser
            180                 185                 190


Asp Phe Phe Phe Phe Val Asn Asp Phe Ser Ile Leu Arg Thr Leu Leu
        195                 200                 205


Pro Leu Val Ser Arg Arg Val Cys Thr Thr Ala Gly Gly Val Pro Val
    210                 215                 220
```

```
Thr Arg Pro Pro Asp Asp Ser Thr Ser Ala Pro Arg Asp Leu Val Leu
225                 230                 235                 240

Ser Glu Pro Ser Ser Gln Ser Leu Arg Val Gln Trp Thr Ala Ala Ser
                245                 250                 255

Gly Pro Val Thr Gly Tyr Lys Val Gln Tyr Thr Pro Leu Thr Gly Leu
            260                 265                 270

Gly Gln Pro Leu Pro Ser Glu Arg Gln Glu Val Asn Val Pro Ala Gly
        275                 280                 285

Glu Thr Ser Val Arg Leu Arg Gly Leu Arg Pro Leu Thr Glu Tyr Gln
    290                 295                 300

Val Thr Val Ile Ala Leu Tyr Ala Asn Ser Ile Gly Glu Ala Val Ser
305                 310                 315                 320

Gly Thr Ala Arg Thr Thr Ala Leu Glu Gly Pro Glu Leu Thr Ile Gln
                325                 330                 335

Asn Thr Thr Ala His Ser Leu Leu Val Ala Trp Arg Ser Val Pro Gly
            340                 345                 350

Ala Thr Gly Tyr Arg Val Thr Trp Arg Val Leu Ser Gly Gly Pro Thr
        355                 360                 365

Gln Gln Gln Glu Leu Gly Pro Gly Gln Gly Ser Val Leu Leu Arg Asp
    370                 375                 380

Leu Glu Pro Gly Thr Asp Tyr Glu Val Thr Val Ser Thr Leu Phe Gly
385                 390                 395                 400

Arg Ser Val Gly Pro Ala Thr Ser Leu Met Ala Arg Thr Asp Ala Ser
                405                 410                 415

Val Glu Gln Thr Leu Arg Pro Val Ile Leu Gly Pro Thr Ser Ile Leu
            420                 425                 430

Leu Ser Trp Asn Leu Val Pro Glu Ala Arg Gly Tyr Arg Leu Glu Trp
        435                 440                 445

Arg Arg Glu Thr Gly Leu Glu Pro Pro Gln Lys Val Val Leu Pro Ser
    450                 455                 460

Asp Val Thr Arg Tyr Gln Leu Asp Gly Leu Gln Pro Gly Thr Glu Tyr
465                 470                 475                 480

Arg Leu Thr Leu Tyr Thr Leu Leu Glu Gly His Glu Val Ala Thr Pro
                485                 490                 495
```

```
Ala Thr Val Val Pro Thr Gly Pro Glu Leu Pro Val Ser Pro Val Thr
            500                 505                 510

Asp Leu Gln Ala Thr Glu Leu Pro Gly Gln Arg Val Arg Val Ser Trp
        515                 520                 525

Ser Pro Val Pro Gly Ala Thr Gln Tyr Arg Ile Ile Val Arg Ser Thr
    530                 535                 540

Gln Gly Val Glu Arg Thr Leu Val Leu Pro Gly Ser Gln Thr Ala Phe
545                 550                 555                 560

Asp Leu Asp Asp Val Gln Ala Gly Leu Ser Tyr Thr Val Arg Val Ser
                565                 570                 575

Ala Arg Val Gly Pro Arg Glu Gly Ser Ala Ser Val Leu Thr Val Arg
            580                 585                 590

Arg Glu Pro Glu Thr Pro Leu Ala Val Pro Gly Leu Arg Val Val Val
        595                 600                 605

Ser Asp Ala Thr Arg Val Arg Val Ala Trp Gly Pro Val Pro Gly Ala
    610                 615                 620

Ser Gly Phe Arg Ile Ser Trp Ser Thr Gly Ser Gly Pro Glu Ser Ser
625                 630                 635                 640

Gln Thr Leu Pro Pro Asp Ser Thr Ala Thr Asp Ile Thr Gly Leu Gln
                645                 650                 655

Pro Gly Thr Thr Tyr Gln Val Ala Val Ser Val Leu Arg Gly Arg Glu
            660                 665                 670

Glu Gly Pro Ala Ala Val Ile Val Ala Arg Thr Asp Pro Leu Gly Pro
        675                 680                 685

Val Arg Thr Val His Val Thr Gln Ala Ser Ser Ser Ser Val Thr Ile
    690                 695                 700

Thr Trp Thr Arg Val Pro Gly Ala Thr Gly Tyr Arg Val Ser Trp His
705                 710                 715                 720

Ser Ala His Gly Pro Glu Lys Ser Gln Leu Val Ser Gly Glu Ala Thr
                725                 730                 735

Val Ala Glu Leu Asp Gly Leu Glu Pro Asp Thr Glu Tyr Thr Val His
            740                 745                 750

Val Arg Ala His Val Ala Gly Val Asp Gly Pro Pro Ala Ser Val Val
        755                 760                 765
```

```
Val Arg Thr Ala Pro Glu Pro Val Gly Arg Val Ser Arg Leu Gln Ile
    770                 775                 780

Leu Asn Ala Ser Ser Asp Val Leu Arg Ile Thr Trp Val Gly Val Thr
785                 790                 795                 800

Gly Ala Thr Ala Tyr Arg Leu Ala Trp Gly Arg Ser Glu Gly Gly Pro
                805                 810                 815

Met Arg His Gln Ile Leu Pro Gly Asn Thr Asp Ser Ala Glu Ile Arg
            820                 825                 830

Gly Leu Glu Gly Gly Val Ser Tyr Ser Val Arg Val Thr Ala Leu Val
        835                 840                 845

Gly Asp Arg Glu Gly Thr Pro Val Ser Ile Val Val Thr Thr Pro Pro
    850                 855                 860

Glu Ala Pro Pro Ala Leu Gly Thr Leu His Val Val Gln Arg Gly Glu
865                 870                 875                 880

His Ser Leu Arg Leu Arg Trp Glu Pro Val Pro Arg Ala Gln Gly Phe
                885                 890                 895

Leu Leu His Trp Gln Pro Glu Gly Gly Gln Glu Gln Ser Arg Val Leu
            900                 905                 910

Gly Pro Glu Leu Ser Ser Tyr His Leu Asp Gly Leu Glu Pro Ala Thr
        915                 920                 925

Gln Tyr Arg Val Arg Leu Ser Val Leu Gly Pro Ala Gly Glu Gly Pro
    930                 935                 940

Ser Ala Glu Val Thr Ala Arg Thr Glu Ser Pro Arg Val Pro Ser Ile
945                 950                 955                 960

Glu Leu Arg Val Val Asp Thr Ser Ile Asp Ser Val Thr Leu Ala Trp
                965                 970                 975

Thr Pro Val Ser Arg Ala Ser Ser Tyr Ile Leu Ser Trp Arg Pro Leu
            980                 985                 990

Arg Gly Pro Gly Gln Glu Val Pro  Gly Ser Pro Gln Thr  Leu Pro Gly
        995                 1000                1005

Ile Ser  Ser Ser Gln Arg Val  Thr Gly Leu Glu Pro  Gly Val Ser
    1010                1015                1020

Tyr Ile  Phe Ser Leu Thr Pro  Val Leu Asp Gly Val  Arg Gly Pro
    1025                1030                1035
```

```
Glu Ala  Ser Val Thr Gln Thr  Pro Val Cys Pro Arg  Gly Leu Ala
    1040                1045                1050

Asp Val  Val Phe Leu Pro His  Ala Thr Gln Asp Asn  Ala His Arg
    1055                1060                1065

Ala Glu  Ala Thr Arg Arg Val  Leu Glu Arg Leu Val  Leu Ala Leu
    1070                1075                1080

Gly Pro  Leu Gly Pro Gln Ala  Val Gln Val Gly Leu  Leu Ser Tyr
    1085                1090                1095

Ser His  Arg Pro Ser Pro Leu  Phe Pro Leu Asn Gly  Ser His Asp
    1100                1105                1110

Leu Gly  Ile Ile Leu Gln Arg  Ile Arg Asp Met Pro  Tyr Met Asp
    1115                1120                1125

Pro Ser  Gly Asn Asn Leu Gly  Thr Ala Val Val Thr  Ala His Arg
    1130                1135                1140

Tyr Met  Leu Ala Pro Asp Ala  Pro Gly Arg Arg Gln  His Val Pro
    1145                1150                1155

Gly Val  Met Val Leu Leu Val  Asp Glu Pro Leu Arg  Gly Asp Ile
    1160                1165                1170

Phe Ser  Pro Ile Arg Glu Ala  Gln Ala Ser Gly Leu  Asn Val Val
    1175                1180                1185

Met Leu  Gly Met Ala Gly Ala  Asp Pro Glu Gln Leu  Arg Arg Leu
    1190                1195                1200

Ala Pro  Gly Met Asp Ser Val  Gln Thr Phe Phe Ala  Val Asp Asp
    1205                1210                1215

Gly Pro  Ser Leu Asp Gln Ala  Val Ser Gly Leu Ala  Thr Ala Leu
    1220                1225                1230

Cys Gln  Ala Ser Phe Thr Thr  Gln Pro Arg Pro Glu  Pro Cys Pro
    1235                1240                1245

Val Tyr  Cys Pro Lys Gly Gln  Lys Gly Glu Pro Gly  Glu Met Gly
    1250                1255                1260

Leu Arg  Gly Gln Val Gly Pro  Pro Gly Asp Pro Gly  Leu Pro Gly
    1265                1270                1275

Arg Thr  Gly Ala Pro Gly Pro  Gln Gly Pro Pro Gly  Ser Ala Thr
    1280                1285                1290
```

```
Ala Lys  Gly Glu Arg Gly Phe  Pro Gly Ala Asp Gly  Arg Pro Gly
    1295                 1300                 1305

Ser Pro  Gly Arg Ala Gly Asn  Pro Gly Thr Pro Gly  Ala Pro Gly
    1310                 1315                 1320

Leu Lys  Gly Ser Pro Gly Leu  Pro Gly Pro Arg Gly  Asp Pro Gly
    1325                 1330                 1335

Glu Arg  Gly Pro Arg Gly Pro  Lys Gly Glu Pro Gly  Ala Pro Gly
    1340                 1345                 1350

Gln Val  Ile Gly Gly Glu Gly  Pro Gly Leu Pro Gly  Arg Lys Gly
    1355                 1360                 1365

Asp Pro  Gly Pro Ser Gly Pro  Pro Gly Pro Arg Gly  Pro Leu Gly
    1370                 1375                 1380

Asp Pro  Gly Pro Arg Gly Pro  Pro Gly Leu Pro Gly  Thr Ala Met
    1385                 1390                 1395

Lys Gly  Asp Lys Gly Asp Arg  Gly Glu Arg Gly Pro  Pro Gly Pro
    1400                 1405                 1410

Gly Glu  Gly Gly Ile Ala Pro  Gly Glu Pro Gly Leu  Pro Gly Leu
    1415                 1420                 1425

Pro Gly  Ser Pro Gly Pro Gln  Gly Pro Val Gly Pro  Pro Gly Lys
    1430                 1435                 1440

Lys Gly  Glu Lys Gly Asp Ser  Glu Asp Gly Ala Pro  Gly Leu Pro
    1445                 1450                 1455

Gly Gln  Pro Gly Ser Pro Gly  Glu Gln Gly Pro Arg  Gly Pro Pro
    1460                 1465                 1470

Gly Ala  Ile Gly Pro Lys Gly  Asp Arg Gly Phe Pro  Gly Pro Leu
    1475                 1480                 1485

Gly Glu  Ala Gly Glu Lys Gly  Glu Arg Gly Pro Pro  Gly Pro Ala
    1490                 1495                 1500

Gly Ser  Arg Gly Leu Pro Gly  Val Ala Gly Arg Pro  Gly Ala Lys
    1505                 1510                 1515

Gly Pro  Glu Gly Pro Pro Gly  Pro Thr Gly Arg Gln  Gly Glu Lys
    1520                 1525                 1530

Gly Glu  Pro Gly Arg Pro Gly  Asp Pro Ala Val Val  Gly Pro Ala
    1535                 1540                 1545
```

```
Val Ala  Gly Pro Lys Gly Glu  Lys Gly Asp Val Gly  Pro Ala Gly
    1550                 1555                 1560

Pro Arg  Gly Ala Thr Gly Val  Gln Gly Glu Arg Gly  Pro Pro Gly
    1565                 1570                 1575

Leu Val  Leu Pro Gly Asp Pro  Gly Pro Lys Gly Asp  Pro Gly Asp
    1580                 1585                 1590

Arg Gly  Pro Ile Gly Leu Thr  Gly Arg Ala Gly Pro  Pro Gly Asp
    1595                 1600                 1605

Ser Gly  Pro Pro Gly Glu Lys  Gly Asp Pro Gly Arg  Pro Gly Pro
    1610                 1615                 1620

Pro Gly  Pro Val Gly Pro Arg  Gly Arg Asp Gly Glu  Val Gly Glu
    1625                 1630                 1635

Lys Gly  Asp Glu Gly Pro Pro  Gly Asp Pro Gly Leu  Pro Gly Lys
    1640                 1645                 1650

Ala Gly  Glu Arg Gly Leu Arg  Gly Ala Pro Gly Val  Arg Gly Pro
    1655                 1660                 1665

Val Gly  Glu Lys Gly Asp Gln  Gly Asp Pro Gly Glu  Asp Gly Arg
    1670                 1675                 1680

Asn Gly  Ser Pro Gly Ser Ser  Gly Pro Lys Gly Asp  Arg Gly Glu
    1685                 1690                 1695

Pro Gly  Pro Pro Gly Pro Pro  Gly Arg Leu Val Asp  Thr Gly Pro
    1700                 1705                 1710

Gly Ala  Arg Glu Lys Gly Glu  Pro Gly Asp Arg Gly  Gln Glu Gly
    1715                 1720                 1725

Pro Arg  Gly Pro Lys Gly Asp  Pro Gly Leu Pro Gly  Ala Pro Gly
    1730                 1735                 1740

Glu Arg  Gly Ile Glu Gly Phe  Arg Gly Pro Pro Gly  Pro Gln Gly
    1745                 1750                 1755

Asp Pro  Gly Val Arg Gly Pro  Ala Gly Glu Lys Gly  Asp Arg Gly
    1760                 1765                 1770

Pro Pro  Gly Leu Asp Gly Arg  Ser Gly Leu Asp Gly  Lys Pro Gly
    1775                 1780                 1785

Ala Ala  Gly Pro Ser Gly Pro  Asn Gly Ala Ala Gly  Lys Ala Gly
    1790                 1795                 1800
```

```
Asp Pro  Gly Arg Asp Gly Leu  Pro Gly Leu Arg Gly  Glu Gln Gly
    1805                 1810                 1815

Leu Pro  Gly Pro Ser Gly Pro  Pro Gly Leu Pro Gly  Lys Pro Gly
    1820                 1825                 1830

Glu Asp  Gly Lys Pro Gly Leu  Asn Gly Lys Asn Gly  Glu Pro Gly
    1835                 1840                 1845

Asp Pro  Gly Glu Asp Gly Arg  Lys Gly Glu Lys Gly  Asp Ser Gly
    1850                 1855                 1860

Ala Ser  Gly Arg Glu Gly Arg  Asp Gly Pro Lys Gly  Glu Arg Gly
    1865                 1870                 1875

Ala Pro  Gly Ile Leu Gly Pro  Gln Gly Pro Pro Gly  Leu Pro Gly
    1880                 1885                 1890

Pro Val  Gly Pro Pro Gly Gln  Gly Phe Pro Gly Val  Pro Gly Gly
    1895                 1900                 1905

Thr Gly  Pro Lys Gly Asp Arg  Gly Glu Thr Gly Ser  Lys Gly Glu
    1910                 1915                 1920

Gln Gly  Leu Pro Gly Glu Arg  Gly Leu Arg Gly Glu  Pro Gly Ser
    1925                 1930                 1935

Val Pro  Asn Val Asp Arg Leu  Leu Glu Thr Ala Gly  Ile Lys Ala
    1940                 1945                 1950

Ser Ala  Leu Arg Glu Ile Val  Glu Thr Trp Asp Glu  Ser Ser Gly
    1955                 1960                 1965

Ser Phe  Leu Pro Val Pro Glu  Arg Arg Arg Gly Pro  Lys Gly Asp
    1970                 1975                 1980

Ser Gly  Glu Gln Gly Pro Pro  Gly Lys Glu Gly Pro  Ile Gly Phe
    1985                 1990                 1995

Pro Gly  Glu Arg Gly Leu Lys  Gly Asp Arg Gly Asp  Pro Gly Pro
    2000                 2005                 2010

Gln Gly  Pro Pro Gly Leu Ala  Leu Gly Glu Arg Gly  Pro Pro Gly
    2015                 2020                 2025

Pro Ser  Gly Leu Ala Gly Glu  Pro Gly Lys Pro Gly  Ile Pro Gly
    2030                 2035                 2040

Leu Pro  Gly Arg Ala Gly Gly  Val Gly Glu Ala Gly  Arg Pro Gly
    2045                 2050                 2055
```

```
Glu Arg  Gly Glu Arg Gly Glu  Lys Gly Glu Arg Gly  Glu Gln Gly
    2060                 2065                 2070

Arg Asp  Gly Pro Pro Gly Leu  Pro Gly Thr Pro Gly  Pro Pro Gly
    2075                 2080                 2085

Pro Pro  Gly Pro Lys Val Ser  Val Asp Glu Pro Gly  Pro Gly Leu
    2090                 2095                 2100

Ser Gly  Glu Gln Gly Pro Pro  Gly Leu Lys Gly Ala  Lys Gly Glu
    2105                 2110                 2115

Pro Gly  Ser Asn Gly Asp Gln  Gly Pro Lys Gly Asp  Arg Gly Val
    2120                 2125                 2130

Pro Gly  Ile Lys Gly Asp Arg  Gly Glu Pro Gly Pro  Arg Gly Gln
    2135                 2140                 2145

Asp Gly  Asn Pro Gly Leu Pro  Gly Glu Arg Gly Met  Ala Gly Pro
    2150                 2155                 2160

Glu Gly  Lys Pro Gly Leu Gln  Gly Pro Arg Gly Pro  Pro Gly Pro
    2165                 2170                 2175

Val Gly  Gly His Gly Asp Pro  Gly Pro Pro Gly Ala  Pro Gly Leu
    2180                 2185                 2190

Ala Gly  Pro Ala Gly Pro Gln  Gly Pro Ser Gly Leu  Lys Gly Glu
    2195                 2200                 2205

Pro Gly  Glu Thr Gly Pro Pro  Gly Arg Gly Leu Thr  Gly Pro Thr
    2210                 2215                 2220

Gly Ala  Val Gly Leu Pro Gly  Pro Pro Gly Pro Ser  Gly Leu Val
    2225                 2230                 2235

Gly Pro  Gln Gly Ser Pro Gly  Leu Pro Gly Gln Val  Gly Glu Thr
    2240                 2245                 2250

Gly Lys  Pro Gly Ala Pro Gly  Arg Asp Gly Ala Ser  Gly Lys Asp
    2255                 2260                 2265

Gly Asp  Arg Gly Ser Pro Gly  Val Pro Gly Ser Pro  Gly Leu Pro
    2270                 2275                 2280

Gly Pro  Val Gly Pro Lys Gly  Glu Pro Gly Pro Thr  Gly Ala Pro
    2285                 2290                 2295

Gly Gln  Ala Val Val Gly Leu  Pro Gly Ala Lys Gly  Glu Lys Gly
    2300                 2305                 2310
```

```
Ala Pro  Gly Gly Leu Ala Gly  Asp Leu Val Gly Glu  Pro Gly Ala
    2315                 2320                 2325

Lys Gly  Asp Arg Gly Leu Pro  Gly Pro Arg Gly Glu  Lys Gly Glu
    2330                 2335                 2340

Ala Gly  Arg Ala Gly Glu Pro  Gly Asp Pro Gly Glu  Asp Gly Gln
    2345                 2350                 2355

Lys Gly  Ala Pro Gly Pro Lys  Gly Phe Lys Gly Asp  Pro Gly Val
    2360                 2365                 2370

Gly Val  Pro Gly Ser Pro Gly  Pro Pro Gly Pro Pro  Gly Val Lys
    2375                 2380                 2385

Gly Asp  Leu Gly Leu Pro Gly  Leu Pro Gly Ala Pro  Gly Val Val
    2390                 2395                 2400

Gly Phe  Pro Gly Gln Thr Gly  Pro Arg Gly Glu Met  Gly Gln Pro
    2405                 2410                 2415

Gly Pro  Ser Gly Glu Arg Gly  Leu Ala Gly Pro Pro  Gly Arg Glu
    2420                 2425                 2430

Gly Ile  Pro Gly Pro Leu Gly  Pro Pro Gly Pro Pro  Gly Ser Val
    2435                 2440                 2445

Gly Pro  Pro Gly Ala Ser Gly  Leu Lys Gly Asp Lys  Gly Asp Pro
    2450                 2455                 2460

Gly Val  Gly Leu Pro Gly Pro  Arg Gly Glu Arg Gly  Glu Pro Gly
    2465                 2470                 2475

Ile Arg  Gly Glu Asp Gly Arg  Pro Gly Gln Glu Gly  Pro Arg Gly
    2480                 2485                 2490

Leu Thr  Gly Pro Pro Gly Ser  Arg Gly Glu Arg Gly  Glu Lys Gly
    2495                 2500                 2505

Asp Val  Gly Ser Ala Gly Leu  Lys Gly Asp Lys Gly  Asp Ser Ala
    2510                 2515                 2520

Val Ile  Leu Gly Pro Pro Gly  Pro Arg Gly Ala Lys  Gly Asp Met
    2525                 2530                 2535

Gly Glu  Arg Gly Pro Arg Gly  Leu Asp Gly Asp Lys  Gly Pro Arg
    2540                 2545                 2550

Gly Asp  Asn Gly Asp Pro Gly  Asp Lys Gly Ser Lys  Gly Glu Pro
    2555                 2560                 2565
```

```
Gly Asp  Lys Gly Ser Ala Gly  Leu Pro Gly Leu Arg  Gly Leu Leu
    2570                2575                2580

Gly Pro  Gln Gly Gln Pro Gly  Ala Ala Gly Ile Pro  Gly Asp Pro
    2585                2590                2595

Gly Ser  Pro Gly Lys Asp Gly  Val Pro Gly Ile Arg  Gly Glu Lys
    2600                2605                2610

Gly Asp  Val Gly Phe Met Gly  Pro Arg Gly Leu Lys  Gly Glu Arg
    2615                2620                2625

Gly Val  Lys Gly Ala Cys Gly  Leu Asp Gly Glu Lys  Gly Asp Lys
    2630                2635                2640

Gly Glu  Ala Gly Pro Pro Gly  Arg Pro Gly Leu Ala  Gly His Lys
    2645                2650                2655

Gly Glu  Met Gly Glu Pro Gly  Val Pro Gly Gln Ser  Gly Ala Pro
    2660                2665                2670

Gly Lys  Glu Gly Leu Ile Gly  Pro Lys Gly Asp Arg  Gly Phe Asp
    2675                2680                2685

Gly Gln  Pro Gly Pro Lys Gly  Asp Gln Gly Glu Lys  Gly Glu Arg
    2690                2695                2700

Gly Thr  Pro Gly Ile Gly Gly  Phe Pro Gly Pro Ser  Gly Asn Asp
    2705                2710                2715

Gly Ser  Ala Gly Pro Pro Gly  Pro Pro Gly Ser Val  Gly Pro Arg
    2720                2725                2730

Gly Pro  Glu Gly Leu Gln Gly  Gln Lys Gly Glu Arg  Gly Pro Pro
    2735                2740                2745

Gly Glu  Arg Val Val Gly Ala  Pro Gly Val Pro Gly  Ala Pro Gly
    2750                2755                2760

Glu Arg  Gly Glu Gln Gly Arg  Pro Gly Pro Ala Gly  Pro Arg Gly
    2765                2770                2775

Glu Lys  Gly Glu Ala Ala Leu  Thr Glu Asp Asp Ile  Arg Gly Phe
    2780                2785                2790

Val Arg  Gln Glu Met Ser Gln  His Cys Ala Cys Gln  Gly Gln Phe
    2795                2800                2805

Ile Ala  Ser Gly Ser Arg Pro  Leu Pro Ser Tyr Ala  Ala Asp Thr
    2810                2815                2820
```

```
Ala Gly  Ser Gln Leu His Ala  Val Pro Val Leu Arg  Val Ser His
    2825                2830                2835


Ala Glu  Glu Glu Glu Arg Val  Pro Pro Glu Asp Asp  Glu Tyr Ser
    2840                2845                2850


Glu Tyr  Ser Glu Tyr Ser Val  Glu Glu Tyr Gln Asp  Pro Glu Ala
    2855                2860                2865


Pro Trp  Asp Ser Asp Asp Pro  Cys Ser Leu Pro Leu  Asp Glu Gly
    2870                2875                2880


Ser Cys  Thr Ala Tyr Thr Leu  Arg Trp Tyr His Arg  Ala Val Thr
    2885                2890                2895


Gly Ser  Thr Glu Ala Cys His  Pro Phe Val Tyr Gly  Gly Cys Gly
    2900                2905                2910


Gly Asn  Ala Asn Arg Phe Gly  Thr Arg Glu Ala Cys  Glu Arg Arg
    2915                2920                2925


Cys Pro  Pro Arg Val Val Gln  Ser Gln Gly Thr Gly  Thr Ala Gln
    2930                2935                2940


Asp
```

<210> 491
<211> 529
<212> PRT
<213> Homo sapiens

<400> 491

```
Met Leu Leu Ala Val Leu Tyr Cys Leu Leu Trp Ser Phe Gln Thr Ser
1               5                  10                  15


Ala Gly His Phe Pro Arg Ala Cys Val Ser Ser Lys Asn Leu Met Glu
            20                  25                  30


Lys Glu Cys Cys Pro Pro Trp Ser Gly Asp Arg Ser Pro Cys Gly Gln
        35                  40                  45


Leu Ser Gly Arg Gly Ser Cys Gln Asn Ile Leu Leu Ser Asn Ala Pro
    50                  55                  60


Leu Gly Pro Gln Phe Pro Phe Thr Gly Val Asp Asp Arg Glu Ser Trp
65                  70                  75                  80


Pro Ser Val Phe Tyr Asn Arg Thr Cys Gln Cys Ser Gly Asn Phe Met
                85                  90                  95
```

```
Gly Phe Asn Cys Gly Asn Cys Lys Phe Gly Phe Trp Gly Pro Asn Cys
            100                 105                 110

Thr Glu Arg Arg Leu Leu Val Arg Arg Asn Ile Phe Asp Leu Ser Ala
        115                 120                 125

Pro Glu Lys Asp Lys Phe Phe Ala Tyr Leu Thr Leu Ala Lys His Thr
    130                 135                 140

Ile Ser Ser Asp Tyr Val Ile Pro Ile Gly Thr Tyr Gly Gln Met Lys
145                 150                 155                 160

Asn Gly Ser Thr Pro Met Phe Asn Asp Ile Asn Ile Tyr Asp Leu Phe
                165                 170                 175

Val Trp Met His Tyr Tyr Val Ser Met Asp Ala Leu Leu Gly Gly Ser
            180                 185                 190

Glu Ile Trp Arg Asp Ile Asp Phe Ala His Glu Ala Pro Ala Phe Leu
        195                 200                 205

Pro Trp His Arg Leu Phe Leu Leu Arg Trp Glu Gln Glu Ile Gln Lys
    210                 215                 220

Leu Thr Gly Asp Glu Asn Phe Thr Ile Pro Tyr Trp Asp Trp Arg Asp
225                 230                 235                 240

Ala Glu Lys Cys Asp Ile Cys Thr Asp Glu Tyr Met Gly Gly Gln His
                245                 250                 255

Pro Thr Asn Pro Asn Leu Leu Ser Pro Ala Ser Phe Phe Ser Ser Trp
            260                 265                 270

Gln Ile Val Cys Ser Arg Leu Glu Glu Tyr Asn Ser His Gln Ser Leu
        275                 280                 285

Cys Asn Gly Thr Pro Glu Gly Pro Leu Arg Arg Asn Pro Gly Asn His
    290                 295                 300

Asp Lys Ser Arg Thr Pro Arg Leu Pro Ser Ser Ala Asp Val Glu Phe
305                 310                 315                 320

Cys Leu Ser Leu Thr Gln Tyr Glu Ser Gly Ser Met Asp Lys Ala Ala
                325                 330                 335

Asn Phe Ser Phe Arg Asn Thr Leu Glu Gly Phe Ala Ser Pro Leu Thr
            340                 345                 350

Gly Ile Ala Asp Ala Ser Gln Ser Ser Met His Asn Ala Leu His Ile
        355                 360                 365
```

```
Tyr Met Asn Gly Thr Met Ser Gln Val Gln Gly Ser Ala Asn Asp Pro
    370                 375                 380

Ile Phe Leu Leu His His Ala Phe Val Asp Ser Ile Phe Glu Gln Trp
385                 390                 395                 400

Leu Arg Arg His Arg Pro Leu Gln Glu Val Tyr Pro Glu Ala Asn Ala
                405                 410                 415

Pro Ile Gly His Asn Arg Glu Ser Tyr Met Val Pro Phe Ile Pro Leu
            420                 425                 430

Tyr Arg Asn Gly Asp Phe Phe Ile Ser Ser Lys Asp Leu Gly Tyr Asp
        435                 440                 445

Tyr Ser Tyr Leu Gln Asp Ser Asp Pro Asp Ser Phe Gln Asp Tyr Ile
    450                 455                 460

Lys Ser Tyr Leu Glu Gln Ala Ser Arg Ile Trp Ser Trp Leu Leu Gly
465                 470                 475                 480

Ala Ala Met Val Gly Ala Val Leu Thr Ala Leu Leu Ala Gly Leu Val
                485                 490                 495

Ser Leu Leu Cys Arg His Lys Arg Lys Gln Leu Pro Glu Glu Lys Gln
            500                 505                 510

Pro Leu Leu Met Glu Lys Glu Asp Tyr His Ser Leu Tyr Gln Ser His
        515                 520                 525

Leu
```

<210> 492
<211> 1669
<212> PRT
<213> Homo sapiens

<400> 492

```
Met Gly Pro Arg Leu Ser Val Trp Leu Leu Leu Leu Pro Ala Ala Leu
1               5                   10                  15

Leu Leu His Glu Glu His Ser Arg Ala Ala Ala Lys Gly Gly Cys Ala
            20                  25                  30

Gly Ser Gly Cys Gly Lys Cys Asp Cys His Gly Val Lys Gly Gln Lys
        35                  40                  45

Gly Glu Arg Gly Leu Pro Gly Leu Gln Gly Val Ile Gly Phe Pro Gly
    50                  55                  60

Met Gln Gly Pro Glu Gly Pro Gln Gly Pro Pro Gly Gln Lys Gly Asp
```

65 70 75 80

Thr Gly Glu Pro Gly Leu Pro Gly Thr Lys Gly Thr Arg Gly Pro Pro
85 90 95

Gly Ala Ser Gly Tyr Pro Gly Asn Pro Gly Leu Pro Gly Ile Pro Gly
100 105 110

Gln Asp Gly Pro Pro Gly Pro Pro Gly Ile Pro Gly Cys Asn Gly Thr
115 120 125

Lys Gly Glu Arg Gly Pro Leu Gly Pro Pro Gly Leu Pro Gly Phe Ala
130 135 140

Gly Asn Pro Gly Pro Pro Gly Leu Pro Gly Met Lys Gly Asp Pro Gly
145 150 155 160

Glu Ile Leu Gly His Val Pro Gly Met Leu Leu Lys Gly Glu Arg Gly
165 170 175

Phe Pro Gly Ile Pro Gly Thr Pro Gly Pro Pro Gly Leu Pro Gly Leu
180 185 190

Gln Gly Pro Val Gly Pro Pro Gly Phe Thr Gly Pro Pro Gly Pro Pro
195 200 205

Gly Pro Pro Gly Pro Pro Gly Glu Lys Gly Gln Met Gly Leu Ser Phe
210 215 220

Gln Gly Pro Lys Gly Asp Lys Gly Asp Gln Gly Val Ser Gly Pro Pro
225 230 235 240

Gly Val Pro Gly Gln Ala Gln Val Gln Glu Lys Gly Asp Phe Ala Thr
245 250 255

Lys Gly Glu Lys Gly Gln Lys Gly Glu Pro Gly Phe Gln Gly Met Pro
260 265 270

Gly Val Gly Glu Lys Gly Glu Pro Gly Lys Pro Gly Pro Arg Gly Lys
275 280 285

Pro Gly Lys Asp Gly Asp Lys Gly Glu Lys Gly Ser Pro Gly Phe Pro
290 295 300

Gly Glu Pro Gly Tyr Pro Gly Leu Ile Gly Arg Gln Gly Pro Gln Gly
305 310 315 320

Glu Lys Gly Glu Ala Gly Pro Pro Gly Pro Pro Gly Ile Val Ile Gly
325 330 335

Thr Gly Pro Leu Gly Glu Lys Gly Glu Arg Gly Tyr Pro Gly Thr Pro

```
            340                 345                 350

Gly Pro Arg Gly Glu Pro Gly Pro Lys Gly Phe Pro Gly Leu Pro Gly
        355                 360                 365

Gln Pro Gly Pro Pro Gly Leu Pro Val Pro Gly Gln Ala Gly Ala Pro
    370                 375                 380

Gly Phe Pro Gly Glu Arg Gly Glu Lys Gly Asp Arg Gly Phe Pro Gly
385                 390                 395                 400

Thr Ser Leu Pro Gly Pro Ser Gly Arg Asp Gly Leu Pro Gly Pro Pro
                405                 410                 415

Gly Ser Pro Gly Pro Pro Gly Gln Pro Gly Tyr Thr Asn Gly Ile Val
            420                 425                 430

Glu Cys Gln Pro Gly Pro Pro Gly Asp Gln Gly Pro Pro Gly Ile Pro
        435                 440                 445

Gly Gln Pro Gly Phe Ile Gly Glu Ile Gly Glu Lys Gly Gln Lys Gly
    450                 455                 460

Glu Ser Cys Leu Ile Cys Asp Ile Asp Gly Tyr Arg Gly Pro Pro Gly
465                 470                 475                 480

Pro Gln Gly Pro Pro Gly Glu Ile Gly Phe Pro Gly Gln Pro Gly Ala
                485                 490                 495

Lys Gly Asp Arg Gly Leu Pro Gly Arg Asp Gly Val Ala Gly Val Pro
            500                 505                 510

Gly Pro Gln Gly Thr Pro Gly Leu Ile Gly Gln Pro Gly Ala Lys Gly
        515                 520                 525

Glu Pro Gly Glu Phe Tyr Phe Asp Leu Arg Leu Lys Gly Asp Lys Gly
    530                 535                 540

Asp Pro Gly Phe Pro Gly Gln Pro Gly Met Thr Gly Arg Ala Gly Ser
545                 550                 555                 560

Pro Gly Arg Asp Gly His Pro Gly Leu Pro Gly Pro Lys Gly Ser Pro
                565                 570                 575

Gly Ser Val Gly Leu Lys Gly Glu Arg Gly Pro Pro Gly Gly Val Gly
            580                 585                 590

Phe Pro Gly Ser Arg Gly Asp Thr Gly Pro Pro Gly Pro Pro Gly Tyr
        595                 600                 605

Gly Pro Ala Gly Pro Ile Gly Asp Lys Gly Gln Ala Gly Phe Pro Gly
```

610 615 620

Gly Pro Gly Ser Pro Gly Leu Pro Gly Pro Lys Gly Glu Pro Gly Lys
625 630 635 640

Ile Val Pro Leu Pro Gly Pro Pro Gly Ala Glu Gly Leu Pro Gly Ser
645 650 655

Pro Gly Phe Pro Gly Pro Gln Gly Asp Arg Gly Phe Pro Gly Thr Pro
660 665 670

Gly Arg Pro Gly Leu Pro Gly Glu Lys Gly Ala Val Gly Gln Pro Gly
675 680 685

Ile Gly Phe Pro Gly Pro Pro Gly Pro Lys Gly Val Asp Gly Leu Pro
690 695 700

Gly Asp Met Gly Pro Pro Gly Thr Pro Gly Arg Pro Gly Phe Asn Gly
705 710 715 720

Leu Pro Gly Asn Pro Gly Val Gln Gly Gln Lys Gly Glu Pro Gly Val
725 730 735

Gly Leu Pro Gly Leu Lys Gly Leu Pro Gly Leu Pro Gly Ile Pro Gly
740 745 750

Thr Pro Gly Glu Lys Gly Ser Ile Gly Val Pro Gly Val Pro Gly Glu
755 760 765

His Gly Ala Ile Gly Pro Pro Gly Leu Gln Gly Ile Arg Gly Glu Pro
770 775 780

Gly Pro Pro Gly Leu Pro Gly Ser Val Gly Ser Pro Gly Val Pro Gly
785 790 795 800

Ile Gly Pro Pro Gly Ala Arg Gly Pro Pro Gly Gly Gln Gly Pro Pro
805 810 815

Gly Leu Ser Gly Pro Pro Gly Ile Lys Gly Glu Lys Gly Phe Pro Gly
820 825 830

Phe Pro Gly Leu Asp Met Pro Gly Pro Lys Gly Asp Lys Gly Ala Gln
835 840 845

Gly Leu Pro Gly Ile Thr Gly Gln Ser Gly Leu Pro Gly Leu Pro Gly
850 855 860

Gln Gln Gly Ala Pro Gly Ile Pro Gly Phe Pro Gly Ser Lys Gly Glu
865 870 875 880

Met Gly Val Met Gly Thr Pro Gly Gln Pro Gly Ser Pro Gly Pro Val

885 890 895

Gly Ala Pro Gly Leu Pro Gly Glu Lys Gly Asp His Gly Phe Pro Gly
900 905 910

Ser Ser Gly Pro Arg Gly Asp Pro Gly Leu Lys Gly Asp Lys Gly Asp
915 920 925

Val Gly Leu Pro Gly Lys Pro Gly Ser Met Asp Lys Val Asp Met Gly
930 935 940

Ser Met Lys Gly Gln Lys Gly Asp Gln Gly Glu Lys Gly Gln Ile Gly
945 950 955 960

Pro Ile Gly Glu Lys Gly Ser Arg Gly Asp Pro Gly Thr Pro Gly Val
965 970 975

Pro Gly Lys Asp Gly Gln Ala Gly Gln Pro Gly Gln Pro Gly Pro Lys
980 985 990

Gly Asp Pro Gly Ile Ser Gly Thr Pro Gly Ala Pro Gly Leu Pro Gly
995 1000 1005

Pro Lys Gly Ser Val Gly Gly Met Gly Leu Pro Gly Thr Pro Gly
1010 1015 1020

Glu Lys Gly Val Pro Gly Ile Pro Gly Pro Gln Gly Ser Pro Gly
1025 1030 1035

Leu Pro Gly Asp Lys Gly Ala Lys Gly Glu Lys Gly Gln Ala Gly
1040 1045 1050

Pro Pro Gly Ile Gly Ile Pro Gly Leu Arg Gly Glu Lys Gly Asp
1055 1060 1065

Gln Gly Ile Ala Gly Phe Pro Gly Ser Pro Gly Glu Lys Gly Glu
1070 1075 1080

Lys Gly Ser Ile Gly Ile Pro Gly Met Pro Gly Ser Pro Gly Leu
1085 1090 1095

Lys Gly Ser Pro Gly Ser Val Gly Tyr Pro Gly Ser Pro Gly Leu
1100 1105 1110

Pro Gly Glu Lys Gly Asp Lys Gly Leu Pro Gly Leu Asp Gly Ile
1115 1120 1125

Pro Gly Val Lys Gly Glu Ala Gly Leu Pro Gly Thr Pro Gly Pro
1130 1135 1140

Thr Gly Pro Ala Gly Gln Lys Gly Glu Pro Gly Ser Asp Gly Ile

```
    1145                1150                1155

Pro Gly  Ser Ala Gly Glu Lys  Gly Glu Pro Gly Leu  Pro Gly Arg
    1160                1165                1170

Gly Phe  Pro Gly Phe Pro Gly  Ala Lys Gly Asp Lys  Gly Ser Lys
    1175                1180                1185

Gly Glu  Val Gly Phe Pro Gly  Leu Ala Gly Ser Pro  Gly Ile Pro
    1190                1195                1200

Gly Ser  Lys Gly Glu Gln Gly  Phe Met Gly Pro Pro  Gly Pro Gln
    1205                1210                1215

Gly Gln  Pro Gly Leu Pro Gly  Ser Pro Gly His Ala  Thr Glu Gly
    1220                1225                1230

Pro Lys  Gly Asp Arg Gly Pro  Gln Gly Gln Pro Gly  Leu Pro Gly
    1235                1240                1245

Leu Pro  Gly Pro Met Gly Pro  Pro Gly Leu Pro Gly  Ile Asp Gly
    1250                1255                1260

Val Lys  Gly Asp Lys Gly Asn  Pro Gly Trp Pro Gly  Ala Pro Gly
    1265                1270                1275

Val Pro  Gly Pro Lys Gly Asp  Pro Gly Phe Gln Gly  Met Pro Gly
    1280                1285                1290

Ile Gly  Gly Ser Pro Gly Ile  Thr Gly Ser Lys Gly  Asp Met Gly
    1295                1300                1305

Pro Pro  Gly Val Pro Gly Phe  Gln Gly Pro Lys Gly  Leu Pro Gly
    1310                1315                1320

Leu Gln  Gly Ile Lys Gly Asp  Gln Gly Asp Gln Gly  Val Pro Gly
    1325                1330                1335

Ala Lys  Gly Leu Pro Gly Pro  Pro Gly Pro Pro Gly  Pro Tyr Asp
    1340                1345                1350

Ile Ile  Lys Gly Glu Pro Gly  Leu Pro Gly Pro Glu  Gly Pro Pro
    1355                1360                1365

Gly Leu  Lys Gly Leu Gln Gly  Leu Pro Gly Pro Lys  Gly Gln Gln
    1370                1375                1380

Gly Val  Thr Gly Leu Val Gly  Ile Pro Gly Pro Pro  Gly Ile Pro
    1385                1390                1395

Gly Phe  Asp Gly Ala Pro Gly  Gln Lys Gly Glu Met  Gly Pro Ala
```

1400 1405 1410

Gly Pro Thr Gly Pro Arg Gly Phe Pro Gly Pro Pro Gly Pro Asp
1415 1420 1425

Gly Leu Pro Gly Ser Met Gly Pro Pro Gly Thr Pro Ser Val Asp
1430 1435 1440

His Gly Phe Leu Val Thr Arg His Ser Gln Thr Ile Asp Asp Pro
1445 1450 1455

Gln Cys Pro Ser Gly Thr Lys Ile Leu Tyr His Gly Tyr Ser Leu
1460 1465 1470

Leu Tyr Val Gln Gly Asn Glu Arg Ala His Gly Gln Asp Leu Gly
1475 1480 1485

Thr Ala Gly Ser Cys Leu Arg Lys Phe Ser Thr Met Pro Phe Leu
1490 1495 1500

Phe Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn Asp
1505 1510 1515

Tyr Ser Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser Met
1520 1525 1530

Ala Pro Ile Thr Gly Glu Asn Ile Arg Pro Phe Ile Ser Arg Cys
1535 1540 1545

Ala Val Cys Glu Ala Pro Ala Met Val Met Ala Val His Ser Gln
1550 1555 1560

Thr Ile Gln Ile Pro Pro Cys Pro Ser Gly Trp Ser Ser Leu Trp
1565 1570 1575

Ile Gly Tyr Ser Phe Val Met His Thr Ser Ala Gly Ala Glu Gly
1580 1585 1590

Ser Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu Glu Glu Phe
1595 1600 1605

Arg Ser Ala Pro Phe Ile Glu Cys His Gly Arg Gly Thr Cys Asn
1610 1615 1620

Tyr Tyr Ala Asn Ala Tyr Ser Phe Trp Leu Ala Thr Ile Glu Arg
1625 1630 1635

Ser Glu Met Phe Lys Lys Pro Thr Pro Ser Thr Leu Lys Ala Gly
1640 1645 1650

Glu Leu Arg Thr His Val Ser Arg Cys Gln Val Cys Met Arg Arg

1655 1660 1665

Thr

<210> 493
<211> 1712
<212> PRT
<213> Homo sapiens

<400> 493

Met Gly Arg Asp Gln Arg Ala Val Ala Gly Pro Ala Leu Arg Arg Trp
1 5 10 15

Leu Leu Leu Gly Thr Val Thr Val Gly Phe Leu Ala Gln Ser Val Leu
20 25 30

Ala Gly Val Lys Lys Phe Asp Val Pro Cys Gly Gly Arg Asp Cys Ser
35 40 45

Gly Gly Cys Gln Cys Tyr Pro Glu Lys Gly Gly Arg Gly Gln Pro Gly
50 55 60

Pro Val Gly Pro Gln Gly Tyr Asn Gly Pro Pro Gly Leu Gln Gly Phe
65 70 75 80

Pro Gly Leu Gln Gly Arg Lys Gly Asp Lys Gly Glu Arg Gly Ala Pro
85 90 95

Gly Val Thr Gly Pro Lys Gly Asp Val Gly Ala Arg Gly Val Ser Gly
100 105 110

Phe Pro Gly Ala Asp Gly Ile Pro Gly His Pro Gly Gln Gly Gly Pro
115 120 125

Arg Gly Arg Pro Gly Tyr Asp Gly Cys Asn Gly Thr Gln Gly Asp Ser
130 135 140

Gly Pro Gln Gly Pro Pro Gly Ser Glu Gly Phe Thr Gly Pro Pro Gly
145 150 155 160

Pro Gln Gly Pro Lys Gly Gln Lys Gly Glu Pro Tyr Ala Leu Pro Lys
165 170 175

Glu Glu Arg Asp Arg Tyr Arg Gly Glu Pro Gly Glu Pro Gly Leu Val
180 185 190

Gly Phe Gln Gly Pro Pro Gly Arg Pro Gly His Val Gly Gln Met Gly
195 200 205

Pro Val Gly Ala Pro Gly Arg Pro Gly Pro Pro Gly Pro Pro Gly Pro
210 215 220

```
Lys Gly Gln Gln Gly Asn Arg Gly Leu Gly Phe Tyr Gly Val Lys Gly
225                 230                 235                 240

Glu Lys Gly Asp Val Gly Gln Pro Gly Pro Asn Gly Ile Pro Ser Asp
                245                 250                 255

Thr Leu His Pro Ile Ile Ala Pro Thr Gly Val Thr Phe His Pro Asp
            260                 265                 270

Gln Tyr Lys Gly Glu Lys Gly Ser Glu Gly Glu Pro Gly Ile Arg Gly
        275                 280                 285

Ile Ser Leu Lys Gly Glu Glu Gly Ile Met Gly Phe Pro Gly Leu Arg
    290                 295                 300

Gly Tyr Pro Gly Leu Ser Gly Glu Lys Gly Ser Pro Gly Gln Lys Gly
305                 310                 315                 320

Ser Arg Gly Leu Asp Gly Tyr Gln Gly Pro Asp Gly Pro Arg Gly Pro
                325                 330                 335

Lys Gly Glu Ala Gly Asp Pro Gly Pro Pro Gly Leu Pro Ala Tyr Ser
            340                 345                 350

Pro His Pro Ser Leu Ala Lys Gly Ala Arg Gly Asp Pro Gly Phe Pro
        355                 360                 365

Gly Ala Gln Gly Glu Pro Gly Ser Gln Gly Glu Pro Gly Asp Pro Gly
    370                 375                 380

Leu Pro Gly Pro Pro Gly Leu Ser Ile Gly Asp Gly Asp Gln Arg Arg
385                 390                 395                 400

Gly Leu Pro Gly Glu Met Gly Pro Lys Gly Phe Ile Gly Asp Pro Gly
                405                 410                 415

Ile Pro Ala Leu Tyr Gly Gly Pro Pro Gly Pro Asp Gly Lys Arg Gly
            420                 425                 430

Pro Pro Gly Pro Pro Gly Leu Pro Gly Pro Pro Gly Pro Asp Gly Phe
        435                 440                 445

Leu Phe Gly Leu Lys Gly Ala Lys Gly Arg Ala Gly Phe Pro Gly Leu
    450                 455                 460

Pro Gly Ser Pro Gly Ala Arg Gly Pro Lys Gly Trp Lys Gly Asp Ala
465                 470                 475                 480

Gly Glu Cys Arg Cys Thr Glu Gly Asp Glu Ala Ile Lys Gly Leu Pro
                485                 490                 495
```

```
Gly Leu Pro Gly Pro Lys Gly Phe Ala Gly Ile Asn Gly Glu Pro Gly
            500                 505                 510

Arg Lys Gly Asp Arg Gly Asp Pro Gly Gln His Gly Leu Pro Gly Phe
        515                 520                 525

Pro Gly Leu Lys Gly Val Pro Gly Asn Ile Gly Ala Pro Gly Pro Lys
    530                 535                 540

Gly Ala Lys Gly Asp Ser Arg Thr Ile Thr Thr Lys Gly Glu Arg Gly
545                 550                 555                 560

Gln Pro Gly Val Pro Gly Val Pro Gly Met Lys Gly Asp Asp Gly Ser
                565                 570                 575

Pro Gly Arg Asp Gly Leu Asp Gly Phe Pro Gly Leu Pro Gly Pro Pro
            580                 585                 590

Gly Asp Gly Ile Lys Gly Pro Pro Gly Asp Pro Gly Tyr Pro Gly Ile
        595                 600                 605

Pro Gly Thr Lys Gly Thr Pro Gly Glu Met Gly Pro Pro Gly Leu Gly
    610                 615                 620

Leu Pro Gly Leu Lys Gly Gln Arg Gly Phe Pro Gly Asp Ala Gly Leu
625                 630                 635                 640

Pro Gly Pro Pro Gly Phe Leu Gly Pro Pro Gly Pro Ala Gly Thr Pro
                645                 650                 655

Gly Gln Ile Asp Cys Asp Thr Asp Val Lys Arg Ala Val Gly Gly Asp
            660                 665                 670

Arg Gln Glu Ala Ile Gln Pro Gly Cys Ile Gly Gly Pro Lys Gly Leu
        675                 680                 685

Pro Gly Leu Pro Gly Pro Pro Gly Pro Thr Gly Ala Lys Gly Leu Arg
    690                 695                 700

Gly Ile Pro Gly Phe Ala Gly Ala Asp Gly Gly Pro Gly Pro Arg Gly
705                 710                 715                 720

Leu Pro Gly Asp Ala Gly Arg Glu Gly Phe Pro Gly Pro Pro Gly Phe
                725                 730                 735

Ile Gly Pro Arg Gly Ser Lys Gly Ala Val Gly Leu Pro Gly Pro Asp
            740                 745                 750

Gly Ser Pro Gly Pro Ile Gly Leu Pro Gly Pro Asp Gly Pro Pro Gly
        755                 760                 765
```

```
Glu Arg Gly Leu Pro Gly Glu Val Leu Gly Ala Gln Pro Gly Pro Arg
    770                 775                 780

Gly Asp Ala Gly Val Pro Gly Gln Pro Gly Leu Lys Gly Leu Pro Gly
785                 790                 795                 800

Asp Arg Gly Pro Pro Gly Phe Arg Gly Ser Gln Gly Met Pro Gly Met
                805                 810                 815

Pro Gly Leu Lys Gly Gln Pro Gly Leu Pro Gly Pro Ser Gly Gln Pro
            820                 825                 830

Gly Leu Tyr Gly Pro Pro Gly Leu His Gly Phe Pro Gly Ala Pro Gly
        835                 840                 845

Gln Glu Gly Pro Leu Gly Leu Pro Gly Ile Pro Gly Arg Glu Gly Leu
    850                 855                 860

Pro Gly Asp Arg Gly Asp Pro Gly Asp Thr Gly Ala Pro Gly Pro Val
865                 870                 875                 880

Gly Met Lys Gly Leu Ser Gly Asp Arg Gly Asp Ala Gly Phe Thr Gly
                885                 890                 895

Glu Gln Gly His Pro Gly Ser Pro Gly Phe Lys Gly Ile Asp Gly Met
            900                 905                 910

Pro Gly Thr Pro Gly Leu Lys Gly Asp Arg Gly Ser Pro Gly Met Asp
        915                 920                 925

Gly Phe Gln Gly Met Pro Gly Leu Lys Gly Arg Pro Gly Phe Pro Gly
    930                 935                 940

Ser Lys Gly Glu Ala Gly Phe Phe Gly Ile Pro Gly Leu Lys Gly Leu
945                 950                 955                 960

Ala Gly Glu Pro Gly Phe Lys Gly Ser Arg Gly Asp Pro Gly Pro Pro
                965                 970                 975

Gly Pro Pro Pro Val Ile Leu Pro Gly Met Lys Asp Ile Lys Gly Glu
            980                 985                 990

Lys Gly Asp Glu Gly Pro Met Gly  Leu Lys Gly Tyr Leu  Gly Ala Lys
        995                 1000                1005

Gly Ile  Gln Gly Met Pro Gly  Ile Pro Gly Leu Ser  Gly Ile Pro
    1010                1015                1020

Gly Leu  Pro Gly Arg Pro Gly  His Ile Lys Gly Val  Lys Gly Asp
    1025                1030                1035
```

```
Ile Gly  Val Pro Gly Ile Pro  Gly Leu Pro Gly Phe  Pro Gly Val
    1040                1045                1050

Ala Gly  Pro Pro Gly Ile Thr  Gly Phe Pro Gly Phe  Ile Gly Ser
    1055                1060                1065

Arg Gly  Asp Lys Gly Ala Pro  Gly Arg Ala Gly Leu  Tyr Gly Glu
    1070                1075                1080

Ile Gly  Ala Thr Gly Asp Phe  Gly Asp Ile Gly Asp  Thr Ile Asn
    1085                1090                1095

Leu Pro  Gly Arg Pro Gly Leu  Lys Gly Glu Arg Gly  Thr Thr Gly
    1100                1105                1110

Ile Pro  Gly Leu Lys Gly Phe  Phe Gly Glu Lys Gly  Thr Glu Gly
    1115                1120                1125

Asp Ile  Gly Phe Pro Gly Ile  Thr Gly Val Thr Gly  Val Gln Gly
    1130                1135                1140

Pro Pro  Gly Leu Lys Gly Gln  Thr Gly Phe Pro Gly  Leu Thr Gly
    1145                1150                1155

Pro Pro  Gly Ser Gln Gly Glu  Leu Gly Arg Ile Gly  Leu Pro Gly
    1160                1165                1170

Gly Lys  Gly Asp Asp Gly Trp  Pro Gly Ala Pro Gly  Leu Pro Gly
    1175                1180                1185

Phe Pro  Gly Leu Arg Gly Ile  Arg Gly Leu His Gly  Leu Pro Gly
    1190                1195                1200

Thr Lys  Gly Phe Pro Gly Ser  Pro Gly Ser Asp Ile  His Gly Asp
    1205                1210                1215

Pro Gly  Phe Pro Gly Pro Pro  Gly Glu Arg Gly Asp  Pro Gly Glu
    1220                1225                1230

Ala Asn  Thr Leu Pro Gly Pro  Val Gly Val Pro Gly  Gln Lys Gly
    1235                1240                1245

Asp Gln  Gly Ala Pro Gly Glu  Arg Gly Pro Pro Gly  Ser Pro Gly
    1250                1255                1260

Leu Gln  Gly Phe Pro Gly Ile  Thr Pro Pro Ser Asn  Ile Ser Gly
    1265                1270                1275

Ala Pro  Gly Asp Lys Gly Ala  Pro Gly Ile Phe Gly  Leu Lys Gly
    1280                1285                1290
```

```
Tyr Arg  Gly Pro Pro Gly Pro  Pro Gly Ser Ala Ala  Leu Pro Gly
    1295                 1300                 1305

Ser Lys  Gly Asp Thr Gly Asn  Pro Gly Ala Pro Gly  Thr Pro Gly
    1310                 1315                 1320

Thr Lys  Gly Trp Ala Gly Asp  Ser Gly Pro Gln Gly  Arg Pro Gly
    1325                 1330                 1335

Val Phe  Gly Leu Pro Gly Glu  Lys Gly Pro Arg Gly  Glu Gln Gly
    1340                 1345                 1350

Phe Met  Gly Asn Thr Gly Pro  Thr Gly Ala Val Gly  Asp Arg Gly
    1355                 1360                 1365

Pro Lys  Gly Pro Lys Gly Asp  Pro Gly Phe Pro Gly  Ala Pro Gly
    1370                 1375                 1380

Thr Val  Gly Ala Pro Gly Ile  Ala Gly Ile Pro Gln  Lys Ile Ala
    1385                 1390                 1395

Val Gln  Pro Gly Thr Val Gly  Pro Gln Gly Arg Arg  Gly Pro Pro
    1400                 1405                 1410

Gly Ala  Pro Gly Glu Met Gly  Pro Gln Gly Pro Pro  Gly Glu Pro
    1415                 1420                 1425

Gly Phe  Arg Gly Ala Pro Gly  Lys Ala Gly Pro Gln  Gly Arg Gly
    1430                 1435                 1440

Gly Val  Ser Ala Val Pro Gly  Phe Arg Gly Asp Glu  Gly Pro Ile
    1445                 1450                 1455

Gly His  Gln Gly Pro Ile Gly  Gln Glu Gly Ala Pro  Gly Arg Pro
    1460                 1465                 1470

Gly Ser  Pro Gly Leu Pro Gly  Met Pro Gly Arg Ser  Val Ser Ile
    1475                 1480                 1485

Gly Tyr  Leu Leu Val Lys His  Ser Gln Thr Asp Gln  Glu Pro Met
    1490                 1495                 1500

Cys Pro  Val Gly Met Asn Lys  Leu Trp Ser Gly Tyr  Ser Leu Leu
    1505                 1510                 1515

Tyr Phe  Glu Gly Gln Glu Lys  Ala His Asn Gln Asp  Leu Gly Leu
    1520                 1525                 1530

Ala Gly  Ser Cys Leu Ala Arg  Phe Ser Thr Met Pro  Phe Leu Tyr
    1535                 1540                 1545
```

```
Cys Asn  Pro Gly Asp Val Cys  Tyr Tyr Ala Ser Arg  Asn Asp Lys
    1550                 1555                 1560

Ser Tyr  Trp Leu Ser Thr Thr  Ala Pro Leu Pro Met  Met Pro Val
    1565                 1570                 1575

Ala Glu  Asp Glu Ile Lys Pro  Tyr Ile Ser Arg Cys  Ser Val Cys
    1580                 1585                 1590

Glu Ala  Pro Ala Ile Ala Ile  Ala Val His Ser Gln  Asp Val Ser
    1595                 1600                 1605

Ile Pro  His Cys Pro Ala Gly  Trp Arg Ser Leu Trp  Ile Gly Tyr
    1610                 1615                 1620

Ser Phe  Leu Met His Thr Ala  Ala Gly Asp Glu Gly  Gly Gly Gln
    1625                 1630                 1635

Ser Leu  Val Ser Pro Gly Ser  Cys Leu Glu Asp Phe  Arg Ala Thr
    1640                 1645                 1650

Pro Phe  Ile Glu Cys Asn Gly  Gly Arg Gly Thr Cys  His Tyr Tyr
    1655                 1660                 1665

Ala Asn  Lys Tyr Ser Phe Trp  Leu Thr Thr Ile Pro  Glu Gln Ser
    1670                 1675                 1680

Phe Gln  Gly Ser Pro Ser Ala  Asp Thr Leu Lys Ala  Gly Leu Ile
    1685                 1690                 1695

Arg Thr  His Ile Ser Arg Cys  Gln Val Cys Met Lys  Asn Leu
    1700                 1705                 1710


<210>  494
<211>  1670
<212>  PRT
<213>  Homo sapiens

<400>  494

Met Ser Ala Arg Thr Ala Pro Arg Pro Gln Val Leu Leu Leu Pro Leu
1               5                  10                  15

Leu Leu Val Leu Leu Ala Ala Ala Pro Ala Ala Ser Lys Gly Cys Val
            20                  25                  30

Cys Lys Asp Lys Gly Gln Cys Phe Cys Asp Gly Ala Lys Gly Glu Lys
        35                  40                  45

Gly Glu Lys Gly Phe Pro Gly Pro Pro Gly Ser Pro Gly Gln Lys Gly
    50                  55                  60
```

```
Phe Thr Gly Pro Glu Gly Leu Pro Gly Pro Gln Gly Pro Lys Gly Phe
65                  70                  75                  80

Pro Gly Leu Pro Gly Leu Thr Gly Ser Lys Gly Val Arg Gly Ile Ser
                85                  90                  95

Gly Leu Pro Gly Phe Ser Gly Ser Pro Gly Leu Pro Gly Thr Pro Gly
            100                 105                 110

Asn Thr Gly Pro Tyr Gly Leu Val Gly Val Pro Gly Cys Ser Gly Ser
        115                 120                 125

Lys Gly Glu Gln Gly Phe Pro Gly Leu Pro Gly Thr Leu Gly Tyr Pro
    130                 135                 140

Gly Ile Pro Gly Ala Ala Gly Leu Lys Gly Gln Lys Gly Ala Pro Ala
145                 150                 155                 160

Lys Glu Glu Asp Ile Glu Leu Asp Ala Lys Gly Asp Pro Gly Leu Pro
                165                 170                 175

Gly Ala Pro Gly Pro Gln Gly Leu Pro Gly Pro Pro Gly Phe Pro Gly
            180                 185                 190

Pro Val Gly Pro Pro Gly Pro Pro Gly Phe Phe Gly Phe Pro Gly Ala
        195                 200                 205

Met Gly Pro Arg Gly Pro Lys Gly His Met Gly Glu Arg Val Ile Gly
    210                 215                 220

His Lys Gly Glu Arg Gly Val Lys Gly Leu Thr Gly Pro Pro Gly Pro
225                 230                 235                 240

Pro Gly Thr Val Ile Val Thr Leu Thr Gly Pro Asp Asn Arg Thr Asp
                245                 250                 255

Leu Lys Gly Glu Lys Gly Asp Lys Gly Ala Met Gly Glu Pro Gly Pro
            260                 265                 270

Pro Gly Pro Ser Gly Leu Pro Gly Glu Ser Tyr Gly Ser Glu Lys Gly
        275                 280                 285

Ala Pro Gly Asp Pro Gly Leu Gln Gly Lys Pro Gly Lys Asp Gly Val
    290                 295                 300

Pro Gly Phe Pro Gly Ser Glu Gly Val Lys Gly Asn Arg Gly Phe Pro
305                 310                 315                 320

Gly Leu Met Gly Glu Asp Gly Ile Lys Gly Gln Lys Gly Asp Ile Gly
                325                 330                 335
```

```
Pro Pro Gly Phe Arg Gly Pro Thr Glu Tyr Tyr Asp Thr Tyr Gln Glu
            340                 345                 350

Lys Gly Asp Glu Gly Thr Pro Gly Pro Pro Gly Pro Arg Gly Ala Arg
        355                 360                 365

Gly Pro Gln Gly Pro Ser Gly Pro Pro Gly Val Pro Gly Ser Pro Gly
    370                 375                 380

Ser Ser Arg Pro Gly Leu Arg Gly Ala Pro Gly Trp Pro Gly Leu Lys
385                 390                 395                 400

Gly Ser Lys Gly Glu Arg Gly Arg Pro Gly Lys Asp Ala Met Gly Thr
                405                 410                 415

Pro Gly Ser Pro Gly Cys Ala Gly Ser Pro Gly Leu Pro Gly Ser Pro
            420                 425                 430

Gly Pro Pro Gly Pro Pro Gly Asp Ile Val Phe Arg Lys Gly Pro Pro
        435                 440                 445

Gly Asp His Gly Leu Pro Gly Tyr Leu Gly Ser Pro Gly Ile Pro Gly
    450                 455                 460

Val Asp Gly Pro Lys Gly Glu Pro Gly Leu Leu Cys Thr Gln Cys Pro
465                 470                 475                 480

Tyr Ile Pro Gly Pro Pro Gly Leu Pro Gly Leu Pro Gly Leu His Gly
                485                 490                 495

Val Lys Gly Ile Pro Gly Arg Gln Gly Ala Ala Gly Leu Lys Gly Ser
            500                 505                 510

Pro Gly Ser Pro Gly Asn Thr Gly Leu Pro Gly Phe Pro Gly Phe Pro
        515                 520                 525

Gly Ala Gln Gly Asp Pro Gly Leu Lys Gly Glu Lys Gly Glu Thr Leu
    530                 535                 540

Gln Pro Glu Gly Gln Val Gly Val Pro Gly Asp Pro Gly Leu Arg Gly
545                 550                 555                 560

Gln Pro Gly Arg Lys Gly Leu Asp Gly Ile Pro Gly Thr Pro Gly Val
                565                 570                 575

Lys Gly Leu Pro Gly Pro Lys Gly Glu Leu Ala Leu Ser Gly Glu Lys
            580                 585                 590

Gly Asp Gln Gly Pro Pro Gly Asp Pro Gly Ser Pro Gly Ser Pro Gly
        595                 600                 605
```

```
Pro Ala Gly Pro Ala Gly Pro Pro Gly Tyr Gly Pro Gln Gly Glu Pro
    610                 615                 620

Gly Leu Gln Gly Thr Gln Gly Val Pro Gly Ala Pro Gly Pro Pro Gly
625                 630                 635                 640

Glu Ala Gly Pro Arg Gly Glu Leu Ser Val Ser Thr Pro Val Pro Gly
                645                 650                 655

Pro Pro Gly Pro Pro Gly Pro Pro Gly His Pro Gly Pro Gln Gly Pro
            660                 665                 670

Pro Gly Ile Pro Gly Ser Leu Gly Lys Cys Gly Asp Pro Gly Leu Pro
        675                 680                 685

Gly Pro Asp Gly Glu Pro Gly Ile Pro Gly Ile Gly Phe Pro Gly Pro
    690                 695                 700

Pro Gly Pro Lys Gly Asp Gln Gly Phe Pro Gly Thr Lys Gly Ser Leu
705                 710                 715                 720

Gly Cys Pro Gly Lys Met Gly Glu Pro Gly Leu Pro Gly Lys Pro Gly
                725                 730                 735

Leu Pro Gly Ala Lys Gly Glu Pro Ala Val Ala Met Pro Gly Gly Pro
            740                 745                 750

Gly Thr Pro Gly Phe Pro Gly Glu Arg Gly Asn Ser Gly Glu His Gly
        755                 760                 765

Glu Ile Gly Leu Pro Gly Leu Pro Gly Leu Pro Gly Thr Pro Gly Asn
    770                 775                 780

Glu Gly Leu Asp Gly Pro Arg Gly Asp Pro Gly Gln Pro Gly Pro Pro
785                 790                 795                 800

Gly Glu Gln Gly Pro Pro Gly Arg Cys Ile Glu Gly Pro Arg Gly Ala
                805                 810                 815

Gln Gly Leu Pro Gly Leu Asn Gly Leu Lys Gly Gln Gln Gly Arg Arg
            820                 825                 830

Gly Lys Thr Gly Pro Lys Gly Asp Pro Gly Ile Pro Gly Leu Asp Arg
        835                 840                 845

Ser Gly Phe Pro Gly Glu Thr Gly Ser Pro Gly Ile Pro Gly His Gln
    850                 855                 860

Gly Glu Met Gly Pro Leu Gly Gln Arg Gly Tyr Pro Gly Asn Pro Gly
865                 870                 875                 880
```

```
Ile Leu Gly Pro Pro Gly Glu Asp Gly Val Ile Gly Met Met Gly Phe
                885                 890                 895

Pro Gly Ala Ile Gly Pro Pro Gly Pro Pro Gly Asn Pro Gly Thr Pro
            900                 905                 910

Gly Gln Arg Gly Ser Pro Gly Ile Pro Gly Val Lys Gly Gln Arg Gly
        915                 920                 925

Thr Pro Gly Ala Lys Gly Glu Gln Gly Asp Lys Gly Asn Pro Gly Pro
    930                 935                 940

Ser Glu Ile Ser His Val Ile Gly Asp Lys Gly Glu Pro Gly Leu Lys
945                 950                 955                 960

Gly Phe Ala Gly Asn Pro Gly Glu Lys Gly Asn Arg Gly Val Pro Gly
                965                 970                 975

Met Pro Gly Leu Lys Gly Leu Lys Gly Leu Pro Gly Pro Ala Gly Pro
            980                 985                 990

Pro Gly Pro Arg Gly Asp Leu Gly  Ser Thr Gly Asn Pro  Gly Glu Pro
        995                 1000                1005

Gly Leu  Arg Gly Ile Pro Gly  Ser Met Gly Asn Met  Gly Met Pro
    1010                1015                1020

Gly Ser  Lys Gly Lys Arg Gly  Thr Leu Gly Phe Pro  Gly Arg Ala
    1025                1030                1035

Gly Arg  Pro Gly Leu Pro Gly  Ile His Gly Leu Gln  Gly Asp Lys
    1040                1045                1050

Gly Glu  Pro Gly Tyr Ser Glu  Gly Thr Arg Pro Gly  Pro Pro Gly
    1055                1060                1065

Pro Thr  Gly Asp Pro Gly Leu  Pro Gly Asp Met Gly  Lys Lys Gly
    1070                1075                1080

Glu Met  Gly Gln Pro Gly Pro  Pro Gly His Leu Gly  Pro Ala Gly
    1085                1090                1095

Pro Glu  Gly Ala Pro Gly Ser  Pro Gly Ser Pro Gly  Leu Pro Gly
    1100                1105                1110

Lys Pro  Gly Pro His Gly Asp  Leu Gly Phe Lys Gly  Ile Lys Gly
    1115                1120                1125

Leu Leu  Gly Pro Pro Gly Ile  Arg Gly Pro Pro Gly  Leu Pro Gly
    1130                1135                1140
```

```
Phe Pro  Gly Ser Pro Gly Pro  Met Gly Ile Arg Gly  Asp Gln Gly
    1145                1150                1155

Arg Asp  Gly Ile Pro Gly Pro  Ala Gly Glu Lys Gly  Glu Thr Gly
    1160                1165                1170

Leu Leu  Arg Ala Pro Pro Gly  Pro Arg Gly Asn Pro  Gly Ala Gln
    1175                1180                1185

Gly Ala  Lys Gly Asp Arg Gly  Ala Pro Gly Phe Pro  Gly Leu Pro
    1190                1195                1200

Gly Arg  Lys Gly Ala Met Gly  Asp Ala Gly Pro Arg  Gly Pro Thr
    1205                1210                1215

Gly Ile  Glu Gly Phe Pro Gly  Pro Pro Gly Leu Pro  Gly Ala Ile
    1220                1225                1230

Ile Pro  Gly Gln Thr Gly Asn  Arg Gly Pro Pro Gly  Ser Arg Gly
    1235                1240                1245

Ser Pro  Gly Ala Pro Gly Pro  Pro Gly Pro Pro Gly  Ser His Val
    1250                1255                1260

Ile Gly  Ile Lys Gly Asp Lys  Gly Ser Met Gly His  Pro Gly Pro
    1265                1270                1275

Lys Gly  Pro Pro Gly Thr Ala  Gly Asp Met Gly Pro  Pro Gly Arg
    1280                1285                1290

Leu Gly  Ala Pro Gly Thr Pro  Gly Leu Pro Gly Pro  Arg Gly Asp
    1295                1300                1305

Pro Gly  Phe Gln Gly Phe Pro  Gly Val Lys Gly Glu  Lys Gly Asn
    1310                1315                1320

Pro Gly  Phe Leu Gly Ser Ile  Gly Pro Pro Gly Pro  Ile Gly Pro
    1325                1330                1335

Lys Gly  Pro Pro Gly Val Arg  Gly Asp Pro Gly Thr  Leu Lys Ile
    1340                1345                1350

Ile Ser  Leu Pro Gly Ser Pro  Gly Pro Pro Gly Thr  Pro Gly Glu
    1355                1360                1365

Pro Gly  Met Gln Gly Glu Pro  Gly Pro Pro Gly Pro  Pro Gly Asn
    1370                1375                1380

Leu Gly  Pro Cys Gly Pro Arg  Gly Lys Pro Gly Lys  Asp Gly Lys
    1385                1390                1395
```

```
Pro Gly  Thr Pro Gly Pro Ala  Gly Glu Lys Gly Asn  Lys Gly Ser
    1400                 1405                 1410

Lys Gly  Glu Pro Gly Pro Ala  Gly Ser Asp Gly Leu  Pro Gly Leu
    1415                 1420                 1425

Lys Gly  Lys Arg Gly Asp Ser  Gly Ser Pro Ala Thr  Trp Thr Thr
    1430                 1435                 1440

Arg Gly  Phe Val Phe Thr Arg  His Ser Gln Thr Thr  Ala Ile Pro
    1445                 1450                 1455

Ser Cys  Pro Glu Gly Thr Val  Pro Leu Tyr Ser Gly  Phe Ser Phe
    1460                 1465                 1470

Leu Phe  Val Gln Gly Asn Gln  Arg Ala His Gly Gln  Asp Leu Gly
    1475                 1480                 1485

Thr Leu  Gly Ser Cys Leu Gln  Arg Phe Thr Thr Met  Pro Phe Leu
    1490                 1495                 1500

Phe Cys  Asn Val Asn Asp Val  Cys Asn Phe Ala Ser  Arg Asn Asp
    1505                 1510                 1515

Tyr Ser  Tyr Trp Leu Ser Thr  Pro Ala Leu Met Pro  Met Asn Met
    1520                 1525                 1530

Ala Pro  Ile Thr Gly Arg Ala  Leu Glu Pro Tyr Ile  Ser Arg Cys
    1535                 1540                 1545

Thr Val  Cys Glu Gly Pro Ala  Ile Ala Ile Ala Val  His Ser Gln
    1550                 1555                 1560

Thr Thr  Asp Ile Pro Pro Cys  Pro His Gly Trp Ile  Ser Leu Trp
    1565                 1570                 1575

Lys Gly  Phe Ser Phe Ile Met  Phe Thr Ser Ala Gly  Ser Glu Gly
    1580                 1585                 1590

Thr Gly  Gln Ala Leu Ala Ser  Pro Gly Ser Cys Leu  Glu Glu Phe
    1595                 1600                 1605

Arg Ala  Ser Pro Phe Leu Glu  Cys His Gly Arg Gly  Thr Cys Asn
    1610                 1615                 1620

Tyr Tyr  Ser Asn Ser Tyr Ser  Phe Trp Leu Ala Ser  Leu Asn Pro
    1625                 1630                 1635

Glu Arg  Met Phe Arg Lys Pro  Ile Pro Ser Thr Val  Lys Ala Gly
    1640                 1645                 1650
```

```
Glu Leu  Glu Lys Ile Ile Ser  Arg Cys Gln Val Cys  Met Lys Lys
    1655                 1660                 1665


Arg His
    1670


<210>  495
<211>  1690
<212>  PRT
<213>  Homo sapiens

<400>  495

Met Trp Ser Leu His Ile Val Leu Met Arg Cys Ser Phe Arg Leu Thr
1               5                   10                  15


Lys Ser Leu Ala Thr Gly Pro Trp Ser Leu Ile Leu Ile Leu Phe Ser
            20                  25                  30


Val Gln Tyr Val Tyr Gly Ser Gly Lys Lys Tyr Ile Gly Pro Cys Gly
        35                  40                  45


Gly Arg Asp Cys Ser Val Cys His Cys Val Pro Glu Lys Gly Ser Arg
    50                  55                  60


Gly Pro Pro Gly Pro Pro Gly Pro Gln Gly Pro Ile Gly Pro Leu Gly
65                  70                  75                  80


Ala Pro Gly Pro Ile Gly Leu Ser Gly Glu Lys Gly Met Arg Gly Asp
                85                  90                  95


Arg Gly Pro Pro Gly Ala Ala Gly Asp Lys Gly Asp Lys Gly Pro Thr
            100                 105                 110


Gly Val Pro Gly Phe Pro Gly Leu Asp Gly Ile Pro Gly His Pro Gly
        115                 120                 125


Pro Pro Gly Pro Arg Gly Lys Pro Gly Met Ser Gly His Asn Gly Ser
    130                 135                 140


Arg Gly Asp Pro Gly Phe Pro Gly Gly Arg Gly Ala Leu Gly Pro Gly
145                 150                 155                 160


Gly Pro Leu Gly His Pro Gly Glu Lys Gly Glu Lys Gly Asn Ser Val
                165                 170                 175


Phe Ile Leu Gly Ala Val Lys Gly Ile Gln Gly Asp Arg Gly Asp Pro
            180                 185                 190


Gly Leu Pro Gly Leu Pro Gly Ser Trp Gly Ala Gly Gly Pro Ala Gly
        195                 200                 205
```

```
Pro Thr Gly Tyr Pro Gly Glu Pro Gly Leu Val Gly Pro Pro Gly Gln
    210                 215                 220

Pro Gly Arg Pro Gly Leu Lys Gly Asn Pro Gly Val Gly Val Lys Gly
225                 230                 235                 240

Gln Met Gly Asp Pro Gly Glu Val Gly Gln Gln Gly Ser Pro Gly Pro
                245                 250                 255

Thr Leu Leu Val Glu Pro Pro Asp Phe Cys Leu Tyr Lys Gly Glu Lys
            260                 265                 270

Gly Ile Lys Gly Ile Pro Gly Met Val Gly Leu Pro Gly Pro Pro Gly
        275                 280                 285

Arg Lys Gly Glu Ser Gly Ile Gly Ala Lys Gly Glu Lys Gly Ile Pro
    290                 295                 300

Gly Phe Pro Gly Pro Arg Gly Asp Pro Gly Ser Tyr Gly Ser Pro Gly
305                 310                 315                 320

Phe Pro Gly Leu Lys Gly Glu Leu Gly Leu Val Gly Asp Pro Gly Leu
                325                 330                 335

Phe Gly Leu Ile Gly Pro Lys Gly Asp Pro Gly Asn Arg Gly His Pro
            340                 345                 350

Gly Pro Pro Gly Val Leu Val Thr Pro Pro Leu Pro Leu Lys Gly Pro
        355                 360                 365

Pro Gly Asp Pro Gly Phe Pro Gly Arg Tyr Gly Glu Thr Gly Asp Val
    370                 375                 380

Gly Pro Pro Gly Pro Pro Gly Leu Leu Gly Arg Pro Gly Glu Ala Cys
385                 390                 395                 400

Ala Gly Met Ile Gly Pro Pro Gly Pro Gln Gly Phe Pro Gly Leu Pro
                405                 410                 415

Gly Leu Pro Gly Glu Ala Gly Ile Pro Gly Arg Pro Asp Ser Ala Pro
            420                 425                 430

Gly Lys Pro Gly Lys Pro Gly Ser Pro Gly Leu Pro Gly Ala Pro Gly
        435                 440                 445

Leu Gln Gly Leu Pro Gly Ser Ser Val Ile Tyr Cys Ser Val Gly Asn
    450                 455                 460

Pro Gly Pro Gln Gly Ile Lys Gly Lys Val Gly Pro Pro Gly Gly Arg
465                 470                 475                 480
```

```
Gly Pro Lys Gly Glu Lys Gly Asn Glu Gly Leu Cys Ala Cys Glu Pro
                485                 490                 495

Gly Pro Met Gly Pro Pro Gly Pro Pro Gly Leu Pro Gly Arg Gln Gly
            500                 505                 510

Ser Lys Gly Asp Leu Gly Leu Pro Gly Trp Leu Gly Thr Lys Gly Asp
        515                 520                 525

Pro Gly Pro Pro Gly Ala Glu Gly Pro Pro Gly Leu Pro Gly Lys His
    530                 535                 540

Gly Ala Ser Gly Pro Pro Gly Asn Lys Gly Ala Lys Gly Asp Met Val
545                 550                 555                 560

Val Ser Arg Val Lys Gly His Lys Gly Glu Arg Gly Pro Asp Gly Pro
                565                 570                 575

Pro Gly Phe Pro Gly Gln Pro Gly Ser His Gly Arg Asp Gly His Ala
            580                 585                 590

Gly Glu Lys Gly Asp Pro Gly Pro Pro Gly Asp His Glu Asp Ala Thr
        595                 600                 605

Pro Gly Gly Lys Gly Phe Pro Gly Pro Leu Gly Pro Pro Gly Lys Ala
    610                 615                 620

Gly Pro Val Gly Pro Pro Gly Leu Gly Phe Pro Gly Pro Pro Gly Glu
625                 630                 635                 640

Arg Gly His Pro Gly Val Pro Gly His Pro Gly Val Arg Gly Pro Asp
                645                 650                 655

Gly Leu Lys Gly Gln Lys Gly Asp Thr Ile Ser Cys Asn Val Thr Tyr
            660                 665                 670

Pro Gly Arg His Gly Pro Pro Gly Phe Asp Gly Pro Pro Gly Pro Lys
        675                 680                 685

Gly Phe Pro Gly Pro Gln Gly Ala Pro Gly Leu Ser Gly Ser Asp Gly
    690                 695                 700

His Lys Gly Arg Pro Gly Thr Pro Gly Thr Ala Glu Ile Pro Gly Pro
705                 710                 715                 720

Pro Gly Phe Arg Gly Asp Met Gly Asp Pro Gly Phe Gly Gly Glu Lys
                725                 730                 735

Gly Ser Ser Pro Val Gly Pro Pro Gly Pro Pro Gly Ser Pro Gly Val
            740                 745                 750
```

```
Asn Gly Gln Lys Gly Ile Pro Gly Asp Pro Ala Phe Gly His Leu Gly
        755                 760                 765

Pro Pro Gly Lys Arg Gly Leu Ser Gly Val Pro Gly Ile Lys Gly Pro
    770                 775                 780

Arg Gly Asp Pro Gly Cys Pro Gly Ala Glu Gly Pro Ala Gly Ile Pro
785                 790                 795                 800

Gly Phe Leu Gly Leu Lys Gly Pro Lys Gly Arg Glu Gly His Ala Gly
                805                 810                 815

Phe Pro Gly Val Pro Gly Pro Pro Gly His Ser Cys Glu Arg Gly Ala
            820                 825                 830

Pro Gly Ile Pro Gly Gln Pro Gly Leu Pro Gly Tyr Pro Gly Ser Pro
        835                 840                 845

Gly Ala Pro Gly Gly Lys Gly Gln Pro Gly Asp Val Gly Pro Pro Gly
    850                 855                 860

Pro Ala Gly Met Lys Gly Leu Pro Gly Leu Pro Gly Arg Pro Gly Ala
865                 870                 875                 880

His Gly Pro Pro Gly Leu Pro Gly Ile Pro Gly Pro Phe Gly Asp Asp
                885                 890                 895

Gly Leu Pro Gly Pro Pro Gly Pro Lys Gly Pro Arg Gly Leu Pro Gly
            900                 905                 910

Phe Pro Gly Phe Pro Gly Glu Arg Gly Lys Pro Gly Ala Glu Gly Cys
        915                 920                 925

Pro Gly Ala Lys Gly Glu Pro Gly Glu Lys Gly Met Ser Gly Leu Pro
    930                 935                 940

Gly Asp Arg Gly Leu Arg Gly Ala Lys Gly Ala Ile Gly Pro Pro Gly
945                 950                 955                 960

Asp Glu Gly Glu Met Ala Ile Ile Ser Gln Lys Gly Thr Pro Gly Glu
                965                 970                 975

Pro Gly Pro Pro Gly Asp Asp Gly Phe Pro Gly Glu Arg Gly Asp Lys
            980                 985                 990

Gly Thr Pro Gly Met Gln Gly Arg  Arg Gly Glu Pro Gly  Arg Tyr Gly
        995                 1000                1005

Pro Pro  Gly Phe His Arg Gly  Glu Pro Gly Glu Lys  Gly Gln Pro
    1010                1015                1020
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Gly Pro  Pro Gly Pro Pro Gly  Pro Pro Gly Ser Thr  Gly Leu Arg
    1025                1030                1035

Gly Phe  Ile Gly Phe Pro Gly  Leu Pro Gly Asp Gln  Gly Glu Pro
    1040                1045                1050

Gly Ser  Pro Gly Pro Pro Gly  Phe Ser Gly Ile Asp  Gly Ala Arg
    1055                1060                1065

Gly Pro  Lys Gly Asn Lys Gly  Asp Pro Ala Ser His  Phe Gly Pro
    1070                1075                1080

Pro Gly  Pro Lys Gly Glu Pro  Gly Ser Pro Gly Cys  Pro Gly His
    1085                1090                1095

Phe Gly  Ala Ser Gly Glu Gln  Gly Leu Pro Gly Ile  Gln Gly Pro
    1100                1105                1110

Arg Gly  Ser Pro Gly Arg Pro  Gly Pro Pro Gly Ser  Ser Gly Pro
    1115                1120                1125

Pro Gly  Cys Pro Gly Asp His  Gly Met Pro Gly Leu  Arg Gly Gln
    1130                1135                1140

Pro Gly  Glu Met Gly Asp Pro  Gly Pro Arg Gly Leu  Gln Gly Asp
    1145                1150                1155

Pro Gly  Ile Pro Gly Pro Pro  Gly Ile Lys Gly Pro  Ser Gly Ser
    1160                1165                1170

Pro Gly  Leu Asn Gly Leu His  Gly Leu Lys Gly Gln  Lys Gly Thr
    1175                1180                1185

Lys Gly  Ala Ser Gly Leu His  Asp Val Gly Pro Pro  Gly Pro Val
    1190                1195                1200

Gly Ile  Pro Gly Leu Lys Gly  Glu Arg Gly Asp Pro  Gly Ser Pro
    1205                1210                1215

Gly Ile  Ser Pro Pro Gly Pro  Arg Gly Lys Lys Gly  Pro Pro Gly
    1220                1225                1230

Pro Pro  Gly Ser Ser Gly Pro  Pro Gly Pro Ala Gly  Ala Thr Gly
    1235                1240                1245

Arg Ala  Pro Lys Asp Ile Pro  Asp Pro Gly Pro Pro  Gly Asp Gln
    1250                1255                1260

Gly Pro  Pro Gly Pro Asp Gly  Pro Arg Gly Ala Pro  Gly Pro Pro
    1265                1270                1275
```

```
Gly Leu  Pro Gly Ser Val Asp  Leu Leu Arg Gly Glu  Pro Gly Asp
    1280                 1285                 1290

Cys Gly  Leu Pro Gly Pro Pro  Gly Pro Pro Gly Pro  Pro Gly Pro
    1295                 1300                 1305

Pro Gly  Tyr Lys Gly Phe Pro  Gly Cys Asp Gly Lys  Asp Gly Gln
    1310                 1315                 1320

Lys Gly  Pro Val Gly Phe Pro  Gly Pro Gln Gly Pro  His Gly Phe
    1325                 1330                 1335

Pro Gly  Pro Pro Gly Glu Lys  Gly Leu Pro Gly Pro  Pro Gly Arg
    1340                 1345                 1350

Lys Gly  Pro Thr Gly Leu Pro  Gly Pro Arg Gly Glu  Pro Gly Pro
    1355                 1360                 1365

Pro Ala  Asp Val Asp Asp Cys  Pro Arg Ile Pro Gly  Leu Pro Gly
    1370                 1375                 1380

Ala Pro  Gly Met Arg Gly Pro  Glu Gly Ala Met Gly  Leu Pro Gly
    1385                 1390                 1395

Met Arg  Gly Pro Ser Gly Pro  Gly Cys Lys Gly Glu  Pro Gly Leu
    1400                 1405                 1410

Asp Gly  Arg Arg Gly Val Asp  Gly Val Pro Gly Ser  Pro Gly Pro
    1415                 1420                 1425

Pro Gly  Arg Lys Gly Asp Thr  Gly Glu Asp Gly Tyr  Pro Gly Gly
    1430                 1435                 1440

Pro Gly  Pro Pro Gly Pro Ile  Gly Asp Pro Gly Pro  Lys Gly Phe
    1445                 1450                 1455

Gly Pro  Gly Tyr Leu Gly Gly  Phe Leu Leu Val Leu  His Ser Gln
    1460                 1465                 1470

Thr Asp  Gln Glu Pro Thr Cys  Pro Leu Gly Met Pro  Arg Leu Trp
    1475                 1480                 1485

Thr Gly  Tyr Ser Leu Leu Tyr  Leu Glu Gly Gln Glu  Lys Ala His
    1490                 1495                 1500

Asn Gln  Asp Leu Gly Leu Ala  Gly Ser Cys Leu Pro  Val Phe Ser
    1505                 1510                 1515

Thr Leu  Pro Phe Ala Tyr Cys  Asn Ile His Gln Val  Cys His Tyr
    1520                 1525                 1530
```

Ala Gln Arg Asn Asp Arg Ser Tyr Trp Leu Ala Ser Ala Ala Pro
1535 1540 1545

Leu Pro Met Met Pro Leu Ser Glu Glu Ala Ile Arg Pro Tyr Val
1550 1555 1560

Ser Arg Cys Ala Val Cys Glu Ala Pro Ala Gln Ala Val Ala Val
1565 1570 1575

His Ser Gln Asp Gln Ser Ile Pro Pro Cys Pro Gln Thr Trp Arg
1580 1585 1590

Ser Leu Trp Ile Gly Tyr Ser Phe Leu Met His Thr Gly Ala Gly
1595 1600 1605

Asp Gln Gly Gly Gly Gln Ala Leu Met Ser Pro Gly Ser Cys Leu
1610 1615 1620

Glu Asp Phe Arg Ala Ala Pro Phe Leu Glu Cys Gln Gly Arg Gln
1625 1630 1635

Gly Thr Cys His Phe Phe Ala Asn Lys Tyr Ser Phe Trp Leu Thr
1640 1645 1650

Thr Val Lys Ala Asp Leu Gln Phe Ser Ser Ala Pro Ala Pro Asp
1655 1660 1665

Thr Leu Lys Glu Ser Gln Ala Gln Arg Gln Lys Ile Ser Arg Cys
1670 1675 1680

Gln Val Cys Val Lys Tyr Ser
1685 1690

<210> 496
<211> 1685
<212> PRT
<213> Homo sapiens

<400> 496

Met Lys Leu Arg Gly Val Ser Leu Ala Ala Gly Leu Phe Leu Leu Ala
1 5 10 15

Leu Ser Leu Trp Gly Gln Pro Ala Glu Ala Ala Ala Cys Tyr Gly Cys
20 25 30

Ser Pro Gly Ser Lys Cys Asp Cys Ser Gly Ile Lys Gly Glu Lys Gly
35 40 45

Glu Arg Gly Phe Pro Gly Leu Glu Gly His Pro Gly Leu Pro Gly Phe
50 55 60

Pro Gly Pro Glu Gly Pro Pro Gly Pro Arg Gly Gln Lys Gly Asp Asp

65 70 75 80

Gly Ile Pro Gly Pro Pro Gly Pro Lys Gly Ile Arg Gly Pro Pro Gly
85 90 95

Leu Pro Gly Phe Pro Gly Thr Pro Gly Leu Pro Gly Met Pro Gly His
100 105 110

Asp Gly Ala Pro Gly Pro Gln Gly Ile Pro Gly Cys Asn Gly Thr Lys
115 120 125

Gly Glu Arg Gly Phe Pro Gly Ser Pro Gly Phe Pro Gly Leu Gln Gly
130 135 140

Pro Pro Gly Pro Pro Gly Ile Pro Gly Met Lys Gly Glu Pro Gly Ser
145 150 155 160

Ile Ile Met Ser Ser Leu Pro Gly Pro Lys Gly Asn Pro Gly Tyr Pro
165 170 175

Gly Pro Pro Gly Ile Gln Gly Leu Pro Gly Pro Thr Gly Ile Pro Gly
180 185 190

Pro Ile Gly Pro Pro Gly Pro Pro Gly Leu Met Gly Pro Pro Gly Pro
195 200 205

Pro Gly Leu Pro Gly Pro Lys Gly Asn Met Gly Leu Asn Phe Gln Gly
210 215 220

Pro Lys Gly Glu Lys Gly Glu Gln Gly Leu Gln Gly Pro Pro Gly Pro
225 230 235 240

Pro Gly Gln Ile Ser Glu Gln Lys Arg Pro Ile Asp Val Glu Phe Gln
245 250 255

Lys Gly Asp Gln Gly Leu Pro Gly Asp Arg Gly Pro Pro Gly Pro Pro
260 265 270

Gly Ile Arg Gly Pro Pro Gly Pro Pro Gly Gly Glu Lys Gly Glu Lys
275 280 285

Gly Glu Gln Gly Glu Pro Gly Lys Arg Gly Lys Pro Gly Lys Asp Gly
290 295 300

Glu Asn Gly Gln Pro Gly Ile Pro Gly Leu Pro Gly Asp Pro Gly Tyr
305 310 315 320

Pro Gly Glu Pro Gly Arg Asp Gly Glu Lys Gly Gln Lys Gly Asp Thr
325 330 335

Gly Pro Pro Gly Pro Pro Gly Leu Val Ile Pro Arg Pro Gly Thr Gly

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            340                 345                 350

Ile Thr Ile Gly Glu Lys Gly Asn Ile Gly Leu Pro Gly Leu Pro Gly
        355                 360                 365

Glu Lys Gly Glu Arg Gly Phe Pro Gly Ile Gln Gly Pro Pro Gly Leu
    370                 375                 380

Pro Gly Pro Pro Gly Ala Ala Val Met Gly Pro Pro Gly Pro Pro Gly
385                 390                 395                 400

Phe Pro Gly Glu Arg Gly Gln Lys Gly Asp Glu Gly Pro Pro Gly Ile
                405                 410                 415

Ser Ile Pro Gly Pro Pro Gly Leu Asp Gly Gln Pro Gly Ala Pro Gly
            420                 425                 430

Leu Pro Gly Pro Pro Gly Pro Ala Gly Pro His Ile Pro Pro Ser Asp
        435                 440                 445

Glu Ile Cys Glu Pro Gly Pro Pro Gly Pro Pro Gly Ser Pro Gly Asp
    450                 455                 460

Lys Gly Leu Gln Gly Glu Gln Gly Val Lys Gly Asp Lys Gly Asp Thr
465                 470                 475                 480

Cys Phe Asn Cys Ile Gly Thr Gly Ile Ser Gly Pro Pro Gly Gln Pro
                485                 490                 495

Gly Leu Pro Gly Leu Pro Gly Pro Pro Gly Ser Leu Gly Phe Pro Gly
            500                 505                 510

Gln Lys Gly Glu Lys Gly Gln Ala Gly Ala Thr Gly Pro Lys Gly Leu
        515                 520                 525

Pro Gly Ile Pro Gly Ala Pro Gly Ala Pro Gly Phe Pro Gly Ser Lys
    530                 535                 540

Gly Glu Pro Gly Asp Ile Leu Thr Phe Pro Gly Met Lys Gly Asp Lys
545                 550                 555                 560

Gly Glu Leu Gly Ser Pro Gly Ala Pro Gly Leu Pro Gly Leu Pro Gly
                565                 570                 575

Thr Pro Gly Gln Asp Gly Leu Pro Gly Leu Pro Gly Pro Lys Gly Glu
            580                 585                 590

Pro Gly Gly Ile Thr Phe Lys Gly Glu Arg Gly Pro Pro Gly Asn Pro
        595                 600                 605

Gly Leu Pro Gly Leu Pro Gly Asn Ile Gly Pro Met Gly Pro Pro Gly
```

610 615 620

Phe Gly Pro Pro Gly Pro Val Gly Glu Lys Gly Ile Gln Gly Val Ala
625 630 635 640

Gly Asn Pro Gly Gln Pro Gly Ile Pro Gly Pro Lys Gly Asp Pro Gly
645 650 655

Gln Thr Ile Thr Gln Pro Gly Lys Pro Gly Leu Pro Gly Asn Pro Gly
660 665 670

Arg Asp Gly Asp Val Gly Leu Pro Gly Asp Pro Gly Leu Pro Gly Gln
675 680 685

Pro Gly Leu Pro Gly Ile Pro Gly Ser Lys Gly Glu Pro Gly Ile Pro
690 695 700

Gly Ile Gly Leu Pro Gly Pro Pro Gly Pro Lys Gly Phe Pro Gly Ile
705 710 715 720

Pro Gly Pro Pro Gly Ala Pro Gly Thr Pro Gly Arg Ile Gly Leu Glu
725 730 735

Gly Pro Pro Gly Pro Pro Gly Phe Pro Gly Pro Lys Gly Glu Pro Gly
740 745 750

Phe Ala Leu Pro Gly Pro Pro Gly Pro Pro Gly Leu Pro Gly Phe Lys
755 760 765

Gly Ala Leu Gly Pro Lys Gly Asp Arg Gly Phe Pro Gly Pro Pro Gly
770 775 780

Pro Pro Gly Arg Thr Gly Leu Asp Gly Leu Pro Gly Pro Lys Gly Asp
785 790 795 800

Val Gly Pro Asn Gly Gln Pro Gly Pro Met Gly Pro Pro Gly Leu Pro
805 810 815

Gly Ile Gly Val Gln Gly Pro Pro Gly Pro Pro Gly Ile Pro Gly Pro
820 825 830

Ile Gly Gln Pro Gly Leu His Gly Ile Pro Gly Glu Lys Gly Asp Pro
835 840 845

Gly Pro Pro Gly Leu Asp Val Pro Gly Pro Pro Gly Glu Arg Gly Ser
850 855 860

Pro Gly Ile Pro Gly Ala Pro Gly Pro Ile Gly Pro Pro Gly Ser Pro
865 870 875 880

Gly Leu Pro Gly Lys Ala Gly Ala Ser Gly Phe Pro Gly Thr Lys Gly

885 890 895

Glu Met Gly Met Met Gly Pro Pro Gly Pro Pro Gly Pro Leu Gly Ile
900 905 910

Pro Gly Arg Ser Gly Val Pro Gly Leu Lys Gly Asp Asp Gly Leu Gln
915 920 925

Gly Gln Pro Gly Leu Pro Gly Pro Thr Gly Glu Lys Gly Ser Lys Gly
930 935 940

Glu Pro Gly Leu Pro Gly Pro Pro Gly Pro Met Asp Pro Asn Leu Leu
945 950 955 960

Gly Ser Lys Gly Glu Lys Gly Glu Pro Gly Leu Pro Gly Ile Pro Gly
965 970 975

Val Ser Gly Pro Lys Gly Tyr Gln Gly Leu Pro Gly Asp Pro Gly Gln
980 985 990

Pro Gly Leu Ser Gly Gln Pro Gly Leu Pro Gly Pro Pro Gly Pro Lys
995 1000 1005

Gly Asn Pro Gly Leu Pro Gly Gln Pro Gly Leu Ile Gly Pro Pro
1010 1015 1020

Gly Leu Lys Gly Thr Ile Gly Asp Met Gly Phe Pro Gly Pro Gln
1025 1030 1035

Gly Val Glu Gly Pro Pro Gly Pro Ser Gly Val Pro Gly Gln Pro
1040 1045 1050

Gly Ser Pro Gly Leu Pro Gly Gln Lys Gly Asp Lys Gly Asp Pro
1055 1060 1065

Gly Ile Ser Ser Ile Gly Leu Pro Gly Leu Pro Gly Pro Lys Gly
1070 1075 1080

Glu Pro Gly Leu Pro Gly Tyr Pro Gly Asn Pro Gly Ile Lys Gly
1085 1090 1095

Ser Val Gly Asp Pro Gly Leu Pro Gly Leu Pro Gly Thr Pro Gly
1100 1105 1110

Ala Lys Gly Gln Pro Gly Leu Pro Gly Phe Pro Gly Thr Pro Gly
1115 1120 1125

Pro Pro Gly Pro Lys Gly Ile Ser Gly Pro Pro Gly Asn Pro Gly
1130 1135 1140

Leu Pro Gly Glu Pro Gly Pro Val Gly Gly Gly Gly His Pro Gly

1145 1150 1155

Gln Pro Gly Pro Pro Gly Glu Lys Gly Lys Pro Gly Gln Asp Gly
1160 1165 1170

Ile Pro Gly Pro Ala Gly Gln Lys Gly Glu Pro Gly Gln Pro Gly
1175 1180 1185

Phe Gly Asn Pro Gly Pro Pro Gly Leu Pro Gly Leu Ser Gly Gln
1190 1195 1200

Lys Gly Asp Gly Gly Leu Pro Gly Ile Pro Gly Asn Pro Gly Leu
1205 1210 1215

Pro Gly Pro Lys Gly Glu Pro Gly Phe His Gly Phe Pro Gly Val
1220 1225 1230

Gln Gly Pro Pro Gly Pro Pro Gly Ser Pro Gly Pro Ala Leu Glu
1235 1240 1245

Gly Pro Lys Gly Asn Pro Gly Pro Gln Gly Pro Pro Gly Arg Pro
1250 1255 1260

Gly Leu Pro Gly Pro Glu Gly Pro Pro Gly Leu Pro Gly Asn Gly
1265 1270 1275

Gly Ile Lys Gly Glu Lys Gly Asn Pro Gly Gln Pro Gly Leu Pro
1280 1285 1290

Gly Leu Pro Gly Leu Lys Gly Asp Gln Gly Pro Pro Gly Leu Gln
1295 1300 1305

Gly Asn Pro Gly Arg Pro Gly Leu Asn Gly Met Lys Gly Asp Pro
1310 1315 1320

Gly Leu Pro Gly Val Pro Gly Phe Pro Gly Met Lys Gly Pro Ser
1325 1330 1335

Gly Val Pro Gly Ser Ala Gly Pro Glu Gly Glu Pro Gly Leu Ile
1340 1345 1350

Gly Pro Pro Gly Pro Pro Gly Leu Pro Gly Pro Ser Gly Gln Ser
1355 1360 1365

Ile Ile Ile Lys Gly Asp Ala Gly Pro Pro Gly Ile Pro Gly Gln
1370 1375 1380

Pro Gly Leu Lys Gly Leu Pro Gly Pro Gln Gly Pro Gln Gly Leu
1385 1390 1395

Pro Gly Pro Thr Gly Pro Pro Gly Asp Pro Gly Arg Asn Gly Leu

1400 1405 1410

Pro Gly Phe Asp Gly Ala Gly Gly Arg Lys Gly Asp Pro Gly Leu
1415 1420 1425

Pro Gly Gln Pro Gly Thr Arg Gly Leu Asp Gly Pro Pro Gly Pro
1430 1435 1440

Asp Gly Leu Gln Gly Pro Pro Gly Pro Pro Gly Thr Ser Ser Val
1445 1450 1455

Ala His Gly Phe Leu Ile Thr Arg His Ser Gln Thr Thr Asp Ala
1460 1465 1470

Pro Gln Cys Pro Gln Gly Thr Leu Gln Val Tyr Glu Gly Phe Ser
1475 1480 1485

Leu Leu Tyr Val Gln Gly Asn Lys Arg Ala His Gly Gln Asp Leu
1490 1495 1500

Gly Thr Ala Gly Ser Cys Leu Arg Arg Phe Ser Thr Met Pro Phe
1505 1510 1515

Met Phe Cys Asn Ile Asn Asn Val Cys Asn Phe Ala Ser Arg Asn
1520 1525 1530

Asp Tyr Ser Tyr Trp Leu Ser Thr Pro Glu Pro Met Pro Met Ser
1535 1540 1545

Met Gln Pro Leu Lys Gly Gln Ser Ile Gln Pro Phe Ile Ser Arg
1550 1555 1560

Cys Ala Val Cys Glu Ala Pro Ala Val Val Ile Ala Val His Ser
1565 1570 1575

Gln Thr Ile Gln Ile Pro His Cys Pro Gln Gly Trp Asp Ser Leu
1580 1585 1590

Trp Ile Gly Tyr Ser Phe Met Met His Thr Ser Ala Gly Ala Glu
1595 1600 1605

Gly Ser Gly Gln Ala Leu Ala Ser Pro Gly Ser Cys Leu Glu Glu
1610 1615 1620

Phe Arg Ser Ala Pro Phe Ile Glu Cys His Gly Arg Gly Thr Cys
1625 1630 1635

Asn Tyr Tyr Ala Asn Ser Tyr Ser Phe Trp Leu Ala Thr Val Asp
1640 1645 1650

Val Ser Asp Met Phe Ser Lys Pro Gln Ser Glu Thr Leu Lys Ala

1655 1660 1665

Gly Asp Leu Arg Thr Arg Ile Ser Arg Cys Gln Val Cys Met Lys
1670 1675 1680

Arg Thr
1685

<210> 497
<211> 1691
<212> PRT
<213> Homo sapiens

<400> 497

Met Leu Ile Asn Lys Leu Trp Leu Leu Leu Val Thr Leu Cys Leu Thr
1 5 10 15

Glu Glu Leu Ala Ala Ala Gly Glu Lys Ser Tyr Gly Lys Pro Cys Gly
20 25 30

Gly Gln Asp Cys Ser Gly Ser Cys Gln Cys Phe Pro Glu Lys Gly Ala
35 40 45

Arg Gly Arg Pro Gly Pro Ile Gly Ile Gln Gly Pro Thr Gly Pro Gln
50 55 60

Gly Phe Thr Gly Ser Thr Gly Leu Ser Gly Leu Lys Gly Glu Arg Gly
65 70 75 80

Phe Pro Gly Leu Leu Gly Pro Tyr Gly Pro Lys Gly Asp Lys Gly Pro
85 90 95

Met Gly Val Pro Gly Phe Leu Gly Ile Asn Gly Ile Pro Gly His Pro
100 105 110

Gly Gln Pro Gly Pro Arg Gly Pro Pro Gly Leu Asp Gly Cys Asn Gly
115 120 125

Thr Gln Gly Ala Val Gly Phe Pro Gly Pro Asp Gly Tyr Pro Gly Leu
130 135 140

Leu Gly Pro Pro Gly Leu Pro Gly Gln Lys Gly Ser Lys Gly Asp Pro
145 150 155 160

Val Leu Ala Pro Gly Ser Phe Lys Gly Met Lys Gly Asp Pro Gly Leu
165 170 175

Pro Gly Leu Asp Gly Ile Thr Gly Pro Gln Gly Ala Pro Gly Phe Pro
180 185 190

Gly Ala Val Gly Pro Ala Gly Pro Pro Gly Leu Gln Gly Pro Pro Gly
195 200 205

```
Pro Pro Gly Pro Leu Gly Pro Asp Gly Asn Met Gly Leu Gly Phe Gln
    210                 215                 220

Gly Glu Lys Gly Val Lys Gly Asp Val Gly Leu Pro Gly Pro Ala Gly
225                 230                 235                 240

Pro Pro Pro Ser Thr Gly Glu Leu Glu Phe Met Gly Phe Pro Lys Gly
                245                 250                 255

Lys Lys Gly Ser Lys Gly Glu Pro Gly Pro Lys Gly Phe Pro Gly Ile
            260                 265                 270

Ser Gly Pro Pro Gly Phe Pro Gly Leu Gly Thr Thr Gly Glu Lys Gly
        275                 280                 285

Glu Lys Gly Glu Lys Gly Ile Pro Gly Leu Pro Gly Pro Arg Gly Pro
    290                 295                 300

Met Gly Ser Glu Gly Val Gln Gly Pro Pro Gly Gln Gln Gly Lys Lys
305                 310                 315                 320

Gly Thr Leu Gly Phe Pro Gly Leu Asn Gly Phe Gln Gly Ile Glu Gly
                325                 330                 335

Gln Lys Gly Asp Ile Gly Leu Pro Gly Pro Asp Val Phe Ile Asp Ile
            340                 345                 350

Asp Gly Ala Val Ile Ser Gly Asn Pro Gly Asp Pro Gly Val Pro Gly
        355                 360                 365

Leu Pro Gly Leu Lys Gly Asp Glu Gly Ile Gln Gly Leu Arg Gly Pro
    370                 375                 380

Ser Gly Val Pro Gly Leu Pro Ala Leu Ser Gly Val Pro Gly Ala Leu
385                 390                 395                 400

Gly Pro Gln Gly Phe Pro Gly Leu Lys Gly Asp Gln Gly Asn Pro Gly
                405                 410                 415

Arg Thr Thr Ile Gly Ala Ala Gly Leu Pro Gly Arg Asp Gly Leu Pro
            420                 425                 430

Gly Pro Pro Gly Pro Pro Gly Pro Pro Ser Pro Glu Phe Glu Thr Glu
        435                 440                 445

Thr Leu His Asn Lys Glu Ser Gly Phe Pro Gly Leu Arg Gly Glu Gln
    450                 455                 460

Gly Pro Lys Gly Asn Leu Gly Leu Lys Gly Ile Lys Gly Asp Ser Gly
465                 470                 475                 480
```

```
Phe Cys Ala Cys Asp Gly Gly Val Pro Asn Thr Gly Pro Pro Gly Glu
                485                 490                 495

Pro Gly Pro Pro Gly Pro Trp Gly Leu Ile Gly Leu Pro Gly Leu Lys
            500                 505                 510

Gly Ala Arg Gly Asp Arg Gly Ser Gly Gly Ala Gln Gly Pro Ala Gly
        515                 520                 525

Ala Pro Gly Leu Val Gly Pro Leu Gly Pro Ser Gly Pro Lys Gly Lys
    530                 535                 540

Lys Gly Glu Pro Ile Leu Ser Thr Ile Gln Gly Met Pro Gly Asp Arg
545                 550                 555                 560

Gly Asp Ser Gly Ser Gln Gly Phe Arg Gly Val Ile Gly Glu Pro Gly
                565                 570                 575

Lys Asp Gly Val Pro Gly Leu Pro Gly Leu Pro Gly Leu Pro Gly Asp
            580                 585                 590

Gly Gly Gln Gly Phe Pro Gly Glu Lys Gly Leu Pro Gly Leu Pro Gly
        595                 600                 605

Glu Lys Gly His Pro Gly Pro Pro Gly Leu Pro Gly Asn Gly Leu Pro
    610                 615                 620

Gly Leu Pro Gly Pro Arg Gly Leu Pro Gly Asp Lys Gly Lys Asp Gly
625                 630                 635                 640

Leu Pro Gly Gln Gln Gly Leu Pro Gly Ser Lys Gly Ile Thr Leu Pro
                645                 650                 655

Cys Ile Ile Pro Gly Ser Tyr Gly Pro Ser Gly Phe Pro Gly Thr Pro
            660                 665                 670

Gly Phe Pro Gly Pro Lys Gly Ser Arg Gly Leu Pro Gly Thr Pro Gly
        675                 680                 685

Gln Pro Gly Ser Ser Gly Ser Lys Gly Glu Pro Gly Ser Pro Gly Leu
    690                 695                 700

Val His Leu Pro Glu Leu Pro Gly Phe Pro Gly Pro Arg Gly Glu Lys
705                 710                 715                 720

Gly Leu Pro Gly Phe Pro Gly Leu Pro Gly Lys Asp Gly Leu Pro Gly
                725                 730                 735

Met Ile Gly Ser Pro Gly Leu Pro Gly Ser Lys Gly Ala Thr Gly Asp
            740                 745                 750
```

```
Ile Phe Gly Ala Glu Asn Gly Ala Pro Gly Glu Gln Gly Leu Gln Gly
        755                 760                 765

Leu Thr Gly His Lys Gly Phe Leu Gly Asp Ser Gly Leu Pro Gly Leu
    770                 775                 780

Lys Gly Val His Gly Lys Pro Gly Leu Leu Gly Pro Lys Gly Glu Arg
785                 790                 795                 800

Gly Ser Pro Gly Thr Pro Gly Gln Val Gly Gln Pro Gly Thr Pro Gly
                805                 810                 815

Ser Ser Gly Pro Tyr Gly Ile Lys Gly Lys Ser Gly Leu Pro Gly Ala
            820                 825                 830

Pro Gly Phe Pro Gly Ile Ser Gly His Pro Gly Lys Lys Gly Thr Arg
        835                 840                 845

Gly Lys Lys Gly Pro Pro Gly Ser Ile Val Lys Lys Gly Leu Pro Gly
    850                 855                 860

Leu Lys Gly Leu Pro Gly Asn Pro Gly Leu Val Gly Leu Lys Gly Ser
865                 870                 875                 880

Pro Gly Ser Pro Gly Val Ala Gly Leu Pro Ala Leu Ser Gly Pro Lys
                885                 890                 895

Gly Glu Lys Gly Ser Val Gly Phe Val Gly Phe Pro Gly Ile Pro Gly
            900                 905                 910

Leu Pro Gly Ile Pro Gly Thr Arg Gly Leu Lys Gly Ile Pro Gly Ser
        915                 920                 925

Thr Gly Lys Met Gly Pro Ser Gly Arg Ala Gly Thr Pro Gly Glu Lys
    930                 935                 940

Gly Asp Arg Gly Asn Pro Gly Pro Val Gly Ile Pro Ser Pro Arg Arg
945                 950                 955                 960

Pro Met Ser Asn Leu Trp Leu Lys Gly Asp Lys Gly Ser Gln Gly Ser
                965                 970                 975

Ala Gly Ser Asn Gly Phe Pro Gly Pro Arg Gly Asp Lys Gly Glu Ala
            980                 985                 990

Gly Arg Pro Gly Pro Pro Gly Leu  Pro Gly Ala Pro Gly  Leu Pro Gly
        995                 1000                1005

Ile Ile  Lys Gly Val Ser Gly  Lys Pro Gly Pro Pro  Gly Phe Met
    1010                1015                1020
```

```
Gly Ile  Arg Gly Leu Pro Gly  Leu Lys Gly Ser Ser  Gly Ile Thr
    1025                 1030                 1035

Gly Phe  Pro Gly Met Pro Gly  Glu Ser Gly Ser Gln  Gly Ile Arg
    1040                 1045                 1050

Gly Ser  Pro Gly Leu Pro Gly  Ala Ser Gly Leu Pro  Gly Leu Lys
    1055                 1060                 1065

Gly Asp  Asn Gly Gln Thr Val  Glu Ile Ser Gly Ser  Pro Gly Pro
    1070                 1075                 1080

Lys Gly  Gln Pro Gly Glu Ser  Gly Phe Lys Gly Thr  Lys Gly Arg
    1085                 1090                 1095

Asp Gly  Leu Ile Gly Asn Ile  Gly Phe Pro Gly Asn  Lys Gly Glu
    1100                 1105                 1110

Asp Gly  Lys Val Gly Val Ser  Gly Asp Val Gly Leu  Pro Gly Ala
    1115                 1120                 1125

Pro Gly  Phe Pro Gly Val Ala  Gly Met Arg Gly Glu  Pro Gly Leu
    1130                 1135                 1140

Pro Gly  Ser Ser Gly His Gln  Gly Ala Ile Gly Pro  Leu Gly Ser
    1145                 1150                 1155

Pro Gly  Leu Ile Gly Pro Lys  Gly Phe Pro Gly Phe  Pro Gly Leu
    1160                 1165                 1170

His Gly  Leu Asn Gly Leu Pro  Gly Thr Lys Gly Thr  His Gly Thr
    1175                 1180                 1185

Pro Gly  Pro Ser Ile Thr Gly  Val Pro Gly Pro Ala  Gly Leu Pro
    1190                 1195                 1200

Gly Pro  Lys Gly Glu Lys Gly  Tyr Pro Gly Ile Gly  Ile Gly Ala
    1205                 1210                 1215

Pro Gly  Lys Pro Gly Leu Arg  Gly Gln Lys Gly Asp  Arg Gly Phe
    1220                 1225                 1230

Pro Gly  Leu Gln Gly Pro Ala  Gly Leu Pro Gly Ala  Pro Gly Ile
    1235                 1240                 1245

Ser Leu  Pro Ser Leu Ile Ala  Gly Gln Pro Gly Asp  Pro Gly Arg
    1250                 1255                 1260

Pro Gly  Leu Asp Gly Glu Arg  Gly Arg Pro Gly Pro  Ala Gly Pro
    1265                 1270                 1275
```

```
Pro Gly  Pro Pro Gly Pro Ser  Ser Asn Gln Gly Asp  Thr Gly Asp
    1280                 1285                 1290

Pro Gly  Phe Pro Gly Ile Pro  Gly Pro Lys Gly Pro  Lys Gly Asp
    1295                 1300                 1305

Gln Gly  Ile Pro Gly Phe Ser  Gly Leu Pro Gly Glu  Leu Gly Leu
    1310                 1315                 1320

Lys Gly  Met Arg Gly Glu Pro  Gly Phe Met Gly Thr  Pro Gly Lys
    1325                 1330                 1335

Val Gly  Pro Pro Gly Asp Pro  Gly Phe Pro Gly Met  Lys Gly Lys
    1340                 1345                 1350

Ala Gly  Pro Arg Gly Ser Ser  Gly Leu Gln Gly Asp  Pro Gly Gln
    1355                 1360                 1365

Thr Pro  Thr Ala Glu Ala Val  Gln Val Pro Pro Gly  Pro Leu Gly
    1370                 1375                 1380

Leu Pro  Gly Ile Asp Gly Ile  Pro Gly Leu Thr Gly  Asp Pro Gly
    1385                 1390                 1395

Ala Gln  Gly Pro Val Gly Leu  Gln Gly Ser Lys Gly  Leu Pro Gly
    1400                 1405                 1410

Ile Pro  Gly Lys Asp Gly Pro  Ser Gly Leu Pro Gly  Pro Pro Gly
    1415                 1420                 1425

Ala Leu  Gly Asp Pro Gly Leu  Pro Gly Leu Gln Gly  Pro Pro Gly
    1430                 1435                 1440

Phe Glu  Gly Ala Pro Gly Gln  Gln Gly Pro Phe Gly  Met Pro Gly
    1445                 1450                 1455

Met Pro  Gly Gln Ser Met Arg  Val Gly Tyr Thr Leu  Val Lys His
    1460                 1465                 1470

Ser Gln  Ser Glu Gln Val Pro  Pro Cys Pro Ile Gly  Met Ser Gln
    1475                 1480                 1485

Leu Trp  Val Gly Tyr Ser Leu  Leu Phe Val Glu Gly  Gln Glu Lys
    1490                 1495                 1500

Ala His  Asn Gln Asp Leu Gly  Phe Ala Gly Ser Cys  Leu Pro Arg
    1505                 1510                 1515

Phe Ser  Thr Met Pro Phe Ile  Tyr Cys Asn Ile Asn  Glu Val Cys
    1520                 1525                 1530
```

```
His Tyr  Ala Arg Arg Asn Asp  Lys Ser Tyr Trp Leu  Ser Thr Thr
    1535                1540                1545

Ala Pro  Ile Pro Met Met Pro  Val Ser Gln Thr Gln  Ile Pro Gln
    1550                1555                1560

Tyr Ile  Ser Arg Cys Ser Val  Cys Glu Ala Pro Ser  Gln Ala Ile
    1565                1570                1575

Ala Val  His Ser Gln Asp Ile  Thr Ile Pro Gln Cys  Pro Leu Gly
    1580                1585                1590

Trp Arg  Ser Leu Trp Ile Gly  Tyr Ser Phe Leu Met  His Thr Ala
    1595                1600                1605

Ala Gly  Ala Glu Gly Gly Gly  Gln Ser Leu Val Ser  Pro Gly Ser
    1610                1615                1620

Cys Leu  Glu Asp Phe Arg Ala  Thr Pro Phe Ile Glu  Cys Ser Gly
    1625                1630                1635

Ala Arg  Gly Thr Cys His Tyr  Phe Ala Asn Lys Tyr  Ser Phe Trp
    1640                1645                1650

Leu Thr  Thr Val Glu Glu Arg  Gln Gln Phe Gly Glu  Leu Pro Val
    1655                1660                1665

Ser Glu  Thr Leu Lys Ala Gly  Gln Leu His Thr Arg  Val Ser Arg
    1670                1675                1680

Cys Gln  Val Cys Met Lys Ser  Leu
    1685                1690


<210>  498
<211>  2944
<212>  PRT
<213>  Homo sapiens

<400>  498

Met Thr Leu Arg Leu Leu Val Ala Ala Leu Cys Ala Gly Ile Leu Ala
1               5                  10                  15

Glu Ala Pro Arg Val Arg Ala Gln His Arg Glu Arg Val Thr Cys Thr
            20                  25                  30

Arg Leu Tyr Ala Ala Asp Ile Val Phe Leu Leu Asp Gly Ser Ser Ser
        35                  40                  45

Ile Gly Arg Ser Asn Phe Arg Glu Val Arg Ser Phe Leu Glu Gly Leu
    50                  55                  60
```

```
Val Leu Pro Phe Ser Gly Ala Ala Ser Ala Gln Gly Val Arg Phe Ala
65                  70                  75                  80

Thr Val Gln Tyr Ser Asp Asp Pro Arg Thr Glu Phe Gly Leu Asp Ala
                85                  90                  95

Leu Gly Ser Gly Gly Asp Val Ile Arg Ala Ile Arg Glu Leu Ser Tyr
            100                 105                 110

Lys Gly Gly Asn Thr Arg Thr Gly Ala Ala Ile Leu His Val Ala Asp
        115                 120                 125

His Val Phe Leu Pro Gln Leu Ala Arg Pro Gly Val Pro Lys Val Cys
    130                 135                 140

Ile Leu Ile Thr Asp Gly Lys Ser Gln Asp Leu Val Asp Thr Ala Ala
145                 150                 155                 160

Gln Arg Leu Lys Gly Gln Gly Val Lys Leu Phe Ala Val Gly Ile Lys
                165                 170                 175

Asn Ala Asp Pro Glu Glu Leu Lys Arg Val Ala Ser Gln Pro Thr Ser
            180                 185                 190

Asp Phe Phe Phe Phe Val Asn Asp Phe Ser Ile Leu Arg Thr Leu Leu
        195                 200                 205

Pro Leu Val Ser Arg Arg Val Cys Thr Thr Ala Gly Gly Val Pro Val
    210                 215                 220

Thr Arg Pro Pro Asp Asp Ser Thr Ser Ala Pro Arg Asp Leu Val Leu
225                 230                 235                 240

Ser Glu Pro Ser Ser Gln Ser Leu Arg Val Gln Trp Thr Ala Ala Ser
                245                 250                 255

Gly Pro Val Thr Gly Tyr Lys Val Gln Tyr Thr Pro Leu Thr Gly Leu
            260                 265                 270

Gly Gln Pro Leu Pro Ser Glu Arg Gln Glu Val Asn Val Pro Ala Gly
        275                 280                 285

Glu Thr Ser Val Arg Leu Arg Gly Leu Arg Pro Leu Thr Glu Tyr Gln
    290                 295                 300

Val Thr Val Ile Ala Leu Tyr Ala Asn Ser Ile Gly Glu Ala Val Ser
305                 310                 315                 320

Gly Thr Ala Arg Thr Thr Ala Leu Glu Gly Pro Glu Leu Thr Ile Gln
                325                 330                 335
```

```
Asn Thr Thr Ala His Ser Leu Leu Val Ala Trp Arg Ser Val Pro Gly
            340                 345                 350

Ala Thr Gly Tyr Arg Val Thr Trp Arg Val Leu Ser Gly Gly Pro Thr
        355                 360                 365

Gln Gln Gln Glu Leu Gly Pro Gly Gln Gly Ser Val Leu Leu Arg Asp
    370                 375                 380

Leu Glu Pro Gly Thr Asp Tyr Glu Val Thr Val Ser Thr Leu Phe Gly
385                 390                 395                 400

Arg Ser Val Gly Pro Ala Thr Ser Leu Met Ala Arg Thr Asp Ala Ser
                405                 410                 415

Val Glu Gln Thr Leu Arg Pro Val Ile Leu Gly Pro Thr Ser Ile Leu
            420                 425                 430

Leu Ser Trp Asn Leu Val Pro Glu Ala Arg Gly Tyr Arg Leu Glu Trp
        435                 440                 445

Arg Arg Glu Thr Gly Leu Glu Pro Pro Gln Lys Val Val Leu Pro Ser
    450                 455                 460

Asp Val Thr Arg Tyr Gln Leu Asp Gly Leu Gln Pro Gly Thr Glu Tyr
465                 470                 475                 480

Arg Leu Thr Leu Tyr Thr Leu Leu Glu Gly His Glu Val Ala Thr Pro
                485                 490                 495

Ala Thr Val Val Pro Thr Gly Pro Glu Leu Pro Val Ser Pro Val Thr
            500                 505                 510

Asp Leu Gln Ala Thr Glu Leu Pro Gly Gln Arg Val Arg Val Ser Trp
        515                 520                 525

Ser Pro Val Pro Gly Ala Thr Gln Tyr Arg Ile Ile Val Arg Ser Thr
    530                 535                 540

Gln Gly Val Glu Arg Thr Leu Val Leu Pro Gly Ser Gln Thr Ala Phe
545                 550                 555                 560

Asp Leu Asp Asp Val Gln Ala Gly Leu Ser Tyr Thr Val Arg Val Ser
                565                 570                 575

Ala Arg Val Gly Pro Arg Glu Gly Ser Ala Ser Val Leu Thr Val Arg
            580                 585                 590

Arg Glu Pro Glu Thr Pro Leu Ala Val Pro Gly Leu Arg Val Val Val
        595                 600                 605
```

```
Ser Asp Ala Thr Arg Val Arg Val Ala Trp Gly Pro Val Pro Gly Ala
    610                 615                 620

Ser Gly Phe Arg Ile Ser Trp Ser Thr Gly Ser Gly Pro Glu Ser Ser
625                 630                 635                 640

Gln Thr Leu Pro Pro Asp Ser Thr Ala Thr Asp Ile Thr Gly Leu Gln
                645                 650                 655

Pro Gly Thr Thr Tyr Gln Val Ala Val Ser Val Leu Arg Gly Arg Glu
            660                 665                 670

Glu Gly Pro Ala Ala Val Ile Val Ala Arg Thr Asp Pro Leu Gly Pro
        675                 680                 685

Val Arg Thr Val His Val Thr Gln Ala Ser Ser Ser Ser Val Thr Ile
    690                 695                 700

Thr Trp Thr Arg Val Pro Gly Ala Thr Gly Tyr Arg Val Ser Trp His
705                 710                 715                 720

Ser Ala His Gly Pro Glu Lys Ser Gln Leu Val Ser Gly Glu Ala Thr
                725                 730                 735

Val Ala Glu Leu Asp Gly Leu Glu Pro Asp Thr Glu Tyr Thr Val His
            740                 745                 750

Val Arg Ala His Val Ala Gly Val Asp Gly Pro Pro Ala Ser Val Val
        755                 760                 765

Val Arg Thr Ala Pro Glu Pro Val Gly Arg Val Ser Arg Leu Gln Ile
    770                 775                 780

Leu Asn Ala Ser Ser Asp Val Leu Arg Ile Thr Trp Val Gly Val Thr
785                 790                 795                 800

Gly Ala Thr Ala Tyr Arg Leu Ala Trp Gly Arg Ser Glu Gly Gly Pro
                805                 810                 815

Met Arg His Gln Ile Leu Pro Gly Asn Thr Asp Ser Ala Glu Ile Arg
            820                 825                 830

Gly Leu Glu Gly Gly Val Ser Tyr Ser Val Arg Val Thr Ala Leu Val
        835                 840                 845

Gly Asp Arg Glu Gly Thr Pro Val Ser Ile Val Val Thr Thr Pro Pro
    850                 855                 860

Glu Ala Pro Pro Ala Leu Gly Thr Leu His Val Val Gln Arg Gly Glu
865                 870                 875                 880
```

```
His Ser Leu Arg Leu Arg Trp Glu Pro Val Pro Arg Ala Gln Gly Phe
                885                 890                 895

Leu Leu His Trp Gln Pro Glu Gly Gly Gln Glu Gln Ser Arg Val Leu
            900                 905                 910

Gly Pro Glu Leu Ser Ser Tyr His Leu Asp Gly Leu Glu Pro Ala Thr
        915                 920                 925

Gln Tyr Arg Val Arg Leu Ser Val Leu Gly Pro Ala Gly Glu Gly Pro
    930                 935                 940

Ser Ala Glu Val Thr Ala Arg Thr Glu Ser Pro Arg Val Pro Ser Ile
945                 950                 955                 960

Glu Leu Arg Val Val Asp Thr Ser Ile Asp Ser Val Thr Leu Ala Trp
                965                 970                 975

Thr Pro Val Ser Arg Ala Ser Ser Tyr Ile Leu Ser Trp Arg Pro Leu
            980                 985                 990

Arg Gly Pro Gly Gln Glu Val Pro  Gly Ser Pro Gln Thr  Leu Pro Gly
        995                 1000                1005

Ile Ser  Ser Ser Gln Arg Val  Thr Gly Leu Glu Pro  Gly Val Ser
    1010                1015                1020

Tyr Ile  Phe Ser Leu Thr Pro  Val Leu Asp Gly Val  Arg Gly Pro
    1025                1030                1035

Glu Ala  Ser Val Thr Gln Thr  Pro Val Cys Pro Arg  Gly Leu Ala
    1040                1045                1050

Asp Val  Val Phe Leu Pro His  Ala Thr Gln Asp Asn  Ala His Arg
    1055                1060                1065

Ala Glu  Ala Thr Arg Arg Val  Leu Glu Arg Leu Val  Leu Ala Leu
    1070                1075                1080

Gly Pro  Leu Gly Pro Gln Ala  Val Gln Val Gly Leu  Leu Ser Tyr
    1085                1090                1095

Ser His  Arg Pro Ser Pro Leu  Phe Pro Leu Asn Gly  Ser His Asp
    1100                1105                1110

Leu Gly  Ile Ile Leu Gln Arg  Ile Arg Asp Met Pro  Tyr Met Asp
    1115                1120                1125

Pro Ser  Gly Asn Asn Leu Gly  Thr Ala Val Val Thr  Ala His Arg
    1130                1135                1140
```

```
Tyr Met  Leu Ala Pro Asp Ala  Pro Gly Arg Arg Gln  His Val Pro
    1145                1150                1155

Gly Val  Met Val Leu Leu Val  Asp Glu Pro Leu Arg  Gly Asp Ile
    1160                1165                1170

Phe Ser  Pro Ile Arg Glu Ala  Gln Ala Ser Gly Leu  Asn Val Val
    1175                1180                1185

Met Leu  Gly Met Ala Gly Ala  Asp Pro Glu Gln Leu  Arg Arg Leu
    1190                1195                1200

Ala Pro  Gly Met Asp Ser Val  Gln Thr Phe Phe Ala  Val Asp Asp
    1205                1210                1215

Gly Pro  Ser Leu Asp Gln Ala  Val Ser Gly Leu Ala  Thr Ala Leu
    1220                1225                1230

Cys Gln  Ala Ser Phe Thr Thr  Gln Pro Arg Pro Glu  Pro Cys Pro
    1235                1240                1245

Val Tyr  Cys Pro Lys Gly Gln  Lys Gly Glu Pro Gly  Glu Met Gly
    1250                1255                1260

Leu Arg  Gly Gln Val Gly Pro  Pro Gly Asp Pro Gly  Leu Pro Gly
    1265                1270                1275

Arg Thr  Gly Ala Pro Gly Pro  Gln Gly Pro Pro Gly  Ser Ala Thr
    1280                1285                1290

Ala Lys  Gly Glu Arg Gly Phe  Pro Gly Ala Asp Gly  Arg Pro Gly
    1295                1300                1305

Ser Pro  Gly Arg Ala Gly Asn  Pro Gly Thr Pro Gly  Ala Pro Gly
    1310                1315                1320

Leu Lys  Gly Ser Pro Gly Leu  Pro Gly Pro Arg Gly  Asp Pro Gly
    1325                1330                1335

Glu Arg  Gly Pro Arg Gly Pro  Lys Gly Glu Pro Gly  Ala Pro Gly
    1340                1345                1350

Gln Val  Ile Gly Gly Glu Gly  Pro Gly Leu Pro Gly  Arg Lys Gly
    1355                1360                1365

Asp Pro  Gly Pro Ser Gly Pro  Pro Gly Pro Arg Gly  Pro Leu Gly
    1370                1375                1380

Asp Pro  Gly Pro Arg Gly Pro  Pro Gly Leu Pro Gly  Thr Ala Met
    1385                1390                1395
```

```
Lys Gly  Asp Lys Gly Asp Arg  Gly Glu Arg Gly Pro  Pro Gly Pro
    1400                 1405                 1410

Gly Glu  Gly Gly Ile Ala Pro  Gly Glu Pro Gly Leu  Pro Gly Leu
    1415                 1420                 1425

Pro Gly  Ser Pro Gly Pro Gln  Gly Pro Val Gly Pro  Pro Gly Lys
    1430                 1435                 1440

Lys Gly  Glu Lys Gly Asp Ser  Glu Asp Gly Ala Pro  Gly Leu Pro
    1445                 1450                 1455

Gly Gln  Pro Gly Ser Pro Gly  Glu Gln Gly Pro Arg  Gly Pro Pro
    1460                 1465                 1470

Gly Ala  Ile Gly Pro Lys Gly  Asp Arg Gly Phe Pro  Gly Pro Leu
    1475                 1480                 1485

Gly Glu  Ala Gly Glu Lys Gly  Glu Arg Gly Pro Pro  Gly Pro Ala
    1490                 1495                 1500

Gly Ser  Arg Gly Leu Pro Gly  Val Ala Gly Arg Pro  Gly Ala Lys
    1505                 1510                 1515

Gly Pro  Glu Gly Pro Pro Gly  Pro Thr Gly Arg Gln  Gly Glu Lys
    1520                 1525                 1530

Gly Glu  Pro Gly Arg Pro Gly  Asp Pro Ala Val Val  Gly Pro Ala
    1535                 1540                 1545

Val Ala  Gly Pro Lys Gly Glu  Lys Gly Asp Val Gly  Pro Ala Gly
    1550                 1555                 1560

Pro Arg  Gly Ala Thr Gly Val  Gln Gly Glu Arg Gly  Pro Pro Gly
    1565                 1570                 1575

Leu Val  Leu Pro Gly Asp Pro  Gly Pro Lys Gly Asp  Pro Gly Asp
    1580                 1585                 1590

Arg Gly  Pro Ile Gly Leu Thr  Gly Arg Ala Gly Pro  Pro Gly Asp
    1595                 1600                 1605

Ser Gly  Pro Pro Gly Glu Lys  Gly Asp Pro Gly Arg  Pro Gly Pro
    1610                 1615                 1620

Pro Gly  Pro Val Gly Pro Arg  Gly Arg Asp Gly Glu  Val Gly Glu
    1625                 1630                 1635

Lys Gly  Asp Glu Gly Pro Pro  Gly Asp Pro Gly Leu  Pro Gly Lys
    1640                 1645                 1650
```

```
Ala Gly  Glu Arg Gly Leu Arg  Gly Ala Pro Gly Val  Arg Gly Pro
    1655                 1660                 1665

Val Gly  Glu Lys Gly Asp Gln  Gly Asp Pro Gly Glu  Asp Gly Arg
    1670                 1675                 1680

Asn Gly  Ser Pro Gly Ser Ser  Gly Pro Lys Gly Asp  Arg Gly Glu
    1685                 1690                 1695

Pro Gly  Pro Pro Gly Pro Pro  Gly Arg Leu Val Asp  Thr Gly Pro
    1700                 1705                 1710

Gly Ala  Arg Glu Lys Gly Glu  Pro Gly Asp Arg Gly  Gln Glu Gly
    1715                 1720                 1725

Pro Arg  Gly Pro Lys Gly Asp  Pro Gly Leu Pro Gly  Ala Pro Gly
    1730                 1735                 1740

Glu Arg  Gly Ile Glu Gly Phe  Arg Gly Pro Pro Gly  Pro Gln Gly
    1745                 1750                 1755

Asp Pro  Gly Val Arg Gly Pro  Ala Gly Glu Lys Gly  Asp Arg Gly
    1760                 1765                 1770

Pro Pro  Gly Leu Asp Gly Arg  Ser Gly Leu Asp Gly  Lys Pro Gly
    1775                 1780                 1785

Ala Ala  Gly Pro Ser Gly Pro  Asn Gly Ala Ala Gly  Lys Ala Gly
    1790                 1795                 1800

Asp Pro  Gly Arg Asp Gly Leu  Pro Gly Leu Arg Gly  Glu Gln Gly
    1805                 1810                 1815

Leu Pro  Gly Pro Ser Gly Pro  Pro Gly Leu Pro Gly  Lys Pro Gly
    1820                 1825                 1830

Glu Asp  Gly Lys Pro Gly Leu  Asn Gly Lys Asn Gly  Glu Pro Gly
    1835                 1840                 1845

Asp Pro  Gly Glu Asp Gly Arg  Lys Gly Glu Lys Gly  Asp Ser Gly
    1850                 1855                 1860

Ala Ser  Gly Arg Glu Gly Arg  Asp Gly Pro Lys Gly  Glu Arg Gly
    1865                 1870                 1875

Ala Pro  Gly Ile Leu Gly Pro  Gln Gly Pro Pro Gly  Leu Pro Gly
    1880                 1885                 1890

Pro Val  Gly Pro Pro Gly Gln  Gly Phe Pro Gly Val  Pro Gly Gly
    1895                 1900                 1905
```

```
Thr Gly  Pro Lys Gly Asp Arg  Gly Glu Thr Gly Ser  Lys Gly Glu
    1910                 1915                 1920

Gln Gly  Leu Pro Gly Glu Arg  Gly Leu Arg Gly Glu  Pro Gly Ser
    1925                 1930                 1935

Val Pro  Asn Val Asp Arg Leu  Leu Glu Thr Ala Gly  Ile Lys Ala
    1940                 1945                 1950

Ser Ala  Leu Arg Glu Ile Val  Glu Thr Trp Asp Glu  Ser Ser Gly
    1955                 1960                 1965

Ser Phe  Leu Pro Val Pro Glu  Arg Arg Arg Gly Pro  Lys Gly Asp
    1970                 1975                 1980

Ser Gly  Glu Gln Gly Pro Pro  Gly Lys Glu Gly Pro  Ile Gly Phe
    1985                 1990                 1995

Pro Gly  Glu Arg Gly Leu Lys  Gly Asp Arg Gly Asp  Pro Gly Pro
    2000                 2005                 2010

Gln Gly  Pro Pro Gly Leu Ala  Leu Gly Glu Arg Gly  Pro Pro Gly
    2015                 2020                 2025

Pro Ser  Gly Leu Ala Gly Glu  Pro Gly Lys Pro Gly  Ile Pro Gly
    2030                 2035                 2040

Leu Pro  Gly Arg Ala Gly Gly  Val Gly Glu Ala Gly  Arg Pro Gly
    2045                 2050                 2055

Glu Arg  Gly Glu Arg Gly Glu  Lys Gly Glu Arg Gly  Glu Gln Gly
    2060                 2065                 2070

Arg Asp  Gly Pro Pro Gly Leu  Pro Gly Thr Pro Gly  Pro Pro Gly
    2075                 2080                 2085

Pro Pro  Gly Pro Lys Val Ser  Val Asp Glu Pro Gly  Pro Gly Leu
    2090                 2095                 2100

Ser Gly  Glu Gln Gly Pro Pro  Gly Leu Lys Gly Ala  Lys Gly Glu
    2105                 2110                 2115

Pro Gly  Ser Asn Gly Asp Gln  Gly Pro Lys Gly Asp  Arg Gly Val
    2120                 2125                 2130

Pro Gly  Ile Lys Gly Asp Arg  Gly Glu Pro Gly Pro  Arg Gly Gln
    2135                 2140                 2145

Asp Gly  Asn Pro Gly Leu Pro  Gly Glu Arg Gly Met  Ala Gly Pro
    2150                 2155                 2160
```

```
Glu Gly  Lys Pro Gly Leu Gln  Gly Pro Arg Gly Pro  Pro Gly Pro
    2165                 2170                 2175

Val Gly  Gly His Gly Asp Pro  Gly Pro Pro Gly Ala  Pro Gly Leu
    2180                 2185                 2190

Ala Gly  Pro Ala Gly Pro Gln  Gly Pro Ser Gly Leu  Lys Gly Glu
    2195                 2200                 2205

Pro Gly  Glu Thr Gly Pro Pro  Gly Arg Gly Leu Thr  Gly Pro Thr
    2210                 2215                 2220

Gly Ala  Val Gly Leu Pro Gly  Pro Pro Gly Pro Ser  Gly Leu Val
    2225                 2230                 2235

Gly Pro  Gln Gly Ser Pro Gly  Leu Pro Gly Gln Val  Gly Glu Thr
    2240                 2245                 2250

Gly Lys  Pro Gly Ala Pro Gly  Arg Asp Gly Ala Ser  Gly Lys Asp
    2255                 2260                 2265

Gly Asp  Arg Gly Ser Pro Gly  Val Pro Gly Ser Pro  Gly Leu Pro
    2270                 2275                 2280

Gly Pro  Val Gly Pro Lys Gly  Glu Pro Gly Pro Thr  Gly Ala Pro
    2285                 2290                 2295

Gly Gln  Ala Val Val Gly Leu  Pro Gly Ala Lys Gly  Glu Lys Gly
    2300                 2305                 2310

Ala Pro  Gly Gly Leu Ala Gly  Asp Leu Val Gly Glu  Pro Gly Ala
    2315                 2320                 2325

Lys Gly  Asp Arg Gly Leu Pro  Gly Pro Arg Gly Glu  Lys Gly Glu
    2330                 2335                 2340

Ala Gly  Arg Ala Gly Glu Pro  Gly Asp Pro Gly Glu  Asp Gly Gln
    2345                 2350                 2355

Lys Gly  Ala Pro Gly Pro Lys  Gly Phe Lys Gly Asp  Pro Gly Val
    2360                 2365                 2370

Gly Val  Pro Gly Ser Pro Gly  Pro Pro Gly Pro Pro  Gly Val Lys
    2375                 2380                 2385

Gly Asp  Leu Gly Leu Pro Gly  Leu Pro Gly Ala Pro  Gly Val Val
    2390                 2395                 2400

Gly Phe  Pro Gly Gln Thr Gly  Pro Arg Gly Glu Met  Gly Gln Pro
    2405                 2410                 2415
```

```
Gly Pro  Ser Gly Glu Arg Gly  Leu Ala Gly Pro Pro  Gly Arg Glu
    2420                 2425                 2430

Gly Ile  Pro Gly Pro Leu Gly  Pro Pro Gly Pro Pro  Gly Ser Val
    2435                 2440                 2445

Gly Pro  Pro Gly Ala Ser Gly  Leu Lys Gly Asp Lys  Gly Asp Pro
    2450                 2455                 2460

Gly Val  Gly Leu Pro Gly Pro  Arg Gly Glu Arg Gly  Glu Pro Gly
    2465                 2470                 2475

Ile Arg  Gly Glu Asp Gly Arg  Pro Gly Gln Glu Gly  Pro Arg Gly
    2480                 2485                 2490

Leu Thr  Gly Pro Pro Gly Ser  Arg Gly Glu Arg Gly  Glu Lys Gly
    2495                 2500                 2505

Asp Val  Gly Ser Ala Gly Leu  Lys Gly Asp Lys Gly  Asp Ser Ala
    2510                 2515                 2520

Val Ile  Leu Gly Pro Pro Gly  Pro Arg Gly Ala Lys  Gly Asp Met
    2525                 2530                 2535

Gly Glu  Arg Gly Pro Arg Gly  Leu Asp Gly Asp Lys  Gly Pro Arg
    2540                 2545                 2550

Gly Asp  Asn Gly Asp Pro Gly  Asp Lys Gly Ser Lys  Gly Glu Pro
    2555                 2560                 2565

Gly Asp  Lys Gly Ser Ala Gly  Leu Pro Gly Leu Arg  Gly Leu Leu
    2570                 2575                 2580

Gly Pro  Gln Gly Gln Pro Gly  Ala Ala Gly Ile Pro  Gly Asp Pro
    2585                 2590                 2595

Gly Ser  Pro Gly Lys Asp Gly  Val Pro Gly Ile Arg  Gly Glu Lys
    2600                 2605                 2610

Gly Asp  Val Gly Phe Met Gly  Pro Arg Gly Leu Lys  Gly Glu Arg
    2615                 2620                 2625

Gly Val  Lys Gly Ala Cys Gly  Leu Asp Gly Glu Lys  Gly Asp Lys
    2630                 2635                 2640

Gly Glu  Ala Gly Pro Pro Gly  Arg Pro Gly Leu Ala  Gly His Lys
    2645                 2650                 2655

Gly Glu  Met Gly Glu Pro Gly  Val Pro Gly Gln Ser  Gly Ala Pro
    2660                 2665                 2670
```

```
Gly Lys  Glu Gly Leu Ile Gly  Pro Lys Gly Asp Arg  Gly Phe Asp
    2675                 2680                 2685

Gly Gln  Pro Gly Pro Lys Gly  Asp Gln Gly Glu Lys  Gly Glu Arg
    2690                 2695                 2700

Gly Thr  Pro Gly Ile Gly Gly  Phe Pro Gly Pro Ser  Gly Asn Asp
    2705                 2710                 2715

Gly Ser  Ala Gly Pro Pro Gly  Pro Pro Gly Ser Val  Gly Pro Arg
    2720                 2725                 2730

Gly Pro  Glu Gly Leu Gln Gly  Gln Lys Gly Glu Arg  Gly Pro Pro
    2735                 2740                 2745

Gly Glu  Arg Val Val Gly Ala  Pro Gly Val Pro Gly  Ala Pro Gly
    2750                 2755                 2760

Glu Arg  Gly Glu Gln Gly Arg  Pro Gly Pro Ala Gly  Pro Arg Gly
    2765                 2770                 2775

Glu Lys  Gly Glu Ala Ala Leu  Thr Glu Asp Asp Ile  Arg Gly Phe
    2780                 2785                 2790

Val Arg  Gln Glu Met Ser Gln  His Cys Ala Cys Gln  Gly Gln Phe
    2795                 2800                 2805

Ile Ala  Ser Gly Ser Arg Pro  Leu Pro Ser Tyr Ala  Ala Asp Thr
    2810                 2815                 2820

Ala Gly  Ser Gln Leu His Ala  Val Pro Val Leu Arg  Val Ser His
    2825                 2830                 2835

Ala Glu  Glu Glu Glu Arg Val  Pro Pro Glu Asp Asp  Glu Tyr Ser
    2840                 2845                 2850

Glu Tyr  Ser Glu Tyr Ser Val  Glu Glu Tyr Gln Asp  Pro Glu Ala
    2855                 2860                 2865

Pro Trp  Asp Ser Asp Asp Pro  Cys Ser Leu Pro Leu  Asp Glu Gly
    2870                 2875                 2880

Ser Cys  Thr Ala Tyr Thr Leu  Arg Trp Tyr His Arg  Ala Val Thr
    2885                 2890                 2895

Gly Ser  Thr Glu Ala Cys His  Pro Phe Val Tyr Gly  Gly Cys Gly
    2900                 2905                 2910

Gly Asn  Ala Asn Arg Phe Gly  Thr Arg Glu Ala Cys  Glu Arg Arg
    2915                 2920                 2925
```

```
Cys Pro  Pro Arg Val Val Gln  Ser Gln Gly Thr Gly  Thr Ala Gln
    2930                2935                2940

Asp
```

<210> 499
<211> 1838
<212> PRT
<213> Homo sapiens

<400> 499

```
Met Asp Val His Thr Arg Trp Lys Ala Arg Ser Ala Leu Arg Pro Gly
1               5                  10                  15

Ala Pro Leu Leu Pro Pro Leu Leu Leu Leu Leu Trp Ala Pro Pro
            20                  25                  30

Pro Ser Arg Ala Ala Gln Pro Ala Asp Leu Leu Lys Val Leu Asp Phe
        35                  40                  45

His Asn Leu Pro Asp Gly Ile Thr Lys Thr Thr Gly Phe Cys Ala Thr
    50                  55                  60

Arg Arg Ser Ser Lys Gly Pro Asp Val Ala Tyr Arg Val Thr Lys Asp
65                  70                  75                  80

Ala Gln Leu Ser Ala Pro Thr Lys Gln Leu Tyr Pro Ala Ser Ala Phe
                85                  90                  95

Pro Glu Asp Phe Ser Ile Leu Thr Thr Val Lys Ala Lys Lys Gly Ser
            100                 105                 110

Gln Ala Phe Leu Val Ser Ile Tyr Asn Glu Gln Gly Ile Gln Gln Ile
        115                 120                 125

Gly Leu Glu Leu Gly Arg Ser Pro Val Phe Leu Tyr Glu Asp His Thr
    130                 135                 140

Gly Lys Pro Gly Pro Glu Asp Tyr Pro Leu Phe Arg Gly Ile Asn Leu
145                 150                 155                 160

Ser Asp Gly Lys Trp His Arg Ile Ala Leu Ser Val His Lys Lys Asn
                165                 170                 175

Val Thr Leu Ile Leu Asp Cys Lys Lys Lys Thr Thr Lys Phe Leu Asp
            180                 185                 190

Arg Ser Asp His Pro Met Ile Asp Ile Asn Gly Ile Ile Val Phe Gly
        195                 200                 205
```

```
Thr Arg Ile Leu Asp Glu Glu Val Phe Glu Gly Asp Ile Gln Gln Leu
    210                 215                 220

Leu Phe Val Ser Asp His Arg Ala Ala Tyr Asp Tyr Cys Glu His Tyr
225                 230                 235                 240

Ser Pro Asp Cys Asp Thr Ala Val Pro Asp Thr Pro Gln Ser Gln Asp
                245                 250                 255

Pro Asn Pro Asp Glu Tyr Tyr Thr Glu Gly Asp Gly Glu Gly Glu Thr
            260                 265                 270

Tyr Tyr Tyr Glu Tyr Pro Tyr Tyr Glu Asp Pro Glu Asp Leu Gly Lys
        275                 280                 285

Glu Pro Thr Pro Ser Lys Lys Pro Val Glu Ala Ala Lys Glu Thr Thr
    290                 295                 300

Glu Val Pro Glu Glu Leu Thr Pro Thr Pro Thr Glu Ala Ala Pro Met
305                 310                 315                 320

Pro Glu Thr Ser Glu Gly Ala Gly Lys Glu Glu Asp Val Gly Ile Gly
                325                 330                 335

Asp Tyr Asp Tyr Val Pro Ser Glu Asp Tyr Tyr Thr Pro Ser Pro Tyr
            340                 345                 350

Asp Asp Leu Thr Tyr Gly Glu Gly Glu Glu Asn Pro Asp Gln Pro Thr
        355                 360                 365

Asp Pro Gly Ala Gly Ala Glu Ile Pro Thr Ser Thr Ala Asp Thr Ser
    370                 375                 380

Asn Ser Ser Asn Pro Ala Pro Pro Pro Gly Glu Gly Ala Asp Asp Leu
385                 390                 395                 400

Glu Gly Glu Phe Thr Glu Glu Thr Ile Arg Asn Leu Asp Glu Asn Tyr
                405                 410                 415

Tyr Asp Pro Tyr Tyr Asp Pro Thr Ser Ser Pro Ser Glu Ile Gly Pro
            420                 425                 430

Gly Met Pro Ala Asn Gln Asp Thr Ile Tyr Glu Gly Ile Gly Gly Pro
        435                 440                 445

Arg Gly Glu Lys Gly Gln Lys Gly Glu Pro Ala Ile Ile Glu Pro Gly
    450                 455                 460

Met Leu Ile Glu Gly Pro Pro Gly Pro Glu Gly Pro Ala Gly Leu Pro
465                 470                 475                 480
```

```
Gly Pro Pro Gly Thr Met Gly Pro Thr Gly Gln Val Gly Asp Pro Gly
                485                 490                 495

Glu Arg Gly Pro Pro Gly Arg Pro Gly Leu Pro Gly Ala Asp Gly Leu
            500                 505                 510

Pro Gly Pro Pro Gly Thr Met Leu Met Leu Pro Phe Arg Phe Gly Gly
        515                 520                 525

Gly Gly Asp Ala Gly Ser Lys Gly Pro Met Val Ser Ala Gln Glu Ser
    530                 535                 540

Gln Ala Gln Ala Ile Leu Gln Gln Ala Arg Leu Ala Leu Arg Gly Pro
545                 550                 555                 560

Ala Gly Pro Met Gly Leu Thr Gly Arg Pro Gly Pro Val Gly Pro Pro
                565                 570                 575

Gly Ser Gly Gly Leu Lys Gly Glu Pro Gly Asp Val Gly Pro Gln Gly
            580                 585                 590

Pro Arg Gly Val Gln Gly Pro Pro Gly Pro Ala Gly Lys Pro Gly Arg
        595                 600                 605

Arg Gly Arg Ala Gly Ser Asp Gly Ala Arg Gly Met Pro Gly Gln Thr
    610                 615                 620

Gly Pro Lys Gly Asp Arg Gly Phe Asp Gly Leu Ala Gly Leu Pro Gly
625                 630                 635                 640

Glu Lys Gly His Arg Gly Asp Pro Gly Pro Ser Gly Pro Pro Gly Pro
                645                 650                 655

Pro Gly Asp Asp Gly Glu Arg Gly Asp Asp Gly Glu Val Gly Pro Arg
            660                 665                 670

Gly Leu Pro Gly Glu Pro Gly Pro Arg Gly Leu Leu Gly Pro Lys Gly
        675                 680                 685

Pro Pro Gly Pro Pro Gly Pro Pro Gly Val Thr Gly Met Asp Gly Gln
    690                 695                 700

Pro Gly Pro Lys Gly Asn Val Gly Pro Gln Gly Glu Pro Gly Pro Pro
705                 710                 715                 720

Gly Gln Gln Gly Asn Pro Gly Ala Gln Gly Leu Pro Gly Pro Gln Gly
                725                 730                 735

Ala Ile Gly Pro Pro Gly Glu Lys Gly Pro Leu Gly Lys Pro Gly Leu
            740                 745                 750
```

```
Pro Gly Met Pro Gly Ala Asp Gly Pro Pro Gly His Pro Gly Lys Glu
        755                 760                 765

Gly Pro Pro Gly Glu Lys Gly Gly Gln Gly Pro Pro Gly Pro Gln Gly
    770                 775                 780

Pro Ile Gly Tyr Pro Gly Pro Arg Gly Val Lys Gly Ala Asp Gly Ile
785                 790                 795                 800

Arg Gly Leu Lys Gly Thr Lys Gly Glu Lys Gly Glu Asp Gly Phe Pro
                805                 810                 815

Gly Phe Lys Gly Asp Met Gly Ile Lys Gly Asp Arg Gly Glu Ile Gly
            820                 825                 830

Pro Pro Gly Pro Arg Gly Glu Asp Gly Pro Glu Gly Pro Lys Gly Arg
        835                 840                 845

Gly Gly Pro Asn Gly Asp Pro Gly Pro Leu Gly Pro Pro Gly Glu Lys
    850                 855                 860

Gly Lys Leu Gly Val Pro Gly Leu Pro Gly Tyr Pro Gly Arg Gln Gly
865                 870                 875                 880

Pro Lys Gly Ser Ile Gly Phe Pro Gly Phe Pro Gly Ala Asn Gly Glu
                885                 890                 895

Lys Gly Gly Arg Gly Thr Pro Gly Lys Pro Gly Pro Arg Gly Gln Arg
            900                 905                 910

Gly Pro Thr Gly Pro Arg Gly Glu Arg Gly Pro Arg Gly Ile Thr Gly
        915                 920                 925

Lys Pro Gly Pro Lys Gly Asn Ser Gly Gly Asp Gly Pro Ala Gly Pro
    930                 935                 940

Pro Gly Glu Arg Gly Pro Asn Gly Pro Gln Gly Pro Thr Gly Phe Pro
945                 950                 955                 960

Gly Pro Lys Gly Pro Pro Gly Pro Pro Gly Lys Asp Gly Leu Pro Gly
                965                 970                 975

His Pro Gly Gln Arg Gly Glu Thr Gly Phe Gln Gly Lys Thr Gly Pro
            980                 985                 990

Pro Gly Pro Pro Gly Val Val Gly  Pro Gln Gly Pro Thr  Gly Glu Thr
        995                 1000                1005

Gly Pro  Met Gly Glu Arg Gly  His Pro Gly Pro Pro  Gly Pro Pro
    1010                1015                1020
```

```
Gly Glu  Gln Gly Leu Pro Gly  Leu Ala Gly Lys Glu  Gly Thr Lys
    1025                1030                1035

Gly Asp  Pro Gly Pro Ala Gly  Leu Pro Gly Lys Asp  Gly Pro Pro
    1040                1045                1050

Gly Leu  Arg Gly Phe Pro Gly  Asp Arg Gly Leu Pro  Gly Pro Val
    1055                1060                1065

Gly Ala  Leu Gly Leu Lys Gly  Asn Glu Gly Pro Pro  Gly Pro Pro
    1070                1075                1080

Gly Pro  Ala Gly Ser Pro Gly  Glu Arg Gly Pro Ala  Gly Ala Ala
    1085                1090                1095

Gly Pro  Ile Gly Ile Pro Gly  Arg Pro Gly Pro Gln  Gly Pro Pro
    1100                1105                1110

Gly Pro  Ala Gly Glu Lys Gly  Ala Pro Gly Glu Lys  Gly Pro Gln
    1115                1120                1125

Gly Pro  Ala Gly Arg Asp Gly  Leu Gln Gly Pro Val  Gly Leu Pro
    1130                1135                1140

Gly Pro  Ala Gly Pro Val Gly  Pro Pro Gly Glu Asp  Gly Asp Lys
    1145                1150                1155

Gly Glu  Ile Gly Glu Pro Gly  Gln Lys Gly Ser Lys  Gly Asp Lys
    1160                1165                1170

Gly Glu  Gln Gly Pro Pro Gly  Pro Thr Gly Pro Gln  Gly Pro Ile
    1175                1180                1185

Gly Gln  Pro Gly Pro Ser Gly  Ala Asp Gly Glu Pro  Gly Pro Arg
    1190                1195                1200

Gly Gln  Gln Gly Leu Phe Gly  Gln Lys Gly Asp Glu  Gly Pro Arg
    1205                1210                1215

Gly Phe  Pro Gly Pro Pro Gly  Pro Val Gly Leu Gln  Gly Leu Pro
    1220                1225                1230

Gly Pro  Pro Gly Glu Lys Gly  Glu Thr Gly Asp Val  Gly Gln Met
    1235                1240                1245

Gly Pro  Pro Gly Pro Pro Gly  Pro Arg Gly Pro Ser  Gly Ala Pro
    1250                1255                1260

Gly Ala  Asp Gly Pro Gln Gly  Pro Pro Gly Gly Ile  Gly Asn Pro
    1265                1270                1275
```

```
Gly Ala  Val Gly Glu Lys Gly  Glu Pro Gly Glu Ala  Gly Glu Pro
    1280                1285                1290

Gly Leu  Pro Gly Glu Gly Gly  Pro Pro Gly Pro Lys  Gly Glu Arg
    1295                1300                1305

Gly Glu  Lys Gly Glu Ser Gly  Pro Ser Gly Ala Ala  Gly Pro Pro
    1310                1315                1320

Gly Pro  Lys Gly Pro Pro Gly  Asp Asp Gly Pro Lys  Gly Ser Pro
    1325                1330                1335

Gly Pro  Val Gly Phe Pro Gly  Asp Pro Gly Pro Pro  Gly Glu Pro
    1340                1345                1350

Gly Pro  Ala Gly Gln Asp Gly  Pro Pro Gly Asp Lys  Gly Asp Asp
    1355                1360                1365

Gly Glu  Pro Gly Gln Thr Gly  Ser Pro Gly Pro Thr  Gly Glu Pro
    1370                1375                1380

Gly Pro  Ser Gly Pro Pro Gly  Lys Arg Gly Pro Pro  Gly Pro Ala
    1385                1390                1395

Gly Pro  Glu Gly Arg Gln Gly  Glu Lys Gly Ala Lys  Gly Glu Ala
    1400                1405                1410

Gly Leu  Glu Gly Pro Pro Gly  Lys Thr Gly Pro Ile  Gly Pro Gln
    1415                1420                1425

Gly Ala  Pro Gly Lys Pro Gly  Pro Asp Gly Leu Arg  Gly Ile Pro
    1430                1435                1440

Gly Pro  Val Gly Glu Gln Gly  Leu Pro Gly Ser Pro  Gly Pro Asp
    1445                1450                1455

Gly Pro  Pro Gly Pro Met Gly  Pro Pro Gly Leu Pro  Gly Leu Lys
    1460                1465                1470

Gly Asp  Ser Gly Pro Lys Gly  Glu Lys Gly His Pro  Gly Leu Ile
    1475                1480                1485

Gly Leu  Ile Gly Pro Pro Gly  Glu Gln Gly Glu Lys  Gly Asp Arg
    1490                1495                1500

Gly Leu  Pro Gly Pro Gln Gly  Ser Ser Gly Pro Lys  Gly Glu Gln
    1505                1510                1515

Gly Ile  Thr Gly Pro Ser Gly  Pro Ile Gly Pro Pro  Gly Pro Pro
    1520                1525                1530
```

```
Gly Leu  Pro Gly Pro Pro Gly  Pro Lys Gly Ala Lys  Gly Ser Ser
    1535                1540                1545

Gly Pro  Thr Gly Pro Lys Gly  Glu Ala Gly His Pro  Gly Pro Pro
    1550                1555                1560

Gly Pro  Pro Gly Pro Pro Gly  Glu Val Ile Gln Pro  Leu Pro Ile
    1565                1570                1575

Gln Ala  Ser Arg Thr Arg Arg  Asn Ile Asp Ala Ser  Gln Leu Leu
    1580                1585                1590

Asp Asp  Gly Asn Gly Glu Asn  Tyr Val Asp Tyr Ala  Asp Gly Met
    1595                1600                1605

Glu Glu  Ile Phe Gly Ser Leu  Asn Ser Leu Lys Leu  Glu Ile Glu
    1610                1615                1620

Gln Met  Lys Arg Pro Leu Gly  Thr Gln Gln Asn Pro  Ala Arg Thr
    1625                1630                1635

Cys Lys  Asp Leu Gln Leu Cys  His Pro Asp Phe Pro  Asp Gly Glu
    1640                1645                1650

Tyr Trp  Val Asp Pro Asn Gln  Gly Cys Ser Arg Asp  Ser Phe Lys
    1655                1660                1665

Val Tyr  Cys Asn Phe Thr Ala  Gly Gly Ser Thr Cys  Val Phe Pro
    1670                1675                1680

Asp Lys  Lys Ser Glu Gly Ala  Arg Ile Thr Ser Trp  Pro Lys Glu
    1685                1690                1695

Asn Pro  Gly Ser Trp Phe Ser  Glu Phe Lys Arg Gly  Lys Leu Leu
    1700                1705                1710

Ser Tyr  Val Asp Ala Glu Gly  Asn Pro Val Gly Val  Val Gln Met
    1715                1720                1725

Thr Phe  Leu Arg Leu Leu Ser  Ala Ser Ala His Gln  Asn Val Thr
    1730                1735                1740

Tyr His  Cys Tyr Gln Ser Val  Ala Trp Gln Asp Ala  Ala Thr Gly
    1745                1750                1755

Ser Tyr  Asp Lys Ala Leu Arg  Phe Leu Gly Ser Asn  Asp Glu Glu
    1760                1765                1770

Met Ser  Tyr Asp Asn Asn Pro  Tyr Ile Arg Ala Leu  Val Asp Gly
    1775                1780                1785
```

Cys Ala Thr Lys Lys Gly Tyr Gln Lys Thr Val Leu Glu Ile Asp
1790 1795 1800

Thr Pro Lys Val Glu Gln Val Pro Ile Val Asp Ile Met Phe Asn
1805 1810 1815

Asp Phe Gly Glu Ala Ser Gln Lys Phe Gly Phe Glu Val Gly Pro
1820 1825 1830

Ala Cys Phe Met Gly
1835

<210> 500
<211> 1499
<212> PRT
<213> Homo sapiens

<400> 500

Met Met Ala Asn Trp Ala Glu Ala Arg Pro Leu Leu Ile Leu Ile Val
1 5 10 15

Leu Leu Gly Gln Phe Val Ser Ile Lys Ala Gln Glu Glu Asp Glu Asp
20 25 30

Glu Gly Tyr Gly Glu Glu Ile Ala Cys Thr Gln Asn Gly Gln Met Tyr
35 40 45

Leu Asn Arg Asp Ile Trp Lys Pro Ala Pro Cys Gln Ile Cys Val Cys
50 55 60

Asp Asn Gly Ala Ile Leu Cys Asp Lys Ile Glu Cys Gln Asp Val Leu
65 70 75 80

Asp Cys Ala Asp Pro Val Thr Pro Pro Gly Glu Cys Cys Pro Val Cys
85 90 95

Ser Gln Thr Pro Gly Gly Gly Asn Thr Asn Phe Gly Arg Gly Arg Lys
100 105 110

Gly Gln Lys Gly Glu Pro Gly Leu Val Pro Val Val Thr Gly Ile Arg
115 120 125

Gly Arg Pro Gly Pro Ala Gly Pro Pro Gly Ser Gln Gly Pro Arg Gly
130 135 140

Glu Arg Gly Pro Lys Gly Arg Pro Gly Pro Arg Gly Pro Gln Gly Ile
145 150 155 160

Asp Gly Glu Pro Gly Val Pro Gly Gln Pro Gly Ala Pro Gly Pro Pro
165 170 175

Gly His Pro Ser His Pro Gly Pro Asp Gly Leu Ser Arg Pro Phe Ser

180 185 190

Ala Gln Met Ala Gly Leu Asp Glu Lys Ser Gly Leu Gly Ser Gln Val
195 200 205

Gly Leu Met Pro Gly Ser Val Gly Pro Val Gly Pro Arg Gly Pro Gln
210 215 220

Gly Leu Gln Gly Gln Gln Gly Gly Ala Gly Pro Thr Gly Pro Pro Gly
225 230 235 240

Glu Pro Gly Asp Pro Gly Pro Met Gly Pro Ile Gly Ser Arg Gly Pro
245 250 255

Glu Gly Pro Pro Gly Lys Pro Gly Glu Asp Gly Glu Pro Gly Arg Asn
260 265 270

Gly Asn Pro Gly Glu Val Gly Phe Ala Gly Ser Pro Gly Ala Arg Gly
275 280 285

Phe Pro Gly Ala Pro Gly Leu Pro Gly Leu Lys Gly His Arg Gly His
290 295 300

Lys Gly Leu Glu Gly Pro Lys Gly Glu Val Gly Ala Pro Gly Ser Lys
305 310 315 320

Gly Glu Ala Gly Pro Thr Gly Pro Met Gly Ala Met Gly Pro Leu Gly
325 330 335

Pro Arg Gly Met Pro Gly Glu Arg Gly Arg Leu Gly Pro Gln Gly Ala
340 345 350

Pro Gly Gln Arg Gly Ala His Gly Met Pro Gly Lys Pro Gly Pro Met
355 360 365

Gly Pro Leu Gly Ile Pro Gly Ser Ser Gly Phe Pro Gly Asn Pro Gly
370 375 380

Met Lys Gly Glu Ala Gly Pro Thr Gly Ala Arg Gly Pro Glu Gly Pro
385 390 395 400

Gln Gly Gln Arg Gly Glu Thr Gly Pro Pro Gly Pro Val Gly Ser Pro
405 410 415

Gly Leu Pro Gly Ala Ile Gly Thr Asp Gly Thr Pro Gly Ala Lys Gly
420 425 430

Pro Thr Gly Ser Pro Gly Thr Ser Gly Pro Pro Gly Ser Ala Gly Pro
435 440 445

Pro Gly Ser Pro Gly Pro Gln Gly Ser Thr Gly Pro Gln Gly Ile Arg

```
    450                 455                 460

Gly Gln Pro Gly Asp Pro Gly Val Pro Gly Phe Lys Gly Glu Ala Gly
465                 470                 475                 480

Pro Lys Gly Glu Pro Gly Pro His Gly Ile Gln Gly Pro Ile Gly Pro
                485                 490                 495

Pro Gly Glu Glu Gly Lys Arg Gly Pro Arg Gly Asp Pro Gly Thr Val
            500                 505                 510

Gly Pro Pro Gly Pro Val Gly Glu Arg Gly Ala Pro Gly Asn Arg Gly
        515                 520                 525

Phe Pro Gly Ser Asp Gly Leu Pro Gly Pro Lys Gly Ala Gln Gly Glu
    530                 535                 540

Arg Gly Pro Val Gly Ser Ser Gly Pro Lys Gly Ser Gln Gly Asp Pro
545                 550                 555                 560

Gly Arg Pro Gly Glu Pro Gly Leu Pro Gly Ala Arg Gly Leu Thr Gly
                565                 570                 575

Asn Pro Gly Val Gln Gly Pro Glu Gly Lys Leu Gly Pro Leu Gly Ala
            580                 585                 590

Pro Gly Glu Asp Gly Arg Pro Gly Pro Pro Gly Ser Ile Gly Ile Arg
        595                 600                 605

Gly Gln Pro Gly Ser Met Gly Leu Pro Gly Pro Lys Gly Ser Ser Gly
    610                 615                 620

Asp Pro Gly Lys Pro Gly Glu Ala Gly Asn Ala Gly Val Pro Gly Gln
625                 630                 635                 640

Arg Gly Ala Pro Gly Lys Asp Gly Glu Val Gly Pro Ser Gly Pro Val
                645                 650                 655

Gly Pro Pro Gly Leu Ala Gly Glu Arg Gly Glu Gln Gly Pro Pro Gly
            660                 665                 670

Pro Thr Gly Phe Gln Gly Leu Pro Gly Pro Pro Gly Pro Pro Gly Glu
        675                 680                 685

Gly Gly Lys Pro Gly Asp Gln Gly Val Pro Gly Asp Pro Gly Ala Val
    690                 695                 700

Gly Pro Leu Gly Pro Arg Gly Glu Arg Gly Asn Pro Gly Glu Arg Gly
705                 710                 715                 720

Glu Pro Gly Ile Thr Gly Leu Pro Gly Glu Lys Gly Met Ala Gly Gly
```

725 730 735

His Gly Pro Asp Gly Pro Lys Gly Ser Pro Gly Pro Ser Gly Thr Pro
740 745 750

Gly Asp Thr Gly Pro Pro Gly Leu Gln Gly Met Pro Gly Glu Arg Gly
755 760 765

Ile Ala Gly Thr Pro Gly Pro Lys Gly Asp Arg Gly Gly Ile Gly Glu
770 775 780

Lys Gly Ala Glu Gly Thr Ala Gly Asn Asp Gly Ala Arg Gly Leu Pro
785 790 795 800

Gly Pro Leu Gly Pro Pro Gly Pro Ala Gly Pro Thr Gly Glu Lys Gly
805 810 815

Glu Pro Gly Pro Arg Gly Leu Val Gly Pro Pro Gly Ser Arg Gly Asn
820 825 830

Pro Gly Ser Arg Gly Glu Asn Gly Pro Thr Gly Ala Val Gly Phe Ala
835 840 845

Gly Pro Gln Gly Pro Asp Gly Gln Pro Gly Val Lys Gly Glu Pro Gly
850 855 860

Glu Pro Gly Gln Lys Gly Asp Ala Gly Ser Pro Gly Pro Gln Gly Leu
865 870 875 880

Ala Gly Ser Pro Gly Pro His Gly Pro Asn Gly Val Pro Gly Leu Lys
885 890 895

Gly Gly Arg Gly Thr Gln Gly Pro Pro Gly Ala Thr Gly Phe Pro Gly
900 905 910

Ser Ala Gly Arg Val Gly Pro Pro Gly Pro Ala Gly Ala Pro Gly Pro
915 920 925

Ala Gly Pro Leu Gly Glu Pro Gly Lys Glu Gly Pro Pro Gly Leu Arg
930 935 940

Gly Asp Pro Gly Ser His Gly Arg Val Gly Asp Arg Gly Pro Ala Gly
945 950 955 960

Pro Pro Gly Gly Pro Gly Asp Lys Gly Asp Pro Gly Glu Asp Gly Gln
965 970 975

Pro Gly Pro Asp Gly Pro Pro Gly Pro Ala Gly Thr Thr Gly Gln Arg
980 985 990

Gly Ile Val Gly Met Pro Gly Gln Arg Gly Glu Arg Gly Met Pro Gly

995 1000 1005

Leu Pro Gly Pro Ala Gly Thr Pro Gly Lys Val Gly Pro Thr Gly
1010 1015 1020

Ala Thr Gly Asp Lys Gly Pro Pro Gly Pro Val Gly Pro Pro Gly
1025 1030 1035

Ser Asn Gly Pro Val Gly Glu Pro Gly Pro Glu Gly Pro Ala Gly
1040 1045 1050

Asn Asp Gly Thr Pro Gly Arg Asp Gly Ala Val Gly Glu Arg Gly
1055 1060 1065

Asp Arg Gly Asp Pro Gly Pro Ala Gly Leu Pro Gly Ser Gln Gly
1070 1075 1080

Ala Pro Gly Thr Pro Gly Pro Val Gly Ala Pro Gly Asp Ala Gly
1085 1090 1095

Gln Arg Gly Asp Pro Gly Ser Arg Gly Pro Ile Gly Pro Pro Gly
1100 1105 1110

Arg Ala Gly Lys Arg Gly Leu Pro Gly Pro Gln Gly Pro Arg Gly
1115 1120 1125

Asp Lys Gly Asp His Gly Asp Arg Gly Asp Arg Gly Gln Lys Gly
1130 1135 1140

His Arg Gly Phe Thr Gly Leu Gln Gly Leu Pro Gly Pro Pro Gly
1145 1150 1155

Pro Asn Gly Glu Gln Gly Ser Ala Gly Ile Pro Gly Pro Phe Gly
1160 1165 1170

Pro Arg Gly Pro Pro Gly Pro Val Gly Pro Ser Gly Lys Glu Gly
1175 1180 1185

Asn Pro Gly Pro Leu Gly Pro Ile Gly Pro Pro Gly Val Arg Gly
1190 1195 1200

Ser Val Gly Glu Ala Gly Pro Glu Gly Pro Pro Gly Glu Pro Gly
1205 1210 1215

Pro Pro Gly Pro Pro Gly Pro Pro Gly His Leu Thr Ala Ala Leu
1220 1225 1230

Gly Asp Ile Met Gly His Tyr Asp Glu Ser Met Pro Asp Pro Leu
1235 1240 1245

Pro Glu Phe Thr Glu Asp Gln Ala Ala Pro Asp Asp Lys Asn Lys

1250 1255 1260

Thr Asp Pro Gly Val His Ala Thr Leu Lys Ser Leu Ser Ser Gln
1265 1270 1275

Ile Glu Thr Met Arg Ser Pro Asp Gly Ser Lys Lys His Pro Ala
1280 1285 1290

Arg Thr Cys Asp Asp Leu Lys Leu Cys His Ser Ala Lys Gln Ser
1295 1300 1305

Gly Glu Tyr Trp Ile Asp Pro Asn Gln Gly Ser Val Glu Asp Ala
1310 1315 1320

Ile Lys Val Tyr Cys Asn Met Glu Thr Gly Glu Thr Cys Ile Ser
1325 1330 1335

Ala Asn Pro Ser Ser Val Pro Arg Lys Thr Trp Trp Ala Ser Lys
1340 1345 1350

Ser Pro Asp Asn Lys Pro Val Trp Tyr Gly Leu Asp Met Asn Arg
1355 1360 1365

Gly Ser Gln Phe Ala Tyr Gly Asp His Gln Ser Pro Asn Thr Ala
1370 1375 1380

Ile Thr Gln Met Thr Phe Leu Arg Leu Leu Ser Lys Glu Ala Ser
1385 1390 1395

Gln Asn Ile Thr Tyr Ile Cys Lys Asn Ser Val Gly Tyr Met Asp
1400 1405 1410

Asp Gln Ala Lys Asn Leu Lys Lys Ala Val Val Leu Lys Gly Ala
1415 1420 1425

Asn Asp Leu Asp Ile Lys Ala Glu Gly Asn Ile Arg Phe Arg Tyr
1430 1435 1440

Ile Val Leu Gln Asp Thr Cys Ser Lys Arg Asn Gly Asn Val Gly
1445 1450 1455

Lys Thr Val Phe Glu Tyr Arg Thr Gln Asn Val Ala Arg Leu Pro
1460 1465 1470

Ile Ile Asp Leu Ala Pro Val Asp Val Gly Gly Thr Asp Gln Glu
1475 1480 1485

Phe Gly Val Glu Ile Gly Pro Val Cys Phe Val
1490 1495

<210> 501

<211> 1745
<212> PRT
<213> Homo sapiens

<400> 501

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Met Gly Asn Arg Arg Asp Leu Gly Gln Pro Arg Ala Gly Leu Cys Leu
1               5                  10                  15

Leu Leu Ala Ala Leu Gln Leu Leu Pro Gly Thr Gln Ala Asp Pro Val
            20                  25                  30

Asp Val Leu Lys Ala Leu Gly Val Gln Gly Gly Gln Ala Gly Val Pro
        35                  40                  45

Glu Gly Pro Gly Phe Cys Pro Gln Arg Thr Pro Glu Gly Asp Arg Ala
    50                  55                  60

Phe Arg Ile Gly Gln Ala Ser Thr Leu Gly Ile Pro Thr Trp Glu Leu
65                  70                  75                  80

Phe Pro Glu Gly His Phe Pro Glu Asn Phe Ser Leu Leu Ile Thr Leu
                85                  90                  95

Arg Gly Gln Pro Ala Asn Gln Ser Val Leu Leu Ser Ile Tyr Asp Glu
            100                 105                 110

Arg Gly Ala Arg Gln Leu Gly Leu Ala Leu Gly Pro Ala Leu Gly Leu
        115                 120                 125

Leu Gly Asp Pro Phe Arg Pro Leu Pro Gln Gln Val Asn Leu Thr Asp
    130                 135                 140

Gly Arg Trp His Arg Val Ala Val Ser Ile Asp Gly Glu Met Val Thr
145                 150                 155                 160

Leu Val Ala Asp Cys Glu Ala Gln Pro Pro Val Leu Gly His Gly Pro
                165                 170                 175

Arg Phe Ile Ser Ile Ala Gly Leu Thr Val Leu Gly Thr Gln Asp Leu
            180                 185                 190

Gly Glu Lys Thr Phe Glu Gly Asp Ile Gln Glu Leu Leu Ile Ser Pro
        195                 200                 205

Asp Pro Gln Ala Ala Phe Gln Ala Cys Glu Arg Tyr Leu Pro Asp Cys
    210                 215                 220

Asp Asn Leu Ala Pro Ala Ala Thr Val Ala Pro Gln Gly Glu Pro Glu
225                 230                 235                 240

Thr Pro Arg Pro Arg Arg Lys Gly Lys Gly Lys Gly Arg Lys Lys Gly
                245                 250                 255
```

```
Arg Gly Arg Lys Gly Lys Gly Arg Lys Lys Asn Lys Glu Ile Trp Thr
            260                 265                 270

Ser Ser Pro Pro Pro Asp Ser Ala Glu Asn Gln Thr Ser Thr Asp Ile
        275                 280                 285

Pro Lys Thr Glu Thr Pro Ala Pro Asn Leu Pro Pro Thr Pro Thr Pro
    290                 295                 300

Leu Val Val Thr Ser Thr Val Thr Thr Gly Leu Asn Ala Thr Ile Leu
305                 310                 315                 320

Glu Arg Ser Leu Asp Pro Asp Ser Gly Thr Glu Leu Gly Thr Leu Glu
                325                 330                 335

Thr Lys Ala Ala Arg Glu Asp Glu Glu Gly Asp Asp Ser Thr Met Gly
            340                 345                 350

Pro Asp Phe Arg Ala Ala Glu Tyr Pro Ser Arg Thr Gln Phe Gln Ile
        355                 360                 365

Phe Pro Gly Ala Gly Glu Lys Gly Ala Lys Gly Glu Pro Ala Val Ile
    370                 375                 380

Glu Lys Gly Gln Gln Phe Glu Gly Pro Pro Gly Ala Pro Gly Pro Gln
385                 390                 395                 400

Gly Val Val Gly Pro Ser Gly Pro Pro Gly Pro Pro Gly Phe Pro Gly
                405                 410                 415

Asp Pro Gly Pro Pro Gly Pro Ala Gly Leu Pro Gly Ile Pro Gly Ile
            420                 425                 430

Asp Gly Ile Arg Gly Pro Pro Gly Thr Val Ile Met Met Pro Phe Gln
        435                 440                 445

Phe Ala Gly Gly Ser Phe Lys Gly Pro Pro Val Ser Phe Gln Gln Ala
    450                 455                 460

Gln Ala Gln Ala Val Leu Gln Gln Thr Gln Leu Ser Met Lys Gly Pro
465                 470                 475                 480

Pro Gly Pro Val Gly Leu Thr Gly Arg Pro Gly Pro Val Gly Leu Pro
                485                 490                 495

Gly His Pro Gly Leu Lys Gly Glu Glu Gly Ala Glu Gly Pro Gln Gly
            500                 505                 510

Pro Arg Gly Leu Gln Gly Pro His Gly Pro Pro Gly Arg Val Gly Lys
        515                 520                 525
```

```
Met Gly Arg Pro Gly Ala Asp Gly Ala Arg Gly Leu Pro Gly Asp Thr
    530                 535                 540

Gly Pro Lys Gly Asp Arg Gly Phe Asp Gly Leu Pro Gly Leu Pro Gly
545                 550                 555                 560

Glu Lys Gly Gln Arg Gly Asp Phe Gly His Val Gly Gln Pro Gly Pro
                565                 570                 575

Pro Gly Glu Asp Gly Glu Arg Gly Ala Glu Gly Pro Pro Gly Pro Thr
            580                 585                 590

Gly Gln Ala Gly Glu Pro Gly Pro Arg Gly Leu Leu Gly Pro Arg Gly
        595                 600                 605

Ser Pro Gly Pro Thr Gly Arg Pro Gly Val Thr Gly Ile Asp Gly Ala
    610                 615                 620

Pro Gly Ala Lys Gly Asn Val Gly Pro Pro Gly Glu Pro Gly Pro Pro
625                 630                 635                 640

Gly Gln Gln Gly Asn His Gly Ser Gln Gly Leu Pro Gly Pro Gln Gly
                645                 650                 655

Leu Ile Gly Thr Pro Gly Glu Lys Gly Pro Pro Gly Asn Pro Gly Ile
            660                 665                 670

Pro Gly Leu Pro Gly Ser Asp Gly Pro Leu Gly His Pro Gly His Glu
        675                 680                 685

Gly Pro Thr Gly Glu Lys Gly Ala Gln Gly Pro Pro Gly Ser Ala Gly
    690                 695                 700

Pro Pro Gly Tyr Pro Gly Pro Arg Gly Val Lys Gly Thr Ser Gly Asn
705                 710                 715                 720

Arg Gly Leu Gln Gly Glu Lys Gly Glu Lys Gly Glu Asp Gly Phe Pro
                725                 730                 735

Gly Phe Lys Gly Asp Val Gly Leu Lys Gly Asp Gln Gly Lys Pro Gly
            740                 745                 750

Ala Pro Gly Pro Arg Gly Glu Asp Gly Pro Glu Gly Pro Lys Gly Gln
        755                 760                 765

Ala Gly Gln Ala Gly Glu Glu Gly Pro Pro Gly Ser Ala Gly Glu Lys
    770                 775                 780

Gly Lys Leu Gly Val Pro Gly Leu Pro Gly Tyr Pro Gly Arg Pro Gly
785                 790                 795                 800
```

```
Pro Lys Gly Ser Ile Gly Phe Pro Gly Pro Leu Gly Pro Ile Gly Glu
                805                 810                 815

Lys Gly Lys Ser Gly Lys Thr Gly Gln Pro Gly Leu Glu Gly Glu Arg
            820                 825                 830

Gly Pro Pro Gly Ser Arg Gly Glu Arg Gly Gln Pro Gly Ala Thr Gly
        835                 840                 845

Gln Pro Gly Pro Lys Gly Asp Val Gly Gln Asp Gly Ala Pro Gly Ile
    850                 855                 860

Pro Gly Glu Lys Gly Leu Pro Gly Leu Gln Gly Pro Pro Gly Phe Pro
865                 870                 875                 880

Gly Pro Lys Gly Pro Pro Gly His Gln Gly Lys Asp Gly Arg Pro Gly
                885                 890                 895

His Pro Gly Gln Arg Gly Glu Leu Gly Phe Gln Gly Gln Thr Gly Pro
            900                 905                 910

Pro Gly Pro Ala Gly Val Leu Gly Pro Gln Gly Lys Thr Gly Glu Val
        915                 920                 925

Gly Pro Leu Gly Glu Arg Gly Pro Pro Gly Pro Pro Gly Pro Pro Gly
    930                 935                 940

Glu Gln Gly Leu Pro Gly Leu Glu Gly Arg Glu Gly Ala Lys Gly Glu
945                 950                 955                 960

Leu Gly Pro Pro Gly Pro Leu Gly Lys Glu Gly Pro Ala Gly Leu Arg
                965                 970                 975

Gly Phe Pro Gly Pro Lys Gly Gly Pro Gly Asp Pro Gly Pro Thr Gly
            980                 985                 990

Leu Lys Gly Asp Lys Gly Pro Pro  Gly Pro Val Gly Ala  Asn Gly Ser
        995                 1000                1005

Pro Gly  Glu Arg Gly Pro Leu  Gly Pro Ala Gly Gly  Ile Gly Leu
    1010                1015                1020

Pro Gly  Gln Ser Gly Ser Glu  Gly Pro Val Gly Pro  Ala Gly Lys
    1025                1030                1035

Lys Gly  Ser Arg Gly Glu Arg  Gly Pro Pro Gly Pro  Thr Gly Lys
    1040                1045                1050

Asp Gly  Ile Pro Gly Pro Leu  Gly Pro Leu Gly Pro  Pro Gly Ala
    1055                1060                1065
```

```
Ala Gly  Pro Ser Gly Glu Glu  Gly Asp Lys Gly Asp  Val Gly Ala
    1070                1075                1080

Pro Gly  His Lys Gly Ser Lys  Gly Asp Lys Gly Asp  Ala Gly Pro
    1085                1090                1095

Pro Gly  Gln Pro Gly Ile Arg  Gly Pro Ala Gly His  Pro Gly Pro
    1100                1105                1110

Pro Gly  Ala Asp Gly Ala Gln  Gly Arg Arg Gly Pro  Pro Gly Leu
    1115                1120                1125

Phe Gly  Gln Lys Gly Asp Asp  Gly Val Arg Gly Phe  Val Gly Val
    1130                1135                1140

Ile Gly  Pro Pro Gly Leu Gln  Gly Leu Pro Gly Pro  Pro Gly Glu
    1145                1150                1155

Lys Gly  Glu Val Gly Asp Val  Gly Ser Met Gly Pro  His Gly Ala
    1160                1165                1170

Pro Gly  Pro Arg Gly Pro Gln  Gly Pro Thr Gly Ser  Glu Gly Thr
    1175                1180                1185

Pro Gly  Leu Pro Gly Gly Val  Gly Gln Pro Gly Ala  Val Gly Glu
    1190                1195                1200

Lys Gly  Glu Arg Gly Asp Ala  Gly Asp Pro Gly Pro  Pro Gly Ala
    1205                1210                1215

Pro Gly  Ile Pro Gly Pro Lys  Gly Asp Ile Gly Glu  Lys Gly Asp
    1220                1225                1230

Ser Gly  Pro Ser Gly Ala Ala  Gly Pro Pro Gly Lys  Lys Gly Pro
    1235                1240                1245

Pro Gly  Glu Asp Gly Ala Lys  Gly Ser Val Gly Pro  Thr Gly Leu
    1250                1255                1260

Pro Gly  Asp Leu Gly Pro Pro  Gly Asp Pro Gly Val  Ser Gly Ile
    1265                1270                1275

Asp Gly  Ser Pro Gly Glu Lys  Gly Asp Pro Gly Asp  Val Gly Gly
    1280                1285                1290

Pro Gly  Pro Pro Gly Ala Ser  Gly Glu Pro Gly Ala  Pro Gly Pro
    1295                1300                1305

Pro Gly  Lys Arg Gly Pro Ser  Gly His Met Gly Arg  Glu Gly Arg
    1310                1315                1320
```

```
Glu Gly  Glu Lys Gly Ala Lys  Gly Glu Pro Gly Pro  Asp Gly Pro
    1325                 1330                 1335

Pro Gly  Arg Thr Gly Pro Met  Gly Ala Arg Gly Pro  Pro Gly Arg
    1340                 1345                 1350

Val Gly  Pro Glu Gly Leu Arg  Gly Ile Pro Gly Pro  Val Gly Glu
    1355                 1360                 1365

Pro Gly  Leu Leu Gly Ala Pro  Gly Gln Met Gly Pro  Pro Gly Pro
    1370                 1375                 1380

Leu Gly  Pro Ser Gly Leu Pro  Gly Leu Lys Gly Asp  Thr Gly Pro
    1385                 1390                 1395

Lys Gly  Glu Lys Gly His Ile  Gly Leu Ile Gly Leu  Ile Gly Pro
    1400                 1405                 1410

Pro Gly  Glu Ala Gly Glu Lys  Gly Asp Gln Gly Leu  Pro Gly Val
    1415                 1420                 1425

Gln Gly  Pro Pro Gly Pro Lys  Gly Asp Pro Gly Pro  Pro Gly Pro
    1430                 1435                 1440

Ile Gly  Ser Leu Gly His Pro  Gly Pro Pro Gly Val  Ala Gly Pro
    1445                 1450                 1455

Leu Gly  Gln Lys Gly Ser Lys  Gly Ser Pro Gly Ser  Met Gly Pro
    1460                 1465                 1470

Arg Gly  Asp Thr Gly Pro Ala  Gly Pro Pro Gly Pro  Pro Gly Ala
    1475                 1480                 1485

Pro Ala  Glu Leu His Gly Leu  Arg Arg Arg Arg Arg  Phe Val Pro
    1490                 1495                 1500

Val Pro  Leu Pro Val Val Glu  Gly Gly Leu Glu Glu  Val Leu Ala
    1505                 1510                 1515

Ser Leu  Thr Ser Leu Ser Leu  Glu Leu Glu Gln Leu  Arg Arg Pro
    1520                 1525                 1530

Pro Gly  Thr Ala Glu Arg Pro  Gly Leu Val Cys His  Glu Leu His
    1535                 1540                 1545

Arg Asn  His Pro His Leu Pro  Asp Gly Glu Tyr Trp  Ile Asp Pro
    1550                 1555                 1560

Asn Gln  Gly Cys Ala Arg Asp  Ser Phe Arg Val Phe  Cys Asn Phe
    1565                 1570                 1575
```

```
Thr Ala  Gly Gly Glu Thr Cys  Leu Tyr Pro Asp Lys  Lys Phe Glu
    1580                 1585                 1590

Ile Val  Lys Leu Ala Ser Trp  Ser Lys Glu Lys Pro  Gly Gly Trp
    1595                 1600                 1605

Tyr Ser  Thr Phe Arg Arg Gly  Lys Lys Phe Ser Tyr  Val Asp Ala
    1610                 1615                 1620

Asp Gly  Ser Pro Val Asn Val  Val Gln Leu Asn Phe  Leu Lys Leu
    1625                 1630                 1635

Leu Ser  Ala Thr Ala Arg Gln  Asn Phe Thr Tyr Ser  Cys Gln Asn
    1640                 1645                 1650

Ala Ala  Ala Trp Leu Asp Glu  Ala Thr Gly Asp Tyr  Ser His Ser
    1655                 1660                 1665

Ala Arg  Phe Leu Gly Thr Asn  Gly Glu Glu Leu Ser  Phe Asn Gln
    1670                 1675                 1680

Thr Thr  Ala Ala Thr Val Ser  Val Pro Gln Asp Gly  Cys Arg Leu
    1685                 1690                 1695

Arg Lys  Gly Gln Thr Lys Thr  Leu Phe Glu Phe Ser  Ser Ser Arg
    1700                 1705                 1710

Ala Gly  Phe Leu Pro Leu Trp  Asp Val Ala Ala Thr  Asp Phe Gly
    1715                 1720                 1725

Gln Thr  Asn Gln Lys Phe Gly  Phe Glu Leu Gly Pro  Val Cys Phe
    1730                 1735                 1740

Ser Ser
    1745


<210>  502
<211>  824
<212>  PRT
<213>  Homo sapiens

<400>  502

Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu
1               5                  10                  15

Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu
            20                  25                  30

Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser
        35                  40                  45
```

```
Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr
    50                  55                  60

His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys
65                  70                  75                  80

Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val
                85                  90                  95

Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln
            100                 105                 110

Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu
        115                 120                 125

Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly
    130                 135                 140

Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys
145                 150                 155                 160

Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser
                165                 170                 175

Arg Leu Gln Ser Pro Lys Val Cys Gly Tyr Leu Lys Val Asp Asn Glu
            180                 185                 190

Glu Leu Leu Pro Lys Gly Leu Val Asp Arg Glu Pro Pro Glu Glu Leu
        195                 200                 205

Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro Met Lys Asn Thr
    210                 215                 220

Cys Lys Leu Leu Val Val Ala Asp His Arg Phe Tyr Arg Tyr Met Gly
225                 230                 235                 240

Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile Glu Leu Ile Asp
                245                 250                 255

Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp Asn Ala Gly Phe
            260                 265                 270

Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile Leu Lys Ser Pro
        275                 280                 285

Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met Ala Lys Ser Tyr
    290                 295                 300

Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met Leu Leu Glu Gln
305                 310                 315                 320
```

```
Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val Cys Leu Ala His
                325                 330                 335

Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu Gly Leu Ala Tyr
            340                 345                 350

Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val Cys Pro Lys Ala
        355                 360                 365

Tyr Tyr Ser Pro Val Gly Lys Lys Asn Ile Tyr Leu Asn Ser Gly Leu
    370                 375                 380

Thr Ser Thr Lys Asn Tyr Gly Lys Thr Ile Leu Thr Lys Glu Ala Asp
385                 390                 395                 400

Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly Ala Glu His Asp
                405                 410                 415

Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp Gln Gly Gly Lys
            420                 425                 430

Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His Glu Asn Asn Lys
        435                 440                 445

Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys Thr Ile Glu Ser
    450                 455                 460

Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys Val Cys Gly Asn
465                 470                 475                 480

Ser Arg Val Asp Glu Gly Glu Glu Cys Asp Pro Gly Ile Met Tyr Leu
                485                 490                 495

Asn Asn Asp Thr Cys Cys Asn Ser Asp Cys Thr Leu Lys Glu Gly Val
            500                 505                 510

Gln Cys Ser Asp Arg Asn Ser Pro Cys Cys Lys Asn Cys Gln Phe Glu
        515                 520                 525

Thr Ala Gln Lys Lys Cys Gln Glu Ala Ile Asn Ala Thr Cys Lys Gly
    530                 535                 540

Val Ser Tyr Cys Thr Gly Asn Ser Ser Glu Cys Pro Pro Pro Gly Asn
545                 550                 555                 560

Ala Glu Asp Asp Thr Val Cys Leu Asp Leu Gly Lys Cys Lys Asp Gly
                565                 570                 575

Lys Cys Ile Pro Phe Cys Glu Arg Glu Gln Gln Leu Glu Ser Cys Ala
            580                 585                 590
```

```
Cys Asn Glu Thr Asp Asn Ser Cys Lys Val Cys Cys Arg Asp Leu Ser
        595                 600                 605

Gly Arg Cys Val Pro Tyr Val Asp Ala Glu Gln Lys Asn Leu Phe Leu
    610                 615                 620

Arg Lys Gly Lys Pro Cys Thr Val Gly Phe Cys Asp Met Asn Gly Lys
625                 630                 635                 640

Cys Glu Lys Arg Val Gln Asp Val Ile Glu Arg Phe Trp Asp Phe Ile
                645                 650                 655

Asp Gln Leu Ser Ile Asn Thr Phe Gly Lys Phe Leu Ala Asp Asn Ile
            660                 665                 670

Val Gly Ser Val Leu Val Phe Ser Leu Ile Phe Trp Ile Pro Phe Ser
        675                 680                 685

Ile Leu Val His Cys Val Asp Lys Lys Leu Asp Lys Gln Tyr Glu Ser
    690                 695                 700

Leu Ser Leu Phe His Pro Ser Asn Val Glu Met Leu Ser Ser Met Asp
705                 710                 715                 720

Ser Ala Ser Val Arg Ile Ile Lys Pro Phe Pro Ala Pro Gln Thr Pro
                725                 730                 735

Gly Arg Leu Gln Pro Ala Pro Val Ile Pro Ser Ala Pro Ala Ala Pro
            740                 745                 750

Lys Leu Asp His Gln Arg Met Asp Thr Ile Gln Glu Asp Pro Ser Thr
        755                 760                 765

Asp Ser His Met Asp Glu Asp Gly Phe Glu Lys Asp Pro Phe Pro Asn
    770                 775                 780

Ser Ser Thr Ala Ala Lys Ser Phe Glu Asp Leu Thr Asp His Pro Val
785                 790                 795                 800

Thr Arg Ser Glu Lys Ala Ala Ser Phe Lys Leu Gln Arg Gln Asn Arg
                805                 810                 815

Val Asp Ser Lys Glu Thr Glu Cys
            820

<210>  503
<211>  423
<212>  PRT
<213>  Homo sapiens

<400>  503
```

```
Met Arg Ser Leu Gly Ala Asn Met Ala Ala Ala Leu Arg Ala Ala Gly
1               5                  10                  15

Val Leu Leu Arg Asp Pro Leu Ala Ser Ser Ser Trp Arg Val Cys Gln
            20                  25                  30

Pro Trp Arg Trp Lys Ser Gly Ala Ala Ala Ala Ala Val Thr Thr Glu
        35                  40                  45

Thr Ala Gln His Ala Gln Gly Ala Lys Pro Gln Val Gln Pro Gln Lys
    50                  55                  60

Arg Lys Pro Lys Thr Gly Ile Leu Met Leu Asn Met Gly Gly Pro Glu
65                  70                  75                  80

Thr Leu Gly Asp Val His Asp Phe Leu Leu Arg Leu Phe Leu Asp Arg
                85                  90                  95

Asp Leu Met Thr Leu Pro Ile Gln Asn Lys Leu Ala Pro Phe Ile Ala
            100                 105                 110

Lys Arg Arg Thr Pro Lys Ile Gln Glu Gln Tyr Arg Arg Ile Gly Gly
        115                 120                 125

Gly Ser Pro Ile Lys Ile Trp Thr Ser Lys Gln Gly Glu Gly Met Val
    130                 135                 140

Lys Leu Leu Asp Glu Leu Ser Pro Asn Thr Ala Pro His Lys Tyr Tyr
145                 150                 155                 160

Ile Gly Phe Arg Tyr Val His Pro Leu Thr Glu Glu Ala Ile Glu Glu
                165                 170                 175

Met Glu Arg Asp Gly Leu Glu Arg Ala Ile Ala Phe Thr Gln Tyr Pro
            180                 185                 190

Gln Tyr Ser Cys Ser Thr Thr Gly Ser Ser Leu Asn Ala Ile Tyr Arg
        195                 200                 205

Tyr Tyr Asn Gln Val Gly Arg Lys Pro Thr Met Lys Trp Ser Thr Ile
    210                 215                 220

Asp Arg Trp Pro Thr His His Leu Leu Ile Gln Cys Phe Ala Asp His
225                 230                 235                 240

Ile Leu Lys Glu Leu Asp His Phe Pro Leu Glu Lys Arg Ser Glu Val
                245                 250                 255

Val Ile Leu Phe Ser Ala His Ser Leu Pro Met Ser Val Val Asn Arg
            260                 265                 270
```

Gly Asp Pro Tyr Pro Gln Glu Val Ser Ala Thr Val Gln Lys Val Met
275 280 285

Glu Arg Leu Glu Tyr Cys Asn Pro Tyr Arg Leu Val Trp Gln Ser Lys
290 295 300

Val Gly Pro Met Pro Trp Leu Gly Pro Gln Thr Asp Glu Ser Ile Lys
305 310 315 320

Gly Leu Cys Glu Arg Gly Arg Lys Asn Ile Leu Leu Val Pro Ile Ala
325 330 335

Phe Thr Ser Asp His Ile Glu Thr Leu Tyr Glu Leu Asp Ile Glu Tyr
340 345 350

Ser Gln Val Leu Ala Lys Glu Cys Gly Val Glu Asn Ile Arg Arg Ala
355 360 365

Glu Ser Leu Asn Gly Asn Pro Leu Phe Ser Lys Ala Leu Ala Asp Leu
370 375 380

Val His Ser His Ile Gln Ser Asn Glu Leu Cys Ser Lys Gln Leu Thr
385 390 395 400

Leu Ser Cys Pro Leu Cys Val Asn Pro Val Cys Arg Glu Thr Lys Ser
405 410 415

Phe Phe Thr Ser Gln Gln Leu
420

<210> 504
<211> 307
<212> PRT
<213> Homo sapiens

<400> 504

Met Gly Gly Leu Thr Ala Ser Asp Val His Pro Thr Leu Gly Val Gln
1 5 10 15

Leu Phe Ser Ala Gly Ile Ala Ala Cys Leu Ala Asp Val Ile Thr Phe
20 25 30

Pro Leu Asp Thr Ala Lys Val Arg Leu Gln Val Gln Gly Glu Cys Pro
35 40 45

Thr Ser Ser Val Ile Arg Tyr Lys Gly Val Leu Gly Thr Ile Thr Ala
50 55 60

Val Val Lys Thr Glu Gly Arg Met Lys Leu Tyr Ser Gly Leu Pro Ala
65 70 75 80

Gly Leu Gln Arg Gln Ile Ser Ser Ala Ser Leu Arg Ile Gly Leu Tyr

85 90 95

Asp Thr Val Gln Glu Phe Leu Thr Ala Gly Lys Glu Thr Ala Pro Ser
100 105 110

Leu Gly Ser Lys Ile Leu Ala Gly Leu Thr Thr Gly Gly Val Ala Val
115 120 125

Phe Ile Gly Gln Pro Thr Glu Val Val Lys Val Arg Leu Gln Ala Gln
130 135 140

Ser His Leu His Gly Ile Lys Pro Arg Tyr Thr Gly Thr Tyr Asn Ala
145 150 155 160

Tyr Arg Ile Ile Ala Thr Thr Glu Gly Leu Thr Gly Leu Trp Lys Gly
165 170 175

Thr Thr Pro Asn Leu Met Arg Ser Val Ile Ile Asn Cys Thr Glu Leu
180 185 190

Val Thr Tyr Asp Leu Met Lys Glu Ala Phe Val Lys Asn Asn Ile Leu
195 200 205

Ala Asp Asp Val Pro Cys His Leu Val Ser Ala Leu Ile Ala Gly Phe
210 215 220

Cys Ala Thr Ala Met Ser Ser Pro Val Asp Val Val Lys Thr Arg Phe
225 230 235 240

Ile Asn Ser Pro Pro Gly Gln Tyr Lys Ser Val Pro Asn Cys Ala Met
245 250 255

Lys Val Phe Thr Asn Glu Gly Pro Thr Ala Phe Phe Lys Gly Leu Val
260 265 270

Pro Ser Phe Leu Arg Leu Gly Ser Trp Asn Val Ile Met Phe Val Cys
275 280 285

Phe Glu Gln Leu Lys Arg Glu Leu Ser Lys Ser Arg Gln Thr Met Asp
290 295 300

Cys Ala Thr
305

<210> 505
<211> 1118
<212> PRT
<213> Homo sapiens

<400> 505

Met Ala Arg Ser Pro Gly Arg Ala Tyr Ala Leu Leu Leu Leu Leu Ile
1 5 10 15

```
Cys Phe Asn Val Gly Ser Gly Leu His Leu Gln Val Leu Ser Thr Arg
            20                  25                  30

Asn Glu Asn Lys Leu Leu Pro Lys His Pro His Leu Val Arg Gln Lys
        35                  40                  45

Arg Ala Trp Ile Thr Ala Pro Val Ala Leu Arg Glu Gly Glu Asp Leu
    50                  55                  60

Ser Lys Lys Asn Pro Ile Ala Lys Ile His Ser Asp Leu Ala Glu Glu
65                  70                  75                  80

Arg Gly Leu Lys Ile Thr Tyr Lys Tyr Thr Gly Lys Gly Ile Thr Glu
                85                  90                  95

Pro Pro Phe Gly Ile Phe Val Phe Asn Lys Asp Thr Gly Glu Leu Asn
            100                 105                 110

Val Thr Ser Ile Leu Asp Arg Glu Glu Thr Pro Phe Phe Leu Leu Thr
        115                 120                 125

Gly Tyr Ala Leu Asp Ala Arg Gly Asn Asn Val Glu Lys Pro Leu Glu
    130                 135                 140

Leu Arg Ile Lys Val Leu Asp Ile Asn Asp Asn Glu Pro Val Phe Thr
145                 150                 155                 160

Gln Asp Val Phe Val Gly Ser Val Glu Glu Leu Ser Ala Ala His Thr
                165                 170                 175

Leu Val Met Lys Ile Asn Ala Thr Asp Ala Asp Glu Pro Asn Thr Leu
            180                 185                 190

Asn Ser Lys Ile Ser Tyr Arg Ile Val Ser Leu Glu Pro Ala Tyr Pro
        195                 200                 205

Pro Val Phe Tyr Leu Asn Lys Asp Thr Gly Glu Ile Tyr Thr Thr Ser
    210                 215                 220

Val Thr Leu Asp Arg Glu Glu His Ser Ser Tyr Thr Leu Thr Val Glu
225                 230                 235                 240

Ala Arg Asp Gly Asn Gly Glu Val Thr Asp Lys Pro Val Lys Gln Ala
                245                 250                 255

Gln Val Gln Ile Arg Ile Leu Asp Val Asn Asp Asn Ile Pro Val Val
            260                 265                 270

Glu Asn Lys Val Leu Glu Gly Met Val Glu Glu Asn Gln Val Asn Val
        275                 280                 285
```

```
Glu Val Thr Arg Ile Lys Val Phe Asp Ala Asp Glu Ile Gly Ser Asp
    290                 295                 300

Asn Trp Leu Ala Asn Phe Thr Phe Ala Ser Gly Asn Glu Gly Gly Tyr
305                 310                 315                 320

Phe His Ile Glu Thr Asp Ala Gln Thr Asn Glu Gly Ile Val Thr Leu
                325                 330                 335

Ile Lys Glu Val Asp Tyr Glu Glu Met Lys Asn Leu Asp Phe Ser Val
            340                 345                 350

Ile Val Ala Asn Lys Ala Ala Phe His Lys Ser Ile Arg Ser Lys Tyr
        355                 360                 365

Lys Pro Thr Pro Ile Pro Ile Lys Val Lys Val Lys Asn Val Lys Glu
    370                 375                 380

Gly Ile His Phe Lys Ser Ser Val Ile Ser Ile Tyr Val Ser Glu Ser
385                 390                 395                 400

Met Asp Arg Ser Ser Lys Gly Gln Ile Ile Gly Asn Phe Gln Ala Phe
                405                 410                 415

Asp Glu Asp Thr Gly Leu Pro Ala His Ala Arg Tyr Val Lys Leu Glu
            420                 425                 430

Asp Arg Asp Asn Trp Ile Ser Val Asp Ser Val Thr Ser Glu Ile Lys
        435                 440                 445

Leu Ala Lys Leu Pro Asp Phe Glu Ser Arg Tyr Val Gln Asn Gly Thr
    450                 455                 460

Tyr Thr Val Lys Ile Val Ala Ile Ser Glu Asp Tyr Pro Arg Lys Thr
465                 470                 475                 480

Ile Thr Gly Thr Val Leu Ile Asn Val Glu Asp Ile Asn Asp Asn Cys
                485                 490                 495

Pro Thr Leu Ile Glu Pro Val Gln Thr Ile Cys His Asp Ala Glu Tyr
            500                 505                 510

Val Asn Val Thr Ala Glu Asp Leu Asp Gly His Pro Asn Ser Gly Pro
        515                 520                 525

Phe Ser Phe Ser Val Ile Asp Lys Pro Pro Gly Met Ala Glu Lys Trp
    530                 535                 540

Lys Ile Ala Arg Gln Glu Ser Thr Ser Val Leu Leu Gln Gln Ser Glu
545                 550                 555                 560
```

```
Lys Lys Leu Gly Arg Ser Glu Ile Gln Phe Leu Ile Ser Asp Asn Gln
                565                 570                 575

Gly Phe Ser Cys Pro Glu Lys Gln Val Leu Thr Leu Thr Val Cys Glu
            580                 585                 590

Cys Leu His Gly Ser Gly Cys Arg Glu Ala Gln His Asp Ser Tyr Val
        595                 600                 605

Gly Leu Gly Pro Ala Ala Ile Ala Leu Met Ile Leu Ala Phe Leu Leu
    610                 615                 620

Leu Leu Leu Val Pro Leu Leu Leu Leu Met Cys His Cys Gly Lys Gly
625                 630                 635                 640

Ala Lys Gly Phe Thr Pro Ile Pro Gly Thr Ile Glu Met Leu His Pro
                645                 650                 655

Trp Asn Asn Glu Gly Ala Pro Pro Glu Asp Lys Val Val Pro Ser Phe
            660                 665                 670

Leu Pro Val Asp Gln Gly Gly Ser Leu Val Gly Arg Asn Gly Val Gly
        675                 680                 685

Gly Met Ala Lys Glu Ala Thr Met Lys Gly Ser Ser Ser Ala Ser Ile
    690                 695                 700

Val Lys Gly Gln His Glu Met Ser Glu Met Asp Gly Arg Trp Glu Glu
705                 710                 715                 720

His Arg Ser Leu Leu Ser Gly Arg Ala Thr Gln Phe Thr Gly Ala Thr
                725                 730                 735

Gly Ala Ile Met Thr Thr Glu Thr Thr Lys Thr Ala Arg Ala Thr Gly
            740                 745                 750

Ala Ser Arg Asp Met Ala Gly Ala Gln Ala Ala Ala Val Ala Leu Asn
        755                 760                 765

Glu Glu Phe Leu Arg Asn Tyr Phe Thr Asp Lys Ala Ala Ser Tyr Thr
    770                 775                 780

Glu Glu Asp Glu Asn His Thr Ala Lys Asp Cys Leu Leu Val Tyr Ser
785                 790                 795                 800

Gln Glu Glu Thr Glu Ser Leu Asn Ala Ser Ile Gly Cys Cys Ser Phe
                805                 810                 815

Ile Glu Gly Glu Leu Asp Asp Arg Phe Leu Asp Asp Leu Gly Leu Lys
            820                 825                 830
```

```
Phe Lys Thr Leu Ala Glu Val Cys Leu Gly Gln Lys Ile Asp Ile Asn
        835                 840                 845

Lys Glu Ile Glu Gln Arg Gln Lys Pro Ala Thr Glu Thr Ser Met Asn
    850                 855                 860

Thr Ala Ser His Ser Leu Cys Glu Gln Thr Met Val Asn Ser Glu Asn
865                 870                 875                 880

Thr Tyr Ser Ser Gly Ser Ser Phe Pro Val Pro Lys Ser Leu Gln Glu
                885                 890                 895

Ala Asn Ala Glu Lys Val Thr Gln Glu Ile Val Thr Glu Arg Ser Val
            900                 905                 910

Ser Ser Arg Gln Ala Gln Lys Val Ala Thr Pro Leu Pro Asp Pro Met
        915                 920                 925

Ala Ser Arg Asn Val Ile Ala Thr Glu Thr Ser Tyr Val Thr Gly Ser
    930                 935                 940

Thr Met Pro Pro Thr Thr Val Ile Leu Gly Pro Ser Gln Pro Gln Ser
945                 950                 955                 960

Leu Ile Val Thr Glu Arg Val Tyr Ala Pro Ala Ser Thr Leu Val Asp
                965                 970                 975

Gln Pro Tyr Ala Asn Glu Gly Thr Val Val Val Thr Glu Arg Val Ile
            980                 985                 990

Gln Pro His Gly Gly Gly Ser Asn  Pro Leu Glu Gly Thr  Gln His Leu
        995                 1000                1005

Gln Asp  Val Pro Tyr Val Met  Val Arg Glu Arg Glu  Ser Phe Leu
    1010                1015                1020

Ala Pro  Ser Ser Gly Val Gln  Pro Thr Leu Ala Met  Pro Asn Ile
    1025                1030                1035

Ala Val  Gly Gln Asn Val Thr  Val Thr Glu Arg Val  Leu Ala Pro
    1040                1045                1050

Ala Ser  Thr Leu Gln Ser Ser  Tyr Gln Ile Pro Thr  Glu Asn Ser
    1055                1060                1065

Met Thr  Ala Arg Asn Thr Thr  Val Ser Gly Ala Gly  Val Pro Gly
    1070                1075                1080

Pro Leu  Pro Asp Phe Gly Leu  Glu Glu Ser Gly His  Ser Asn Ser
    1085                1090                1095
```

```
Thr Ile  Thr Thr Ser Ser Thr  Arg Val Thr Lys His  Ser Thr Val
    1100                1105                1110


Gln His  Ser Tyr Ser
    1115


<210>  506
<211>  747
<212>  PRT
<213>  Homo sapiens

<400>  506

Met Asn His Ser Pro Leu Lys Thr Ala Leu Ala Tyr Glu Cys Phe Gln
1               5                   10                  15


Asp Gln Asp Asn Ser Thr Leu Ala Leu Pro Ser Asp Gln Lys Met Lys
            20                  25                  30


Thr Gly Thr Ser Gly Arg Gln Arg Val Gln Glu Gln Val Met Met Thr
        35                  40                  45


Val Lys Arg Gln Lys Ser Lys Ser Ser Gln Ser Ser Thr Leu Ser His
    50                  55                  60


Ser Asn Arg Gly Ser Met Tyr Asp Gly Leu Ala Asp Asn Tyr Asn Tyr
65                  70                  75                  80


Gly Thr Thr Ser Arg Ser Ser Tyr Tyr Ser Lys Phe Gln Ala Gly Asn
                85                  90                  95


Gly Ser Trp Gly Tyr Pro Ile Tyr Asn Gly Thr Leu Lys Arg Glu Pro
            100                 105                 110


Asp Asn Arg Arg Phe Ser Ser Tyr Ser Gln Met Glu Asn Trp Ser Arg
        115                 120                 125


His Tyr Pro Arg Gly Ser Cys Asn Thr Thr Gly Ala Gly Ser Asp Ile
    130                 135                 140


Cys Phe Met Gln Lys Ile Lys Ala Ser Arg Ser Glu Pro Asp Leu Tyr
145                 150                 155                 160


Cys Asp Pro Arg Gly Thr Leu Arg Lys Gly Thr Leu Gly Ser Lys Gly
                165                 170                 175


Gln Lys Thr Thr Gln Asn Arg Tyr Ser Phe Tyr Ser Thr Cys Ser Gly
            180                 185                 190


Gln Lys Ala Ile Lys Lys Cys Pro Val Arg Pro Pro Ser Cys Ala Ser
        195                 200                 205
```

```
Lys Gln Asp Pro Val Tyr Ile Pro Pro Ile Ser Cys Asn Lys Asp Leu
    210                 215                 220

Ser Phe Gly His Ser Arg Ala Ser Ser Lys Ile Cys Ser Glu Asp Ile
225                 230                 235                 240

Glu Cys Ser Gly Leu Thr Ile Pro Lys Ala Val Gln Tyr Leu Ser Ser
                245                 250                 255

Gln Asp Glu Lys Tyr Gln Ala Ile Gly Ala Tyr Tyr Ile Gln His Thr
            260                 265                 270

Cys Phe Gln Asp Glu Ser Ala Lys Gln Gln Val Tyr Gln Leu Gly Gly
        275                 280                 285

Ile Cys Lys Leu Val Asp Leu Leu Arg Ser Pro Asn Gln Asn Val Gln
    290                 295                 300

Gln Ala Ala Ala Gly Ala Leu Arg Asn Leu Val Phe Arg Ser Thr Thr
305                 310                 315                 320

Asn Lys Leu Glu Thr Arg Arg Gln Asn Gly Ile Arg Glu Ala Val Ser
                325                 330                 335

Leu Leu Arg Arg Thr Gly Asn Ala Glu Ile Gln Lys Gln Leu Thr Gly
            340                 345                 350

Leu Leu Trp Asn Leu Ser Ser Thr Asp Glu Leu Lys Glu Glu Leu Ile
        355                 360                 365

Ala Asp Ala Leu Pro Val Leu Ala Asp Arg Val Ile Ile Pro Phe Ser
    370                 375                 380

Gly Trp Cys Asp Gly Asn Ser Asn Met Ser Arg Glu Val Val Asp Pro
385                 390                 395                 400

Glu Val Phe Phe Asn Ala Thr Gly Cys Leu Arg Lys Arg Leu Gly Met
                405                 410                 415

Arg Glu Leu Leu Ala Leu Val Pro Gln Arg Ala Thr Ser Ser Arg Val
            420                 425                 430

Asn Leu Ser Ser Ala Asp Ala Gly Arg Gln Thr Met Arg Asn Tyr Ser
        435                 440                 445

Gly Leu Ile Asp Ser Leu Met Ala Tyr Val Gln Asn Cys Val Ala Ala
    450                 455                 460

Ser Arg Cys Asp Asp Lys Ser Val Glu Asn Cys Met Cys Val Leu His
465                 470                 475                 480
```

```
Asn Leu Ser Tyr Arg Leu Asp Ala Glu Val Pro Thr Arg Tyr Arg Gln
                485                 490                 495

Leu Glu Tyr Asn Ala Arg Asn Ala Tyr Thr Glu Lys Ser Ser Thr Gly
            500                 505                 510

Cys Phe Ser Asn Lys Ser Asp Lys Met Met Asn Asn Asn Tyr Asp Cys
        515                 520                 525

Pro Leu Pro Glu Glu Glu Thr Asn Pro Lys Gly Ser Gly Trp Leu Tyr
    530                 535                 540

His Ser Asp Ala Ile Arg Thr Tyr Leu Asn Leu Met Gly Lys Ser Lys
545                 550                 555                 560

Lys Asp Ala Thr Leu Glu Ala Cys Ala Gly Ala Leu Gln Asn Leu Thr
                565                 570                 575

Ala Ser Lys Gly Leu Met Ser Ser Gly Met Ser Gln Leu Ile Gly Leu
            580                 585                 590

Lys Glu Lys Gly Leu Pro Gln Ile Ala Arg Leu Leu Gln Ser Gly Asn
        595                 600                 605

Ser Asp Val Val Arg Ser Gly Ala Ser Leu Leu Ser Asn Met Ser Arg
    610                 615                 620

His Pro Leu Leu His Arg Val Met Gly Asn Gln Val Phe Pro Glu Val
625                 630                 635                 640

Thr Arg Leu Leu Thr Ser His Thr Gly Asn Thr Ser Asn Ser Glu Asp
                645                 650                 655

Ile Leu Ser Ser Ala Cys Tyr Thr Val Arg Asn Leu Met Ala Ser Gln
            660                 665                 670

Pro Gln Leu Ala Lys Gln Tyr Phe Ser Ser Ser Met Leu Asn Asn Ile
        675                 680                 685

Ile Asn Leu Cys Arg Ser Ser Ala Ser Pro Lys Ala Ala Glu Ala Ala
    690                 695                 700

Arg Leu Leu Leu Ser Asp Met Trp Ser Ser Lys Glu Leu Gln Gly Val
705                 710                 715                 720

Leu Arg Gln Gln Gly Phe Asp Arg Asn Met Leu Gly Thr Leu Ala Gly
                725                 730                 735

Ala Asn Ser Leu Arg Asn Phe Thr Ser Arg Phe
            740                 745
```

<210> 507
<211> 713
<212> PRT
<213> Homo sapiens

<400> 507

```
Met Ala Thr Gly Gln Asp Arg Val Val Ala Leu Val Asp Met Asp Cys
1               5                  10                  15

Phe Phe Val Gln Val Glu Gln Arg Gln Asn Pro His Leu Arg Asn Lys
            20                  25                  30

Pro Cys Ala Val Val Gln Tyr Lys Ser Trp Lys Gly Gly Gly Ile Ile
        35                  40                  45

Ala Val Ser Tyr Glu Ala Arg Ala Phe Gly Val Thr Arg Ser Met Trp
    50                  55                  60

Ala Asp Asp Ala Lys Lys Leu Cys Pro Asp Leu Leu Leu Ala Gln Val
65                  70                  75                  80

Arg Glu Ser Arg Gly Lys Ala Asn Leu Thr Lys Tyr Arg Glu Ala Ser
                85                  90                  95

Val Glu Val Met Glu Ile Met Ser Arg Phe Ala Val Ile Glu Arg Ala
            100                 105                 110

Ser Ile Asp Glu Ala Tyr Val Asp Leu Thr Ser Ala Val Gln Glu Arg
        115                 120                 125

Leu Gln Lys Leu Gln Gly Gln Pro Ile Ser Ala Asp Leu Leu Pro Ser
    130                 135                 140

Thr Tyr Ile Glu Gly Leu Pro Gln Gly Pro Thr Thr Ala Glu Glu Thr
145                 150                 155                 160

Val Gln Lys Glu Gly Met Arg Lys Gln Gly Leu Phe Gln Trp Leu Asp
                165                 170                 175

Ser Leu Gln Ile Asp Asn Leu Thr Ser Pro Asp Leu Gln Leu Thr Val
            180                 185                 190

Gly Ala Val Ile Val Glu Glu Met Arg Ala Ala Ile Glu Arg Glu Thr
        195                 200                 205

Gly Phe Gln Cys Ser Ala Gly Ile Ser His Asn Lys Val Leu Ala Lys
    210                 215                 220

Leu Ala Cys Gly Leu Asn Lys Pro Asn Arg Gln Thr Leu Val Ser His
225                 230                 235                 240
```

```
Gly Ser Val Pro Gln Leu Phe Ser Gln Met Pro Ile Arg Lys Ile Arg
                245                 250                 255

Ser Leu Gly Gly Lys Leu Gly Ala Ser Val Ile Glu Ile Leu Gly Ile
            260                 265                 270

Glu Tyr Met Gly Glu Leu Thr Gln Phe Thr Glu Ser Gln Leu Gln Ser
        275                 280                 285

His Phe Gly Glu Lys Asn Gly Ser Trp Leu Tyr Ala Met Cys Arg Gly
    290                 295                 300

Ile Glu His Asp Pro Val Lys Pro Arg Gln Leu Pro Lys Thr Ile Gly
305                 310                 315                 320

Cys Ser Lys Asn Phe Pro Gly Lys Thr Ala Leu Ala Thr Arg Glu Gln
                325                 330                 335

Val Gln Trp Trp Leu Leu Gln Leu Ala Gln Glu Leu Glu Glu Arg Leu
            340                 345                 350

Thr Lys Asp Arg Asn Asp Asn Asp Arg Val Ala Thr Gln Leu Val Val
        355                 360                 365

Ser Ile Arg Val Gln Gly Asp Lys Arg Leu Ser Ser Leu Arg Arg Cys
    370                 375                 380

Cys Ala Leu Thr Arg Tyr Asp Ala His Lys Met Ser His Asp Ala Phe
385                 390                 395                 400

Thr Val Ile Lys Asn Cys Asn Thr Ser Gly Ile Gln Thr Glu Trp Ser
                405                 410                 415

Pro Pro Leu Thr Met Leu Phe Leu Cys Ala Thr Lys Phe Ser Ala Ser
            420                 425                 430

Ala Pro Ser Ser Ser Thr Asp Ile Thr Ser Phe Leu Ser Ser Asp Pro
        435                 440                 445

Ser Ser Leu Pro Lys Val Pro Val Thr Ser Ser Glu Ala Lys Thr Gln
    450                 455                 460

Gly Ser Gly Pro Ala Val Thr Ala Thr Lys Lys Ala Thr Thr Ser Leu
465                 470                 475                 480

Glu Ser Phe Phe Gln Lys Ala Ala Glu Arg Gln Lys Val Lys Glu Ala
                485                 490                 495

Ser Leu Ser Ser Leu Thr Ala Pro Thr Gln Ala Pro Met Ser Asn Ser
            500                 505                 510
```

```
Pro Ser Lys Pro Ser Leu Pro Phe Gln Thr Ser Gln Ser Thr Gly Thr
        515                 520                 525

Glu Pro Phe Phe Lys Gln Lys Ser Leu Leu Leu Lys Gln Lys Gln Leu
    530                 535                 540

Asn Asn Ser Ser Val Ser Ser Pro Gln Gln Asn Pro Trp Ser Asn Cys
545                 550                 555                 560

Lys Ala Leu Pro Asn Ser Leu Pro Thr Glu Tyr Pro Gly Cys Val Pro
                565                 570                 575

Val Cys Glu Gly Val Ser Lys Leu Glu Glu Ser Ser Lys Ala Thr Pro
            580                 585                 590

Ala Glu Met Asp Leu Ala His Asn Ser Gln Ser Met His Ala Ser Ser
        595                 600                 605

Ala Ser Lys Ser Val Leu Glu Val Thr Gln Lys Ala Thr Pro Asn Pro
    610                 615                 620

Ser Leu Leu Ala Ala Glu Asp Gln Val Pro Cys Glu Lys Cys Gly Ser
625                 630                 635                 640

Leu Val Pro Val Trp Asp Met Pro Glu His Met Asp Tyr His Phe Ala
                645                 650                 655

Leu Glu Leu Gln Lys Ser Phe Leu Gln Pro His Ser Ser Asn Pro Gln
            660                 665                 670

Val Val Ser Ala Val Ser His Gln Gly Lys Arg Asn Pro Lys Ser Pro
        675                 680                 685

Leu Ala Cys Thr Asn Lys Arg Pro Arg Pro Glu Gly Met Gln Thr Leu
    690                 695                 700

Glu Ser Phe Phe Lys Pro Leu Thr His
705                 710


<210>  508
<211>  115
<212>  PRT
<213>  Homo sapiens

<400>  508

Met Ile Pro Ala Lys Asp Met Ala Lys Val Met Ile Val Met Leu Ala
1               5                   10                  15

Ile Cys Phe Leu Thr Lys Ser Asp Gly Lys Ser Val Lys Lys Arg Ser
            20                  25                  30

Val Ser Glu Ile Gln Leu Met His Asn Leu Gly Lys His Leu Asn Ser
```

35 40 45

Met Glu Arg Val Glu Trp Leu Arg Lys Lys Leu Gln Asp Val His Asn
50 55 60

Phe Val Ala Leu Gly Ala Pro Leu Ala Pro Arg Asp Ala Gly Ser Gln
65 70 75 80

Arg Pro Arg Lys Lys Glu Asp Asn Val Leu Val Glu Ser His Glu Lys
85 90 95

Ser Leu Gly Glu Ala Asp Lys Ala Asp Val Asn Val Leu Thr Lys Ala
100 105 110

Lys Ser Gln
115

<210> 509
<211> 730
<212> PRT
<213> Homo sapiens

<400> 509

Met Pro Gly Val Ala Arg Leu Pro Leu Leu Leu Gly Leu Leu Leu Leu
1 5 10 15

Pro Arg Pro Gly Arg Pro Leu Asp Leu Ala Asp Tyr Thr Tyr Asp Leu
20 25 30

Ala Glu Glu Asp Asp Ser Glu Pro Leu Asn Tyr Lys Asp Pro Cys Lys
35 40 45

Ala Ala Ala Phe Leu Gly Asp Ile Ala Leu Asp Glu Glu Asp Leu Arg
50 55 60

Ala Phe Gln Val Gln Gln Ala Val Asp Leu Arg Arg His Thr Ala Arg
65 70 75 80

Lys Ser Ser Ile Lys Ala Ala Val Pro Gly Asn Thr Ser Thr Pro Ser
85 90 95

Cys Gln Ser Thr Asn Gly Gln Pro Gln Arg Gly Ala Cys Gly Arg Trp
100 105 110

Arg Gly Arg Ser Arg Ser Arg Arg Ala Ala Thr Ser Arg Pro Glu Arg
115 120 125

Val Trp Pro Asp Gly Val Ile Pro Phe Val Ile Gly Gly Asn Phe Thr
130 135 140

Gly Ser Gln Arg Ala Val Phe Arg Gln Ala Met Arg His Trp Glu Lys
145 150 155 160

```
His Thr Cys Val Thr Phe Leu Glu Arg Thr Asp Glu Asp Ser Tyr Ile
                165                 170                 175

Val Phe Thr Tyr Arg Pro Cys Gly Cys Cys Ser Tyr Val Gly Arg Arg
            180                 185                 190

Gly Gly Gly Pro Gln Ala Ile Ser Ile Gly Lys Asn Cys Asp Lys Phe
        195                 200                 205

Gly Ile Val Val His Glu Leu Gly His Val Val Gly Phe Trp His Glu
    210                 215                 220

His Thr Arg Pro Asp Arg Asp Arg His Val Ser Ile Val Arg Glu Asn
225                 230                 235                 240

Ile Gln Pro Gly Gln Glu Tyr Asn Phe Leu Lys Met Glu Pro Gln Glu
                245                 250                 255

Val Glu Ser Leu Gly Glu Thr Tyr Asp Phe Asp Ser Ile Met His Tyr
            260                 265                 270

Ala Arg Asn Thr Phe Ser Arg Gly Ile Phe Leu Asp Thr Ile Val Pro
        275                 280                 285

Lys Tyr Glu Val Asn Gly Val Lys Pro Pro Ile Gly Gln Arg Thr Arg
    290                 295                 300

Leu Ser Lys Gly Asp Ile Ala Gln Ala Arg Lys Leu Tyr Lys Cys Pro
305                 310                 315                 320

Ala Cys Gly Glu Thr Leu Gln Asp Ser Thr Gly Asn Phe Ser Ser Pro
                325                 330                 335

Glu Tyr Pro Asn Gly Tyr Ser Ala His Met His Cys Val Trp Arg Ile
            340                 345                 350

Ser Val Thr Pro Gly Glu Lys Ile Ile Leu Asn Phe Thr Ser Leu Asp
        355                 360                 365

Leu Tyr Arg Ser Arg Leu Cys Trp Tyr Asp Tyr Val Glu Val Arg Asp
    370                 375                 380

Gly Phe Trp Arg Lys Ala Pro Leu Arg Gly Arg Phe Cys Gly Ser Lys
385                 390                 395                 400

Leu Pro Glu Pro Ile Val Ser Thr Asp Ser Arg Leu Trp Val Glu Phe
                405                 410                 415

Arg Ser Ser Ser Asn Trp Val Gly Lys Gly Phe Phe Ala Val Tyr Glu
            420                 425                 430
```

```
Ala Ile Cys Gly Gly Asp Val Lys Lys Asp Tyr Gly His Ile Gln Ser
        435                 440                 445

Pro Asn Tyr Pro Asp Asp Tyr Arg Pro Ser Lys Val Cys Ile Trp Arg
    450                 455                 460

Ile Gln Val Ser Glu Gly Phe His Val Gly Leu Thr Phe Gln Ser Phe
465                 470                 475                 480

Glu Ile Glu Arg His Asp Ser Cys Ala Tyr Asp Tyr Leu Glu Val Arg
                485                 490                 495

Asp Gly His Ser Glu Ser Ser Thr Leu Ile Gly Arg Tyr Cys Gly Tyr
            500                 505                 510

Glu Lys Pro Asp Asp Ile Lys Ser Thr Ser Ser Arg Leu Trp Leu Lys
        515                 520                 525

Phe Val Ser Asp Gly Ser Ile Asn Lys Ala Gly Phe Ala Val Asn Phe
    530                 535                 540

Phe Lys Glu Val Asp Glu Cys Ser Arg Pro Asn Arg Gly Gly Cys Glu
545                 550                 555                 560

Gln Arg Cys Leu Asn Thr Leu Gly Ser Tyr Lys Cys Ser Cys Asp Pro
                565                 570                 575

Gly Tyr Glu Leu Ala Pro Asp Lys Arg Arg Cys Glu Ala Ala Cys Gly
            580                 585                 590

Gly Phe Leu Thr Lys Leu Asn Gly Ser Ile Thr Ser Pro Gly Trp Pro
        595                 600                 605

Lys Glu Tyr Pro Pro Asn Lys Asn Cys Ile Trp Gln Leu Val Ala Pro
    610                 615                 620

Thr Gln Tyr Arg Ile Ser Leu Gln Phe Asp Phe Phe Glu Thr Glu Gly
625                 630                 635                 640

Asn Asp Val Cys Lys Tyr Asp Phe Val Glu Val Arg Ser Gly Leu Thr
                645                 650                 655

Ala Asp Ser Lys Leu His Gly Lys Phe Cys Gly Ser Glu Lys Pro Glu
            660                 665                 670

Val Ile Thr Ser Gln Tyr Asn Asn Met Arg Val Glu Phe Lys Ser Asp
        675                 680                 685

Asn Thr Val Ser Lys Lys Gly Phe Lys Ala His Phe Phe Ser Glu Lys
    690                 695                 700
```

```
Arg Pro Ala Leu Gln Pro Pro Arg Gly Arg Pro His Gln Leu Lys Phe
705                 710                 715                 720


Arg Val Gln Lys Arg Asn Arg Thr Pro Gln
                725                 730


<210>  510
<211>  302
<212>  PRT
<213>  Homo sapiens

<400>  510

Met Pro Gly Val Ala Arg Leu Pro Leu Leu Leu Gly Leu Leu Leu Leu
1               5                   10                  15


Pro Arg Pro Gly Arg Pro Leu Asp Leu Ala Asp Tyr Thr Tyr Asp Leu
            20                  25                  30


Ala Glu Glu Asp Asp Ser Glu Pro Leu Asn Tyr Lys Asp Pro Cys Lys
        35                  40                  45


Ala Ala Ala Phe Leu Gly Asp Ile Ala Leu Asp Glu Glu Asp Leu Arg
    50                  55                  60


Ala Phe Gln Val Gln Gln Ala Val Asp Leu Arg Arg His Thr Ala Arg
65                  70                  75                  80


Lys Ser Ser Ile Lys Ala Ala Val Pro Gly Asn Thr Ser Thr Pro Ser
                85                  90                  95


Cys Gln Ser Thr Asn Gly Gln Pro Gln Arg Gly Ala Cys Gly Arg Trp
            100                 105                 110


Arg Gly Arg Ser Arg Ser Arg Arg Ala Ala Thr Ser Arg Pro Glu Arg
        115                 120                 125


Val Trp Pro Asp Gly Val Ile Pro Phe Val Ile Gly Gly Asn Phe Thr
    130                 135                 140


Gly Ser Gln Arg Ala Val Phe Arg Gln Ala Met Arg His Trp Glu Lys
145                 150                 155                 160


His Thr Cys Val Thr Phe Leu Glu Arg Thr Asp Glu Asp Ser Tyr Ile
                165                 170                 175


Val Phe Thr Tyr Arg Pro Cys Gly Cys Cys Ser Tyr Val Gly Arg Arg
            180                 185                 190


Gly Gly Gly Pro Gln Ala Ile Ser Ile Gly Lys Asn Cys Asp Lys Phe
        195                 200                 205
```

```
Gly Ile Val Val His Glu Leu Gly His Val Val Gly Phe Trp His Glu
    210                 215                 220

His Thr Arg Pro Asp Arg Asp Arg His Val Ser Ile Val Arg Glu Asn
225                 230                 235                 240

Ile Gln Pro Gly Val Leu His Ser Ser Leu Leu Leu Leu Ser Cys Gly
                245                 250                 255

Ser Arg Asn Gly Ala Ser Phe Pro Cys Ser Leu Glu Ser Ser Thr His
            260                 265                 270

Gln Ala Leu Cys Trp Thr Gly Leu Phe Leu Arg Pro Ser Pro Phe Pro
        275                 280                 285

Arg Leu Pro Leu Ala Ala Pro Arg Thr Leu Arg Ala Gly Val
    290                 295                 300


<210>  511
<211>  622
<212>  PRT
<213>  Homo sapiens

<400>  511

Met Pro Gly Val Ala Arg Leu Pro Leu Leu Leu Gly Leu Leu Leu Leu
1               5                   10                  15

Pro Arg Pro Gly Arg Pro Leu Asp Leu Ala Asp Tyr Thr Tyr Asp Leu
            20                  25                  30

Ala Glu Glu Asp Asp Ser Glu Pro Leu Asn Tyr Lys Asp Pro Cys Lys
        35                  40                  45

Ala Ala Ala Phe Leu Gly Asp Ile Ala Leu Asp Glu Glu Asp Leu Arg
    50                  55                  60

Ala Phe Gln Val Gln Gln Ala Val Asp Leu Arg Arg His Thr Ala Arg
65                  70                  75                  80

Lys Ser Ser Ile Lys Ala Ala Val Pro Gly Asn Thr Ser Thr Pro Ser
                85                  90                  95

Cys Gln Ser Thr Asn Gly Gln Pro Gln Arg Gly Ala Cys Gly Arg Trp
            100                 105                 110

Arg Gly Arg Ser Arg Ser Arg Arg Ala Ala Thr Ser Arg Pro Glu Arg
        115                 120                 125

Val Trp Pro Asp Gly Val Ile Pro Phe Val Ile Gly Gly Asn Phe Thr
    130                 135                 140
```

```
Gly Ser Gln Arg Ala Val Phe Arg Gln Ala Met Arg His Trp Glu Lys
145                 150                 155                 160

His Thr Cys Val Thr Phe Leu Glu Arg Thr Asp Glu Asp Ser Tyr Ile
                165                 170                 175

Val Phe Thr Tyr Arg Pro Cys Gly Cys Cys Ser Tyr Val Gly Arg Arg
            180                 185                 190

Gly Gly Gly Pro Gln Ala Ile Ser Ile Gly Lys Asn Cys Asp Lys Phe
        195                 200                 205

Gly Ile Val Val His Glu Leu Gly His Val Val Gly Phe Trp His Glu
    210                 215                 220

His Thr Arg Pro Asp Arg Asp Arg His Val Ser Ile Val Arg Glu Asn
225                 230                 235                 240

Ile Gln Pro Gly Gln Glu Tyr Asn Phe Leu Lys Met Glu Pro Gln Glu
                245                 250                 255

Val Glu Ser Leu Gly Glu Thr Tyr Asp Phe Asp Ser Ile Met His Tyr
            260                 265                 270

Ala Arg Asn Thr Phe Ser Arg Gly Ile Phe Leu Asp Thr Ile Val Pro
        275                 280                 285

Lys Tyr Glu Val Asn Gly Val Lys Pro Pro Ile Gly Gln Arg Thr Arg
    290                 295                 300

Leu Ser Lys Gly Asp Ile Ala Gln Ala Arg Lys Leu Tyr Lys Cys Pro
305                 310                 315                 320

Ala Cys Gly Glu Thr Leu Gln Asp Ser Thr Gly Asn Phe Ser Ser Pro
                325                 330                 335

Glu Tyr Pro Asn Gly Tyr Ser Ala His Met His Cys Val Trp Arg Ile
            340                 345                 350

Ser Val Thr Pro Gly Glu Lys Ile Ile Leu Asn Phe Thr Ser Leu Asp
        355                 360                 365

Leu Tyr Arg Ser Arg Leu Cys Trp Tyr Asp Tyr Val Glu Val Arg Asp
    370                 375                 380

Gly Phe Trp Arg Lys Ala Pro Leu Arg Gly Arg Phe Cys Gly Ser Lys
385                 390                 395                 400

Leu Pro Glu Pro Ile Val Ser Thr Asp Ser Arg Leu Trp Val Glu Phe
                405                 410                 415
```

Arg Ser Ser Ser Asn Trp Val Gly Lys Gly Phe Phe Ala Val Tyr Glu
420 425 430

Ala Ile Cys Gly Gly Asp Val Lys Lys Asp Tyr Gly His Ile Gln Ser
435 440 445

Pro Asn Tyr Pro Asp Asp Tyr Arg Pro Ser Lys Val Cys Ile Trp Arg
450 455 460

Ile Gln Val Ser Glu Gly Phe His Val Gly Leu Thr Phe Gln Ser Phe
465 470 475 480

Glu Ile Glu Arg His Asp Ser Cys Ala Tyr Asp Tyr Leu Glu Val Arg
485 490 495

Asp Gly His Ser Glu Ser Ser Thr Leu Ile Gly Arg Tyr Cys Gly Tyr
500 505 510

Glu Lys Pro Asp Asp Ile Lys Ser Thr Ser Ser Arg Leu Trp Leu Lys
515 520 525

Phe Val Ser Asp Gly Ser Ile Asn Lys Ala Gly Phe Ala Val Asn Phe
530 535 540

Phe Lys Glu Val Asp Glu Cys Ser Arg Pro Asn Arg Gly Gly Cys Glu
545 550 555 560

Gln Arg Cys Leu Asn Thr Leu Gly Ser Tyr Lys Cys Ser Cys Asp Pro
565 570 575

Gly Tyr Glu Leu Ala Pro Asp Lys Arg Arg Cys Glu Gly Cys Tyr Asp
580 585 590

Leu Gln Val Gly Lys Pro Leu Leu Trp Asp Arg His Cys Phe Arg Leu
595 600 605

Ser Thr His Gly Pro Glu Met Leu Gly Thr Ala Leu Arg Gly
610 615 620

<210> 512
<211> 717
<212> PRT
<213> Homo sapiens

<400> 512

Met Pro Gly Val Ala Arg Leu Pro Leu Leu Leu Gly Leu Leu Leu Leu
1 5 10 15

Pro Arg Pro Gly Arg Pro Leu Asp Leu Ala Asp Tyr Thr Tyr Asp Leu
20 25 30

Ala Glu Glu Asp Asp Ser Glu Pro Leu Asn Tyr Lys Asp Pro Cys Lys

```
        35                  40                  45

Ala Ala Ala Phe Leu Gly Asp Ile Ala Leu Asp Glu Glu Asp Leu Arg
    50                  55                  60

Ala Phe Gln Val Gln Gln Ala Val Asp Leu Arg Arg His Thr Ala Arg
65                  70                  75                  80

Lys Ser Ser Ile Lys Ala Ala Val Pro Gly Asn Thr Ser Thr Pro Ser
                85                  90                  95

Cys Gln Ser Thr Asn Gly Gln Pro Gln Arg Gly Ala Cys Gly Arg Trp
            100                 105                 110

Arg Gly Arg Ser Arg Ser Arg Arg Ala Ala Thr Ser Arg Pro Glu Arg
        115                 120                 125

Val Trp Pro Asp Gly Val Ile Pro Phe Val Ile Gly Gly Asn Phe Thr
    130                 135                 140

Gly Ser Gln Arg Ala Val Phe Arg Gln Ala Met Arg His Trp Glu Lys
145                 150                 155                 160

His Thr Cys Val Thr Phe Leu Glu Arg Thr Asp Glu Asp Ser Tyr Ile
                165                 170                 175

Val Phe Thr Tyr Arg Pro Cys Gly Cys Cys Ser Tyr Val Gly Arg Arg
            180                 185                 190

Gly Gly Gly Pro Gln Ala Ile Ser Ile Gly Lys Asn Cys Asp Lys Phe
        195                 200                 205

Gly Ile Val Val His Glu Leu Gly His Val Val Gly Phe Trp His Glu
    210                 215                 220

His Thr Arg Pro Asp Arg Asp Arg His Val Ser Ile Val Arg Glu Asn
225                 230                 235                 240

Ile Gln Pro Gly Gln Glu Tyr Asn Phe Leu Lys Met Glu Pro Gln Glu
                245                 250                 255

Val Glu Ser Leu Gly Glu Thr Tyr Asp Phe Asp Ser Ile Met His Tyr
            260                 265                 270

Ala Arg Asn Thr Phe Ser Arg Gly Ile Phe Leu Asp Thr Ile Val Pro
        275                 280                 285

Lys Tyr Glu Val Asn Gly Val Lys Pro Pro Ile Gly Gln Arg Thr Arg
    290                 295                 300

Leu Ser Lys Gly Asp Ile Ala Gln Ala Arg Lys Leu Tyr Lys Cys Pro
```

```
305                 310                 315                 320

Ala Cys Gly Glu Thr Leu Gln Asp Ser Thr Gly Asn Phe Ser Ser Pro
                325                 330                 335

Glu Tyr Pro Asn Gly Tyr Ser Ala His Met His Cys Val Trp Arg Ile
            340                 345                 350

Ser Val Thr Pro Gly Glu Lys Ile Ile Leu Asn Phe Thr Ser Leu Asp
        355                 360                 365

Leu Tyr Arg Ser Arg Leu Cys Trp Tyr Asp Tyr Val Glu Val Arg Asp
    370                 375                 380

Gly Phe Trp Arg Lys Ala Pro Leu Arg Gly Arg Phe Cys Gly Ser Lys
385                 390                 395                 400

Leu Pro Glu Pro Ile Val Ser Thr Asp Ser Arg Leu Trp Val Glu Phe
                405                 410                 415

Arg Ser Ser Ser Asn Trp Val Gly Lys Gly Phe Phe Ala Val Tyr Glu
            420                 425                 430

Ala Ile Cys Gly Gly Asp Val Lys Lys Asp Tyr Gly His Ile Gln Ser
        435                 440                 445

Pro Asn Tyr Pro Asp Asp Tyr Arg Pro Ser Lys Val Cys Ile Trp Arg
    450                 455                 460

Ile Gln Val Ser Glu Gly Phe His Val Gly Leu Thr Phe Gln Ser Phe
465                 470                 475                 480

Glu Ile Glu Arg His Asp Ser Cys Ala Tyr Asp Tyr Leu Glu Val Arg
                485                 490                 495

Asp Gly His Ser Glu Ser Ser Thr Leu Ile Gly Arg Tyr Cys Gly Tyr
            500                 505                 510

Glu Lys Pro Asp Asp Ile Lys Ser Thr Ser Ser Arg Leu Trp Leu Lys
        515                 520                 525

Phe Val Ser Asp Gly Ser Ile Asn Lys Ala Gly Phe Ala Val Asn Phe
    530                 535                 540

Phe Lys Glu Val Asp Glu Cys Ser Arg Pro Asn Arg Gly Gly Cys Glu
545                 550                 555                 560

Gln Arg Cys Leu Asn Thr Leu Gly Ser Tyr Lys Cys Ser Cys Asp Pro
                565                 570                 575

Gly Tyr Glu Leu Ala Pro Asp Lys Arg Arg Cys Glu Ala Ala Cys Gly
```

580 585 590

Gly Phe Leu Thr Lys Leu Asn Gly Ser Ile Thr Ser Pro Gly Trp Pro
595 600 605

Lys Glu Tyr Pro Pro Asn Lys Asn Cys Ile Trp Gln Leu Val Ala Pro
610 615 620

Thr Gln Tyr Arg Ile Ser Leu Gln Phe Asp Phe Phe Glu Thr Glu Gly
625 630 635 640

Asn Asp Val Cys Lys Tyr Asp Phe Val Glu Val Arg Ser Gly Leu Thr
645 650 655

Ala Asp Ser Lys Leu His Gly Lys Phe Cys Gly Ser Glu Lys Pro Glu
660 665 670

Val Ile Thr Ser Gln Tyr Asn Asn Met Arg Val Glu Phe Lys Ser Asp
675 680 685

Asn Thr Val Ser Lys Lys Gly Phe Lys Ala His Phe Phe Ser Gly Gly
690 695 700

Glu Leu Phe Gly Leu Leu Gly His Pro Pro Arg Arg Pro
705 710 715

<210> 513
<211> 823
<212> PRT
<213> Homo sapiens

<400> 513

Met Pro Gly Val Ala Arg Leu Pro Leu Leu Leu Gly Leu Leu Leu Leu
1 5 10 15

Pro Arg Pro Gly Arg Pro Leu Asp Leu Ala Asp Tyr Thr Tyr Asp Leu
20 25 30

Ala Glu Glu Asp Asp Ser Glu Pro Leu Asn Tyr Lys Asp Pro Cys Lys
35 40 45

Ala Ala Ala Phe Leu Gly Asp Ile Ala Leu Asp Glu Glu Asp Leu Arg
50 55 60

Ala Phe Gln Val Gln Gln Ala Val Asp Leu Arg Arg His Thr Ala Arg
65 70 75 80

Lys Ser Ser Ile Lys Ala Ala Val Pro Gly Asn Thr Ser Thr Pro Ser
85 90 95

Cys Gln Ser Thr Asn Gly Gln Pro Gln Arg Gly Ala Cys Gly Arg Trp
100 105 110

```
Arg Gly Arg Ser Arg Ser Arg Arg Ala Ala Thr Ser Arg Pro Glu Arg
        115                 120                 125

Val Trp Pro Asp Gly Val Ile Pro Phe Val Ile Gly Gly Asn Phe Thr
    130                 135                 140

Gly Ser Gln Arg Ala Val Phe Arg Gln Ala Met Arg His Trp Glu Lys
145                 150                 155                 160

His Thr Cys Val Thr Phe Leu Glu Arg Thr Asp Glu Asp Ser Tyr Ile
                165                 170                 175

Val Phe Thr Tyr Arg Pro Cys Gly Cys Cys Ser Tyr Val Gly Arg Arg
            180                 185                 190

Gly Gly Gly Pro Gln Ala Ile Ser Ile Gly Lys Asn Cys Asp Lys Phe
        195                 200                 205

Gly Ile Val Val His Glu Leu Gly His Val Val Gly Phe Trp His Glu
    210                 215                 220

His Thr Arg Pro Asp Arg Asp Arg His Val Ser Ile Val Arg Glu Asn
225                 230                 235                 240

Ile Gln Pro Gly Gln Glu Tyr Asn Phe Leu Lys Met Glu Pro Gln Glu
                245                 250                 255

Val Glu Ser Leu Gly Glu Thr Tyr Asp Phe Asp Ser Ile Met His Tyr
            260                 265                 270

Ala Arg Asn Thr Phe Ser Arg Gly Ile Phe Leu Asp Thr Ile Val Pro
        275                 280                 285

Lys Tyr Glu Val Asn Gly Val Lys Pro Pro Ile Gly Gln Arg Thr Arg
    290                 295                 300

Leu Ser Lys Gly Asp Ile Ala Gln Ala Arg Lys Leu Tyr Lys Cys Pro
305                 310                 315                 320

Ala Cys Gly Glu Thr Leu Gln Asp Ser Thr Gly Asn Phe Ser Ser Pro
                325                 330                 335

Glu Tyr Pro Asn Gly Tyr Ser Ala His Met His Cys Val Trp Arg Ile
            340                 345                 350

Ser Val Thr Pro Gly Glu Lys Ile Ile Leu Asn Phe Thr Ser Leu Asp
        355                 360                 365

Leu Tyr Arg Ser Arg Leu Cys Trp Tyr Asp Tyr Val Glu Val Arg Asp
    370                 375                 380
```

```
Gly Phe Trp Arg Lys Ala Pro Leu Arg Gly Arg Phe Cys Gly Ser Lys
385                 390                 395                 400

Leu Pro Glu Pro Ile Val Ser Thr Asp Ser Arg Leu Trp Val Glu Phe
                405                 410                 415

Arg Ser Ser Ser Asn Trp Val Gly Lys Gly Phe Phe Ala Val Tyr Glu
            420                 425                 430

Ala Ile Cys Gly Gly Asp Val Lys Lys Asp Tyr Gly His Ile Gln Ser
        435                 440                 445

Pro Asn Tyr Pro Asp Asp Tyr Arg Pro Ser Lys Val Cys Ile Trp Arg
    450                 455                 460

Ile Gln Val Ser Glu Gly Phe His Val Gly Leu Thr Phe Gln Ser Phe
465                 470                 475                 480

Glu Ile Glu Arg His Asp Ser Cys Ala Tyr Asp Tyr Leu Glu Val Arg
                485                 490                 495

Asp Gly His Ser Glu Ser Ser Thr Leu Ile Gly Arg Tyr Cys Gly Tyr
            500                 505                 510

Glu Lys Pro Asp Asp Ile Lys Ser Thr Ser Ser Arg Leu Trp Leu Lys
        515                 520                 525

Phe Val Ser Asp Gly Ser Ile Asn Lys Ala Gly Phe Ala Val Asn Phe
    530                 535                 540

Phe Lys Glu Val Asp Glu Cys Ser Arg Pro Asn Arg Gly Gly Cys Glu
545                 550                 555                 560

Gln Arg Cys Leu Asn Thr Leu Gly Ser Tyr Lys Cys Ser Cys Asp Pro
                565                 570                 575

Gly Tyr Glu Leu Ala Pro Asp Lys Arg Arg Cys Glu Ala Ala Cys Gly
            580                 585                 590

Gly Phe Leu Thr Lys Leu Asn Gly Ser Ile Thr Ser Pro Gly Trp Pro
        595                 600                 605

Lys Glu Tyr Pro Pro Asn Lys Asn Cys Ile Trp Gln Leu Val Ala Pro
    610                 615                 620

Thr Gln Tyr Arg Ile Ser Leu Gln Phe Asp Phe Phe Glu Thr Glu Gly
625                 630                 635                 640

Asn Asp Val Cys Lys Tyr Asp Phe Val Glu Val Arg Ser Gly Leu Thr
                645                 650                 655
```

```
Ala Asp Ser Lys Leu His Gly Lys Phe Cys Gly Ser Glu Lys Pro Glu
            660                 665                 670

Val Ile Thr Ser Gln Tyr Asn Asn Met Arg Val Glu Phe Lys Ser Asp
        675                 680                 685

Asn Thr Val Ser Lys Lys Gly Phe Lys Ala His Phe Phe Ser Val Leu
    690                 695                 700

Glu Gly Ala Gly Asp Arg His Ser His Leu Ser Gly Leu Glu Leu Leu
705                 710                 715                 720

Leu Cys Pro His Ala Leu Val Asp Thr Val Pro Ala Pro Pro Ser Ala
                725                 730                 735

Leu His Gly Asp Thr His Ala His Thr His Thr His Val His Thr His
            740                 745                 750

Cys Pro Ile Ala Gln Glu Thr Cys Arg Gly Pro Pro Leu Gly Ala Ser
        755                 760                 765

Arg Leu Ser Pro Gln Gly Pro Gly His Leu Thr Leu Ala Pro Gln Glu
    770                 775                 780

Gly Ser Tyr Leu Asp Phe Trp Asp Thr His Arg Gly Asp Pro Lys Pro
785                 790                 795                 800

Arg Arg Arg Arg Lys Ser Leu Lys Thr Phe Ser Leu Thr Pro Ala Thr
                805                 810                 815

Phe Arg Gly Ile Trp Ala Leu
            820


<210>  514
<211>  472
<212>  PRT
<213>  Homo sapiens

<400>  514

Met Ala Gly Ala Ser Arg Leu Leu Phe Leu Trp Leu Gly Cys Phe Cys
1               5                   10                  15

Val Ser Leu Ala Gln Gly Glu Arg Pro Lys Pro Pro Phe Pro Glu Leu
            20                  25                  30

Arg Lys Ala Val Pro Gly Asp Arg Thr Ala Gly Gly Gly Pro Asp Ser
        35                  40                  45

Glu Leu Gln Pro Gln Asp Lys Val Ser Glu His Met Leu Arg Leu Tyr
    50                  55                  60
```

```
Asp Arg Tyr Ser Thr Val Gln Ala Ala Arg Thr Pro Gly Ser Leu Glu
65                  70                  75                  80

Gly Gly Ser Gln Pro Trp Arg Pro Arg Leu Leu Arg Glu Gly Asn Thr
                85                  90                  95

Val Arg Ser Phe Arg Ala Ala Ala Ala Glu Thr Leu Glu Arg Lys Gly
            100                 105                 110

Leu Tyr Ile Phe Asn Leu Thr Ser Leu Thr Lys Ser Glu Asn Ile Leu
        115                 120                 125

Ser Ala Thr Leu Tyr Phe Cys Ile Gly Glu Leu Gly Asn Ile Ser Leu
    130                 135                 140

Ser Cys Pro Val Ser Gly Gly Cys Ser His His Ala Gln Arg Lys His
145                 150                 155                 160

Ile Gln Ile Asp Leu Ser Ala Trp Thr Leu Lys Phe Ser Arg Asn Gln
                165                 170                 175

Ser Gln Leu Leu Gly His Leu Ser Val Asp Met Ala Lys Ser His Arg
            180                 185                 190

Asp Ile Met Ser Trp Leu Ser Lys Asp Ile Thr Gln Leu Leu Arg Lys
        195                 200                 205

Ala Lys Glu Asn Glu Glu Phe Leu Ile Gly Phe Asn Ile Thr Ser Lys
    210                 215                 220

Gly Arg Gln Leu Pro Lys Arg Arg Leu Pro Phe Pro Glu Pro Tyr Ile
225                 230                 235                 240

Leu Val Tyr Ala Asn Asp Ala Ala Ile Ser Glu Pro Glu Ser Val Val
                245                 250                 255

Ser Ser Leu Gln Gly His Arg Asn Phe Pro Thr Gly Thr Val Pro Lys
            260                 265                 270

Trp Asp Ser His Ile Arg Ala Ala Leu Ser Ile Glu Arg Arg Lys Lys
        275                 280                 285

Arg Ser Thr Gly Val Leu Leu Pro Leu Gln Asn Asn Glu Leu Pro Gly
    290                 295                 300

Ala Glu Tyr Gln Tyr Lys Lys Asp Glu Val Trp Glu Glu Arg Lys Pro
305                 310                 315                 320

Tyr Lys Thr Leu Gln Ala Gln Ala Pro Glu Lys Ser Lys Asn Lys Lys
                325                 330                 335
```

Lys Gln Arg Lys Gly Pro His Arg Lys Ser Gln Thr Leu Gln Phe Asp
340 345 350

Glu Gln Thr Leu Lys Lys Ala Arg Arg Lys Gln Trp Ile Glu Pro Arg
355 360 365

Asn Cys Ala Arg Arg Tyr Leu Lys Val Asp Phe Ala Asp Ile Gly Trp
370 375 380

Ser Glu Trp Ile Ile Ser Pro Lys Ser Phe Asp Ala Tyr Tyr Cys Ser
385 390 395 400

Gly Ala Cys Gln Phe Pro Met Pro Lys Ser Leu Lys Pro Ser Asn His
405 410 415

Ala Thr Ile Gln Ser Ile Val Arg Ala Val Gly Val Val Pro Gly Ile
420 425 430

Pro Glu Pro Cys Cys Val Pro Glu Lys Met Ser Ser Leu Ser Ile Leu
435 440 445

Phe Phe Asp Glu Asn Lys Asn Val Val Leu Lys Val Tyr Pro Asn Met
450 455 460

Thr Val Glu Ser Cys Ala Cys Arg
465 470

<210> 515
<211> 417
<212> PRT
<213> Homo sapiens

<400> 515

Met His Leu Thr Val Phe Leu Leu Lys Gly Ile Val Gly Phe Leu Trp
1 5 10 15

Ser Cys Trp Val Leu Val Gly Tyr Ala Lys Gly Gly Leu Gly Asp Asn
20 25 30

His Val His Ser Ser Phe Ile Tyr Arg Arg Leu Arg Asn His Glu Arg
35 40 45

Arg Glu Ile Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu Pro His Arg
50 55 60

Pro Arg Pro Phe Ser Pro Gly Lys Gln Ala Ser Ser Ala Pro Leu Phe
65 70 75 80

Met Leu Asp Leu Tyr Asn Ala Met Thr Asn Glu Glu Asn Pro Glu Glu
85 90 95

```
Ser Glu Tyr Ser Val Arg Ala Ser Leu Ala Glu Glu Thr Arg Gly Ala
            100                 105                 110

Arg Lys Gly Tyr Pro Ala Ser Pro Asn Gly Tyr Pro Arg Arg Ile Gln
        115                 120                 125

Leu Ser Arg Thr Thr Pro Leu Thr Thr Gln Ser Pro Pro Leu Ala Ser
    130                 135                 140

Leu His Asp Thr Asn Phe Leu Asn Asp Ala Asp Met Val Met Ser Phe
145                 150                 155                 160

Val Asn Leu Val Glu Arg Asp Lys Asp Phe Ser His Gln Arg Arg His
                165                 170                 175

Tyr Lys Glu Phe Arg Phe Asp Leu Thr Gln Ile Pro His Gly Glu Ala
            180                 185                 190

Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Asp Arg Ser Asn Asn Arg
        195                 200                 205

Phe Glu Asn Glu Thr Ile Lys Ile Ser Ile Tyr Gln Ile Ile Lys Glu
    210                 215                 220

Tyr Thr Asn Arg Asp Ala Asp Leu Phe Leu Leu Asp Thr Arg Lys Ala
225                 230                 235                 240

Gln Ala Leu Asp Val Gly Trp Leu Val Phe Asp Ile Thr Val Thr Ser
                245                 250                 255

Asn His Trp Val Ile Asn Pro Gln Asn Asn Leu Gly Leu Gln Leu Cys
            260                 265                 270

Ala Glu Thr Gly Asp Gly Arg Ser Ile Asn Val Lys Ser Ala Gly Leu
        275                 280                 285

Val Gly Arg Gln Gly Pro Gln Ser Lys Gln Pro Phe Met Val Ala Phe
    290                 295                 300

Phe Lys Ala Ser Glu Val Leu Leu Arg Ser Val Arg Ala Ala Asn Lys
305                 310                 315                 320

Arg Lys Asn Gln Asn Arg Asn Lys Ser Ser Ser His Gln Asp Ser Ser
                325                 330                 335

Arg Met Ser Ser Val Gly Asp Tyr Asn Thr Ser Glu Gln Lys Gln Ala
            340                 345                 350

Cys Lys Lys His Glu Leu Tyr Val Ser Phe Arg Asp Leu Gly Trp Gln
        355                 360                 365
```

Val His Leu Met Phe Pro Asp His Val Pro Lys Pro Cys Cys Ala Pro
370 375 380

Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn
385 390 395 400

Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ser Cys Gly Cys
405 410 415

His

<210> 516
<211> 475
<212> PRT
<213> Homo sapiens

<400> 516

Met Glu Ser Lys Ala Leu Leu Val Leu Thr Leu Ala Val Trp Leu Gln
1 5 10 15

Ser Leu Thr Ala Ser Arg Gly Gly Val Ala Ala Ala Asp Gln Arg Arg
20 25 30

Asp Phe Ile Asp Ile Glu Ser Lys Phe Ala Leu Arg Thr Pro Glu Asp
35 40 45

Thr Ala Glu Asp Thr Cys His Leu Ile Pro Gly Val Ala Glu Ser Val
50 55 60

Ala Thr Cys His Phe Asn His Ser Ser Lys Thr Phe Met Val Ile His
65 70 75 80

Gly Trp Thr Val Thr Gly Met Tyr Glu Ser Trp Val Pro Lys Leu Val
85 90 95

Ala Ala Leu Tyr Lys Arg Glu Pro Asp Ser Asn Val Ile Val Val Asp
100 105 110

Trp Leu Ser Arg Ala Gln Glu His Tyr Pro Val Ser Ala Gly Tyr Thr
115 120 125

Lys Leu Val Gly Gln Asp Val Ala Arg Phe Ile Asn Trp Met Glu Glu
130 135 140

Glu Phe Asn Tyr Pro Leu Asp Asn Val His Leu Leu Gly Tyr Ser Leu
145 150 155 160

Gly Ala His Ala Ala Gly Ile Ala Gly Ser Leu Thr Asn Lys Lys Val
165 170 175

Asn Arg Ile Thr Gly Leu Asp Pro Ala Gly Pro Asn Phe Glu Tyr Ala

```
            180                 185                 190

Glu Ala Pro Ser Arg Leu Ser Pro Asp Asp Ala Asp Phe Val Asp Val
        195                 200                 205

Leu His Thr Phe Thr Arg Gly Ser Pro Gly Arg Ser Ile Gly Ile Gln
    210                 215                 220

Lys Pro Val Gly His Val Asp Ile Tyr Pro Asn Gly Gly Thr Phe Gln
225                 230                 235                 240

Pro Gly Cys Asn Ile Gly Glu Ala Ile Arg Val Ile Ala Glu Arg Gly
                245                 250                 255

Leu Gly Asp Val Asp Gln Leu Val Lys Cys Ser His Glu Arg Ser Ile
            260                 265                 270

His Leu Phe Ile Asp Ser Leu Leu Asn Glu Glu Asn Pro Ser Lys Ala
        275                 280                 285

Tyr Arg Cys Ser Ser Lys Glu Ala Phe Glu Lys Gly Leu Cys Leu Ser
    290                 295                 300

Cys Arg Lys Asn Arg Cys Asn Asn Leu Gly Tyr Glu Ile Asn Lys Val
305                 310                 315                 320

Arg Ala Lys Arg Ser Ser Lys Met Tyr Leu Lys Thr Arg Ser Gln Met
                325                 330                 335

Pro Tyr Lys Val Phe His Tyr Gln Val Lys Ile His Phe Ser Gly Thr
            340                 345                 350

Glu Ser Glu Thr His Thr Asn Gln Ala Phe Glu Ile Ser Leu Tyr Gly
        355                 360                 365

Thr Val Ala Glu Ser Glu Asn Ile Pro Phe Thr Leu Pro Glu Val Ser
    370                 375                 380

Thr Asn Lys Thr Tyr Ser Phe Leu Ile Tyr Thr Glu Val Asp Ile Gly
385                 390                 395                 400

Glu Leu Leu Met Leu Lys Leu Lys Trp Lys Ser Asp Ser Tyr Phe Ser
                405                 410                 415

Trp Ser Asp Trp Trp Ser Ser Pro Gly Phe Ala Ile Gln Lys Ile Arg
            420                 425                 430

Val Lys Ala Gly Glu Thr Gln Lys Lys Val Ile Phe Cys Ser Arg Glu
        435                 440                 445

Lys Val Ser His Leu Gln Lys Gly Lys Ala Pro Ala Val Phe Val Lys
```

450 455 460

Cys His Asp Lys Ser Leu Asn Lys Lys Ser Gly
465 470 475

<210> 517
<211> 499
<212> PRT
<213> Homo sapiens

<400> 517

Met Asp Thr Ser Pro Leu Cys Phe Ser Ile Leu Leu Val Leu Cys Ile
1 5 10 15

Phe Ile Gln Ser Ser Ala Leu Gly Gln Ser Leu Lys Pro Glu Pro Phe
20 25 30

Gly Arg Arg Ala Gln Ala Val Glu Thr Asn Lys Thr Leu His Glu Met
35 40 45

Lys Thr Arg Phe Leu Leu Phe Gly Glu Thr Asn Gln Gly Cys Gln Ile
50 55 60

Arg Ile Asn His Pro Asp Thr Leu Gln Glu Cys Gly Phe Asn Ser Ser
65 70 75 80

Leu Pro Leu Val Met Ile Ile His Gly Trp Ser Val Asp Gly Val Leu
85 90 95

Glu Asn Trp Ile Trp Gln Met Val Ala Ala Leu Lys Ser Gln Pro Ala
100 105 110

Gln Pro Val Asn Val Gly Leu Val Asp Trp Ile Thr Leu Ala His Asp
115 120 125

His Tyr Thr Ile Ala Val Arg Asn Thr Arg Leu Val Gly Lys Glu Val
130 135 140

Ala Ala Leu Leu Arg Trp Leu Glu Glu Ser Val Gln Leu Ser Arg Ser
145 150 155 160

His Val His Leu Ile Gly Tyr Ser Leu Gly Ala His Val Ser Gly Phe
165 170 175

Ala Gly Ser Ser Ile Gly Gly Thr His Lys Ile Gly Arg Ile Thr Gly
180 185 190

Leu Asp Ala Ala Gly Pro Leu Phe Glu Gly Ser Ala Pro Ser Asn Arg
195 200 205

Leu Ser Pro Asp Asp Ala Asn Phe Val Asp Ala Ile His Thr Phe Thr
210 215 220

```
Arg Glu His Met Gly Leu Ser Val Gly Ile Lys Gln Pro Ile Gly His
225                 230                 235                 240

Tyr Asp Phe Tyr Pro Asn Gly Gly Ser Phe Gln Pro Gly Cys His Phe
                245                 250                 255

Leu Glu Leu Tyr Arg His Ile Ala Gln His Gly Phe Asn Ala Ile Thr
            260                 265                 270

Gln Thr Ile Lys Cys Ser His Glu Arg Ser Val His Leu Phe Ile Asp
        275                 280                 285

Ser Leu Leu His Ala Gly Thr Gln Ser Met Ala Tyr Pro Cys Gly Asp
    290                 295                 300

Met Asn Ser Phe Ser Gln Gly Leu Cys Leu Ser Cys Lys Lys Gly Arg
305                 310                 315                 320

Cys Asn Thr Leu Gly Tyr His Val Arg Gln Glu Pro Arg Ser Lys Ser
                325                 330                 335

Lys Arg Leu Phe Leu Val Thr Arg Ala Gln Ser Pro Phe Lys Val Tyr
            340                 345                 350

His Tyr Gln Phe Lys Ile Gln Phe Ile Asn Gln Thr Glu Thr Pro Ile
        355                 360                 365

Gln Thr Thr Phe Thr Met Ser Leu Leu Gly Thr Lys Glu Lys Met Gln
    370                 375                 380

Lys Ile Pro Ile Thr Leu Gly Lys Gly Ile Ala Ser Asn Lys Thr Tyr
385                 390                 395                 400

Ser Phe Leu Ile Thr Leu Asp Val Asp Ile Gly Glu Leu Ile Met Ile
                405                 410                 415

Lys Phe Lys Trp Glu Asn Ser Ala Val Trp Ala Asn Val Trp Asp Thr
            420                 425                 430

Val Gln Thr Ile Ile Pro Trp Ser Thr Gly Pro Arg His Ser Gly Leu
        435                 440                 445

Val Leu Lys Thr Ile Arg Val Lys Ala Gly Glu Thr Gln Gln Arg Met
    450                 455                 460

Thr Phe Cys Ser Glu Asn Thr Asp Asp Leu Leu Leu Arg Pro Thr Gln
465                 470                 475                 480

Glu Lys Ile Phe Val Lys Cys Glu Ile Lys Ser Lys Thr Ser Lys Arg
                485                 490                 495
```

Lys Ile Arg

<210> 518
<211> 465
<212> PRT
<213> Homo sapiens

<400> 518

Met Leu Pro Leu Trp Thr Leu Ser Leu Leu Leu Gly Ala Val Ala Gly
1 5 10 15

Lys Glu Val Cys Tyr Glu Arg Leu Gly Cys Phe Ser Asp Asp Ser Pro
20 25 30

Trp Ser Gly Ile Thr Glu Arg Pro Leu His Ile Leu Pro Trp Ser Pro
35 40 45

Lys Asp Val Asn Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro Asn
50 55 60

Asn Phe Gln Glu Val Ala Ala Asp Ser Ser Ser Ile Ser Gly Ser Asn
65 70 75 80

Phe Lys Thr Asn Arg Lys Thr Arg Phe Ile Ile His Gly Phe Ile Asp
85 90 95

Lys Gly Glu Glu Asn Trp Leu Ala Asn Val Cys Lys Asn Leu Phe Lys
100 105 110

Val Glu Ser Val Asn Cys Ile Cys Val Asp Trp Lys Gly Gly Ser Arg
115 120 125

Thr Gly Tyr Thr Gln Ala Ser Gln Asn Ile Arg Ile Val Gly Ala Glu
130 135 140

Val Ala Tyr Phe Val Glu Phe Leu Gln Ser Ala Phe Gly Tyr Ser Pro
145 150 155 160

Ser Asn Val His Val Ile Gly His Ser Leu Gly Ala His Ala Ala Gly
165 170 175

Glu Ala Gly Arg Arg Thr Asn Gly Thr Ile Gly Arg Ile Thr Gly Leu
180 185 190

Asp Pro Ala Glu Pro Cys Phe Gln Gly Thr Pro Glu Leu Val Arg Leu
195 200 205

Asp Pro Ser Asp Ala Lys Phe Val Asp Val Ile His Thr Asp Gly Ala
210 215 220

```
Pro Ile Val Pro Asn Leu Gly Phe Gly Met Ser Gln Val Val Gly His
225                 230                 235                 240

Leu Asp Phe Phe Pro Asn Gly Gly Val Glu Met Pro Gly Cys Lys Lys
                245                 250                 255

Asn Ile Leu Ser Gln Ile Val Asp Ile Asp Gly Ile Trp Glu Gly Thr
            260                 265                 270

Arg Asp Phe Ala Ala Cys Asn His Leu Arg Ser Tyr Lys Tyr Tyr Thr
        275                 280                 285

Asp Ser Ile Val Asn Pro Asp Gly Phe Ala Gly Phe Pro Cys Ala Ser
    290                 295                 300

Tyr Asn Val Phe Thr Ala Asn Lys Cys Phe Pro Cys Pro Ser Gly Gly
305                 310                 315                 320

Cys Pro Gln Met Gly His Tyr Ala Asp Arg Tyr Pro Gly Lys Thr Asn
                325                 330                 335

Asp Val Gly Gln Lys Phe Tyr Leu Asp Thr Gly Asp Ala Ser Asn Phe
            340                 345                 350

Ala Arg Trp Arg Tyr Lys Val Ser Val Thr Leu Ser Gly Lys Lys Val
        355                 360                 365

Thr Gly His Ile Leu Val Ser Leu Phe Gly Asn Lys Gly Asn Ser Lys
    370                 375                 380

Gln Tyr Glu Ile Phe Lys Gly Thr Leu Lys Pro Asp Ser Thr His Ser
385                 390                 395                 400

Asn Glu Phe Asp Ser Asp Val Asp Val Gly Asp Leu Gln Met Val Lys
                405                 410                 415

Phe Ile Trp Tyr Asn Asn Val Ile Asn Pro Thr Leu Pro Arg Val Gly
            420                 425                 430

Ala Ser Lys Ile Ile Val Glu Thr Asn Val Gly Lys Gln Phe Asn Phe
        435                 440                 445

Cys Ser Pro Glu Thr Val Arg Glu Glu Val Leu Leu Thr Leu Thr Pro
    450                 455                 460

Cys
465


<210>  519
<211>  500
<212>  PRT
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<213> Homo sapiens

<400> 519

```
Met Ser Asn Ser Val Pro Leu Leu Cys Phe Trp Ser Leu Cys Tyr Cys
1               5                  10                  15

Phe Ala Ala Gly Ser Pro Val Pro Phe Gly Pro Glu Gly Arg Leu Glu
            20                  25                  30

Asp Lys Leu His Lys Pro Lys Ala Thr Gln Thr Glu Val Lys Pro Ser
        35                  40                  45

Val Arg Phe Asn Leu Arg Thr Ser Lys Asp Pro Glu His Glu Gly Cys
    50                  55                  60

Tyr Leu Ser Val Gly His Ser Gln Pro Leu Glu Asp Cys Ser Phe Asn
65                  70                  75                  80

Met Thr Ala Lys Thr Phe Phe Ile Ile His Gly Trp Thr Met Ser Gly
                85                  90                  95

Ile Phe Glu Asn Trp Leu His Lys Leu Val Ser Ala Leu His Thr Arg
            100                 105                 110

Glu Lys Asp Ala Asn Val Val Val Val Asp Trp Leu Pro Leu Ala His
        115                 120                 125

Gln Leu Tyr Thr Asp Ala Val Asn Asn Thr Arg Val Val Gly His Ser
    130                 135                 140

Ile Ala Arg Met Leu Asp Trp Leu Gln Glu Lys Asp Asp Phe Ser Leu
145                 150                 155                 160

Gly Asn Val His Leu Ile Gly Tyr Ser Leu Gly Ala His Val Ala Gly
                165                 170                 175

Tyr Ala Gly Asn Phe Val Lys Gly Thr Val Gly Arg Ile Thr Gly Leu
            180                 185                 190

Asp Pro Ala Gly Pro Met Phe Glu Gly Ala Asp Ile His Lys Arg Leu
        195                 200                 205

Ser Pro Asp Asp Ala Asp Phe Val Asp Val Leu His Thr Tyr Thr Arg
    210                 215                 220

Ser Phe Gly Leu Ser Ile Gly Ile Gln Met Pro Val Gly His Ile Asp
225                 230                 235                 240

Ile Tyr Pro Asn Gly Gly Asp Phe Gln Pro Gly Cys Gly Leu Asn Asp
                245                 250                 255
```

```
Val Leu Gly Ser Ile Ala Tyr Gly Thr Ile Thr Glu Val Val Lys Cys
            260                 265                 270

Glu His Glu Arg Ala Val His Leu Phe Val Asp Ser Leu Val Asn Gln
        275                 280                 285

Asp Lys Pro Ser Phe Ala Phe Gln Cys Thr Asp Ser Asn Arg Phe Lys
    290                 295                 300

Lys Gly Ile Cys Leu Ser Cys Arg Lys Asn Arg Cys Asn Ser Ile Gly
305                 310                 315                 320

Tyr Asn Ala Lys Lys Met Arg Asn Lys Arg Asn Ser Lys Met Tyr Leu
                325                 330                 335

Lys Thr Arg Ala Gly Met Pro Phe Arg Val Tyr His Tyr Gln Met Lys
            340                 345                 350

Ile His Val Phe Ser Tyr Lys Asn Met Gly Glu Ile Glu Pro Thr Phe
        355                 360                 365

Tyr Val Thr Leu Tyr Gly Thr Asn Ala Asp Ser Gln Thr Leu Pro Leu
    370                 375                 380

Glu Ile Val Glu Arg Ile Glu Gln Asn Ala Thr Asn Thr Phe Leu Val
385                 390                 395                 400

Tyr Thr Glu Glu Asp Leu Gly Asp Leu Leu Lys Ile Gln Leu Thr Trp
                405                 410                 415

Glu Gly Ala Ser Gln Ser Trp Tyr Asn Leu Trp Lys Glu Phe Arg Ser
            420                 425                 430

Tyr Leu Ser Gln Pro Arg Asn Pro Gly Arg Glu Leu Asn Ile Arg Arg
        435                 440                 445

Ile Arg Val Lys Ser Gly Glu Thr Gln Arg Lys Leu Thr Phe Cys Thr
    450                 455                 460

Glu Asp Pro Glu Asn Thr Ser Ile Ser Pro Gly Arg Glu Leu Trp Phe
465                 470                 475                 480

Arg Lys Cys Arg Asp Gly Trp Arg Met Lys Asn Glu Thr Ser Pro Thr
                485                 490                 495

Val Glu Leu Pro
            500
```

<210> 520
<211> 399
<212> PRT
<213> Homo sapiens

<400> 520

```
Met Lys Met Arg Phe Leu Gly Leu Val Val Cys Leu Val Leu Trp Thr
1               5                  10                  15

Leu His Ser Glu Gly Ser Gly Gly Lys Leu Thr Ala Val Asp Pro Glu
            20                  25                  30

Thr Asn Met Asn Val Ser Glu Ile Ile Ser Tyr Trp Gly Phe Pro Ser
        35                  40                  45

Glu Glu Tyr Leu Val Glu Thr Glu Asp Gly Tyr Ile Leu Cys Leu Asn
    50                  55                  60

Arg Ile Pro His Gly Arg Lys Asn His Ser Asp Lys Gly Pro Lys Pro
65                  70                  75                  80

Val Val Phe Leu Gln His Gly Leu Leu Ala Asp Ser Ser Asn Trp Val
                85                  90                  95

Thr Asn Leu Ala Asn Ser Ser Leu Gly Phe Ile Leu Ala Asp Ala Gly
            100                 105                 110

Phe Asp Val Trp Met Gly Asn Ser Arg Gly Asn Thr Trp Ser Arg Lys
        115                 120                 125

His Lys Thr Leu Ser Val Ser Gln Asp Glu Phe Trp Ala Phe Ser Tyr
    130                 135                 140

Asp Glu Met Ala Lys Tyr Asp Leu Pro Ala Ser Ile Asn Phe Ile Leu
145                 150                 155                 160

Asn Lys Thr Gly Gln Glu Gln Val Tyr Tyr Val Gly His Ser Gln Gly
                165                 170                 175

Thr Thr Ile Gly Phe Ile Ala Phe Ser Gln Ile Pro Glu Leu Ala Lys
            180                 185                 190

Arg Ile Lys Met Phe Phe Ala Leu Gly Pro Val Ala Ser Val Ala Phe
        195                 200                 205

Cys Thr Ser Pro Met Ala Lys Leu Gly Arg Leu Pro Asp His Leu Ile
    210                 215                 220

Lys Asp Leu Phe Gly Asp Lys Glu Phe Leu Pro Gln Ser Ala Phe Leu
225                 230                 235                 240

Lys Trp Leu Gly Thr His Val Cys Thr His Val Ile Leu Lys Glu Leu
                245                 250                 255

Cys Gly Asn Leu Cys Phe Leu Leu Cys Gly Phe Asn Glu Arg Asn Leu
```

260 265 270

Asn Met Ser Arg Val Asp Val Tyr Thr Thr His Ser Pro Ala Gly Thr
275 280 285

Ser Val Gln Asn Met Leu His Trp Ser Gln Ala Val Lys Phe Gln Lys
290 295 300

Phe Gln Ala Phe Asp Trp Gly Ser Ser Ala Lys Asn Tyr Phe His Tyr
305 310 315 320

Asn Gln Ser Tyr Pro Pro Thr Tyr Asn Val Lys Asp Met Leu Val Pro
325 330 335

Thr Ala Val Trp Ser Gly Gly His Asp Trp Leu Ala Asp Val Tyr Asp
340 345 350

Val Asn Ile Leu Leu Thr Gln Ile Thr Asn Leu Val Phe His Glu Ser
355 360 365

Ile Pro Glu Trp Glu His Leu Asp Phe Ile Trp Gly Leu Asp Ala Pro
370 375 380

Trp Arg Leu Tyr Asn Lys Ile Ile Asn Leu Met Arg Lys Tyr Gln
385 390 395

<210> 521
<211> 1076
<212> PRT
<213> Homo sapiens

<400> 521

Met Glu Pro Gly Ser Lys Ser Val Ser Arg Ser Asp Trp Gln Pro Glu
1 5 10 15

Pro His Gln Arg Pro Ile Thr Pro Leu Glu Pro Gly Pro Glu Lys Thr
20 25 30

Pro Ile Ala Gln Pro Glu Ser Lys Thr Leu Gln Gly Ser Asn Thr Gln
35 40 45

Gln Lys Pro Ala Ser Asn Gln Arg Pro Leu Thr Gln Gln Glu Thr Pro
50 55 60

Ala Gln His Asp Ala Glu Ser Gln Lys Glu Pro Arg Ala Gln Gln Lys
65 70 75 80

Ser Ala Ser Gln Glu Glu Phe Leu Ala Pro Gln Lys Pro Ala Pro Gln
85 90 95

Gln Ser Pro Tyr Ile Gln Arg Val Leu Leu Thr Gln Gln Glu Ala Ala
100 105 110

```
Ser Gln Gln Gly Pro Gly Leu Gly Lys Glu Ser Ile Thr Gln Gln Glu
        115                 120                 125

Pro Ala Leu Arg Gln Arg His Val Ala Gln Pro Gly Pro Gly Pro Gly
    130                 135                 140

Glu Pro Pro Pro Ala Gln Gln Glu Ala Glu Ser Thr Pro Ala Ala Gln
145                 150                 155                 160

Ala Lys Pro Gly Ala Lys Arg Glu Pro Ser Ala Pro Thr Glu Ser Thr
                165                 170                 175

Ser Gln Glu Thr Pro Glu Gln Ser Asp Lys Gln Thr Thr Pro Val Gln
            180                 185                 190

Gly Ala Lys Ser Lys Gln Gly Ser Leu Thr Glu Leu Gly Phe Leu Thr
        195                 200                 205

Lys Leu Gln Glu Leu Ser Ile Gln Arg Ser Ala Leu Glu Trp Lys Ala
    210                 215                 220

Leu Ser Glu Trp Val Thr Asp Ser Glu Ser Glu Ser Asp Val Gly Ser
225                 230                 235                 240

Ser Ser Asp Thr Asp Ser Pro Ala Thr Met Gly Gly Met Val Ala Gln
                245                 250                 255

Gly Val Lys Leu Gly Phe Lys Gly Lys Ser Gly Tyr Lys Val Met Ser
            260                 265                 270

Gly Tyr Ser Gly Thr Ser Pro His Glu Lys Thr Ser Ala Arg Asn His
        275                 280                 285

Arg His Tyr Gln Asp Thr Ala Ser Arg Leu Ile His Asn Met Asp Leu
    290                 295                 300

Arg Thr Met Thr Gln Ser Leu Val Thr Leu Ala Glu Asp Asn Ile Ala
305                 310                 315                 320

Phe Phe Ser Ser Gln Gly Pro Gly Glu Thr Ala Gln Arg Leu Ser Gly
                325                 330                 335

Val Phe Ala Gly Val Arg Glu Gln Ala Leu Gly Leu Glu Pro Ala Leu
            340                 345                 350

Gly Arg Leu Leu Gly Val Ala His Leu Phe Asp Leu Asp Pro Glu Thr
        355                 360                 365

Pro Ala Asn Gly Tyr Arg Ser Leu Val His Thr Ala Arg Cys Cys Leu
    370                 375                 380
```

```
Ala His Leu Leu His Lys Ser Arg Tyr Val Ala Ser Asn Arg Arg Ser
385                 390                 395                 400

Ile Phe Phe Arg Thr Ser His Asn Leu Ala Glu Leu Glu Ala Tyr Leu
                405                 410                 415

Ala Ala Leu Thr Gln Leu Arg Ala Leu Val Tyr Tyr Ala Gln Arg Leu
            420                 425                 430

Leu Val Thr Asn Arg Pro Gly Val Leu Phe Phe Glu Gly Asp Glu Gly
        435                 440                 445

Leu Thr Ala Asp Phe Leu Arg Glu Tyr Val Thr Leu His Lys Gly Cys
    450                 455                 460

Phe Tyr Gly Arg Cys Leu Gly Phe Gln Phe Thr Pro Ala Ile Arg Pro
465                 470                 475                 480

Phe Leu Gln Thr Ile Ser Ile Gly Leu Val Ser Phe Gly Glu His Tyr
                485                 490                 495

Lys Arg Asn Glu Thr Gly Leu Ser Val Ala Ala Ser Ser Leu Phe Thr
            500                 505                 510

Ser Gly Arg Phe Ala Ile Asp Pro Glu Leu Arg Gly Ala Glu Phe Glu
        515                 520                 525

Arg Ile Thr Gln Asn Leu Asp Val His Phe Trp Lys Ala Phe Trp Asn
    530                 535                 540

Ile Thr Glu Met Glu Val Leu Ser Ser Leu Ala Asn Met Ala Ser Ala
545                 550                 555                 560

Thr Val Arg Val Ser Arg Leu Leu Ser Leu Pro Pro Glu Ala Phe Glu
                565                 570                 575

Met Pro Leu Thr Ala Asp Pro Thr Leu Thr Val Thr Ile Ser Pro Pro
            580                 585                 590

Leu Ala His Thr Gly Pro Gly Pro Val Leu Val Arg Leu Ile Ser Tyr
        595                 600                 605

Asp Leu Arg Glu Gly Gln Asp Ser Glu Glu Leu Ser Ser Leu Ile Lys
    610                 615                 620

Ser Asn Gly Gln Arg Ser Leu Glu Leu Trp Pro Arg Pro Gln Gln Ala
625                 630                 635                 640

Pro Arg Ser Arg Ser Leu Ile Val His Phe His Gly Gly Gly Phe Val
                645                 650                 655
```

```
Ala Gln Thr Ser Arg Ser His Glu Pro Tyr Leu Lys Ser Trp Ala Gln
            660                 665                 670

Glu Leu Gly Ala Pro Ile Ile Ser Ile Asp Tyr Ser Leu Ala Pro Glu
        675                 680                 685

Ala Pro Phe Pro Arg Ala Leu Glu Glu Cys Phe Phe Ala Tyr Cys Trp
    690                 695                 700

Ala Ile Lys His Cys Ala Leu Leu Gly Ser Thr Gly Glu Arg Ile Cys
705                 710                 715                 720

Leu Ala Gly Asp Ser Ala Gly Gly Asn Leu Cys Phe Thr Val Ala Leu
                725                 730                 735

Arg Ala Ala Ala Tyr Gly Val Arg Val Pro Asp Gly Ile Met Ala Ala
            740                 745                 750

Tyr Pro Ala Thr Met Leu Gln Pro Ala Ala Ser Pro Ser Arg Leu Leu
        755                 760                 765

Ser Leu Met Asp Pro Leu Leu Pro Leu Ser Val Leu Ser Lys Cys Val
    770                 775                 780

Ser Ala Tyr Ala Gly Ala Lys Thr Glu Asp His Ser Asn Ser Asp Gln
785                 790                 795                 800

Lys Ala Leu Gly Met Met Gly Leu Val Arg Arg Asp Thr Ala Leu Leu
                805                 810                 815

Leu Arg Asp Phe Arg Leu Gly Ala Ser Ser Trp Leu Asn Ser Phe Leu
            820                 825                 830

Glu Leu Ser Gly Arg Lys Ser Gln Lys Met Ser Glu Pro Ile Ala Glu
        835                 840                 845

Pro Met Arg Arg Ser Val Ser Glu Ala Ala Leu Ala Gln Pro Gln Gly
    850                 855                 860

Pro Leu Gly Thr Asp Ser Leu Lys Asn Leu Thr Leu Arg Asp Leu Ser
865                 870                 875                 880

Leu Arg Gly Asn Ser Glu Thr Ser Ser Asp Thr Pro Glu Met Ser Leu
                885                 890                 895

Ser Ala Glu Thr Leu Ser Pro Ser Thr Pro Ser Asp Val Asn Phe Leu
            900                 905                 910

Leu Pro Pro Glu Asp Ala Gly Glu Glu Ala Glu Ala Lys Asn Glu Leu
        915                 920                 925
```

```
Ser Pro Met Asp Arg Gly Leu Gly Val Arg Ala Ala Phe Pro Glu Gly
    930                 935                 940

Phe His Pro Arg Arg Ser Ser Gln Gly Ala Thr Gln Met Pro Leu Tyr
945                 950                 955                 960

Ser Ser Pro Ile Val Lys Asn Pro Phe Met Ser Pro Leu Leu Ala Pro
                965                 970                 975

Asp Ser Met Leu Lys Ser Leu Pro Pro Val His Ile Val Ala Cys Ala
            980                 985                 990

Leu Asp Pro Met Leu Asp Asp Ser  Val Met Leu Ala Arg  Arg Leu Arg
        995                 1000                1005

Asn Leu  Gly Gln Pro Val Thr  Leu Arg Val Val Glu  Asp Leu Pro
    1010                1015                1020

His Gly  Phe Leu Thr Leu Ala  Ala Leu Cys Arg Glu  Thr Arg Gln
    1025                1030                1035

Ala Ala  Glu Leu Cys Val Glu  Arg Ile Arg Leu Val  Leu Thr Pro
    1040                1045                1050

Pro Ala  Gly Ala Gly Pro Ser  Gly Glu Thr Gly Ala  Ala Gly Val
    1055                1060                1065

Asp Gly  Gly Cys Gly Gly Arg  His
    1070                1075


<210>  522
<211>  398
<212>  PRT
<213>  Homo sapiens

<400>  522

Met Trp Leu Leu Leu Thr Met Ala Ser Leu Ile Ser Val Leu Gly Thr
1               5                   10                  15

Thr His Gly Leu Phe Gly Lys Leu His Pro Gly Ser Pro Glu Val Thr
            20                  25                  30

Met Asn Ile Ser Gln Met Ile Thr Tyr Trp Gly Tyr Pro Asn Glu Glu
        35                  40                  45

Tyr Glu Val Val Thr Glu Asp Gly Tyr Ile Leu Glu Val Asn Arg Ile
    50                  55                  60

Pro Tyr Gly Lys Lys Asn Ser Gly Asn Thr Gly Gln Arg Pro Val Val
65                  70                  75                  80
```

```
Phe Leu Gln His Gly Leu Leu Ala Ser Ala Thr Asn Trp Ile Ser Asn
                85                  90                  95

Leu Pro Asn Asn Ser Leu Ala Phe Ile Leu Ala Asp Ala Gly Tyr Asp
            100                 105                 110

Val Trp Leu Gly Asn Ser Arg Gly Asn Thr Trp Ala Arg Arg Asn Leu
        115                 120                 125

Tyr Tyr Ser Pro Asp Ser Val Glu Phe Trp Ala Phe Ser Phe Asp Glu
    130                 135                 140

Met Ala Lys Tyr Asp Leu Pro Ala Thr Ile Asp Phe Ile Val Lys Lys
145                 150                 155                 160

Thr Gly Gln Lys Gln Leu His Tyr Val Gly His Ser Gln Gly Thr Thr
                165                 170                 175

Ile Gly Phe Ile Ala Phe Ser Thr Asn Pro Ser Leu Ala Lys Arg Ile
            180                 185                 190

Lys Thr Phe Tyr Ala Leu Ala Pro Val Ala Thr Val Lys Tyr Thr Lys
        195                 200                 205

Ser Leu Ile Asn Lys Leu Arg Phe Val Pro Gln Ser Leu Phe Lys Phe
    210                 215                 220

Ile Phe Gly Asp Lys Ile Phe Tyr Pro His Asn Phe Phe Asp Gln Phe
225                 230                 235                 240

Leu Ala Thr Glu Val Cys Ser Arg Glu Met Leu Asn Leu Leu Cys Ser
                245                 250                 255

Asn Ala Leu Phe Ile Ile Cys Gly Phe Asp Ser Lys Asn Phe Asn Thr
            260                 265                 270

Ser Arg Leu Asp Val Tyr Leu Ser His Asn Pro Ala Gly Thr Ser Val
        275                 280                 285

Gln Asn Met Phe His Trp Thr Gln Ala Val Lys Ser Gly Lys Phe Gln
    290                 295                 300

Ala Tyr Asp Trp Gly Ser Pro Val Gln Asn Arg Met His Tyr Asp Gln
305                 310                 315                 320

Ser Gln Pro Pro Tyr Tyr Asn Val Thr Ala Met Asn Val Pro Ile Ala
                325                 330                 335

Val Trp Asn Gly Gly Lys Asp Leu Leu Ala Asp Pro Gln Asp Val Gly
            340                 345                 350
```

```
Leu Leu Leu Pro Lys Leu Pro Asn Leu Ile Tyr His Lys Glu Ile Pro
        355                 360                 365

Phe Tyr Asn His Leu Asp Phe Ile Trp Ala Met Asp Ala Pro Gln Glu
    370                 375                 380

Val Tyr Asn Asp Ile Val Ser Met Ile Ser Glu Asp Lys Lys
385                 390                 395


<210>  523
<211>  467
<212>  PRT
<213>  Homo sapiens

<400>  523

Met Leu Ile Phe Trp Thr Ile Thr Leu Phe Leu Leu Gly Ala Ala Lys
1               5                   10                  15

Gly Lys Glu Val Cys Tyr Glu Asp Leu Gly Cys Phe Ser Asp Thr Glu
            20                  25                  30

Pro Trp Gly Gly Thr Ala Ile Arg Pro Leu Lys Ile Leu Pro Trp Ser
        35                  40                  45

Pro Glu Lys Ile Gly Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro
    50                  55                  60

Asn Asn Phe Gln Ile Leu Leu Leu Ser Asp Pro Ser Thr Ile Glu Ala
65                  70                  75                  80

Ser Asn Phe Gln Met Asp Arg Lys Thr Arg Phe Ile Ile His Gly Phe
                85                  90                  95

Ile Asp Lys Gly Asp Glu Ser Trp Val Thr Asp Met Cys Lys Lys Leu
            100                 105                 110

Phe Glu Val Glu Glu Val Asn Cys Ile Cys Val Asp Trp Lys Lys Gly
        115                 120                 125

Ser Gln Ala Thr Tyr Thr Gln Ala Ala Asn Asn Val Arg Val Val Gly
    130                 135                 140

Ala Gln Val Ala Gln Met Leu Asp Ile Leu Leu Thr Glu Tyr Ser Tyr
145                 150                 155                 160

Pro Pro Ser Lys Val His Leu Ile Gly His Ser Leu Gly Ala His Val
                165                 170                 175

Ala Gly Glu Ala Gly Ser Lys Thr Pro Gly Leu Ser Arg Ile Thr Gly
            180                 185                 190
```

```
Leu Asp Pro Val Glu Ala Ser Phe Glu Ser Thr Pro Glu Glu Val Arg
        195                 200                 205

Leu Asp Pro Ser Asp Ala Asp Phe Val Asp Val Ile His Thr Asp Ala
    210                 215                 220

Ala Pro Leu Ile Pro Phe Leu Gly Phe Gly Thr Asn Gln Gln Met Gly
225                 230                 235                 240

His Leu Asp Phe Phe Pro Asn Gly Gly Glu Ser Met Pro Gly Cys Lys
                245                 250                 255

Lys Asn Ala Leu Ser Gln Ile Val Asp Leu Asp Gly Ile Trp Ala Gly
            260                 265                 270

Thr Arg Asp Phe Val Ala Cys Asn His Leu Arg Ser Tyr Lys Tyr Tyr
        275                 280                 285

Leu Glu Ser Ile Leu Asn Pro Asp Gly Phe Ala Ala Tyr Pro Cys Thr
    290                 295                 300

Ser Tyr Lys Ser Phe Glu Ser Asp Lys Cys Phe Pro Cys Pro Asp Gln
305                 310                 315                 320

Gly Cys Pro Gln Met Gly His Tyr Ala Asp Lys Phe Ala Gly Arg Thr
                325                 330                 335

Ser Glu Glu Gln Gln Lys Phe Phe Leu Asn Thr Gly Glu Ala Ser Asn
            340                 345                 350

Phe Ala Arg Trp Arg Tyr Gly Val Ser Ile Thr Leu Ser Gly Arg Thr
        355                 360                 365

Ala Thr Gly Gln Ile Lys Val Ala Leu Phe Gly Asn Lys Gly Asn Thr
    370                 375                 380

His Gln Tyr Ser Ile Phe Arg Gly Ile Leu Lys Pro Gly Ser Thr His
385                 390                 395                 400

Ser Tyr Glu Phe Asp Ala Lys Leu Asp Val Gly Thr Ile Glu Lys Val
                405                 410                 415

Lys Phe Leu Trp Asn Asn Asn Val Ile Asn Pro Thr Leu Pro Lys Val
            420                 425                 430

Gly Ala Thr Lys Ile Thr Val Gln Lys Gly Glu Glu Lys Thr Val Tyr
        435                 440                 445

Asn Phe Cys Ser Glu Asp Thr Val Arg Glu Asp Thr Leu Leu Thr Leu
    450                 455                 460
```

Thr Pro Cys
465

<210> 524
<211> 469
<212> PRT
<213> Homo sapiens

<400> 524

Met Leu Pro Pro Trp Thr Leu Gly Leu Leu Leu Leu Ala Thr Val Arg
1 5 10 15

Gly Lys Glu Val Cys Tyr Gly Gln Leu Gly Cys Phe Ser Asp Glu Lys
20 25 30

Pro Trp Ala Gly Thr Leu Gln Arg Pro Val Lys Leu Leu Pro Trp Ser
35 40 45

Pro Glu Asp Ile Asp Thr Arg Phe Leu Leu Tyr Thr Asn Glu Asn Pro
50 55 60

Asn Asn Phe Gln Leu Ile Thr Gly Thr Glu Pro Asp Thr Ile Glu Ala
65 70 75 80

Ser Asn Phe Gln Leu Asp Arg Lys Thr Arg Phe Ile Ile His Gly Phe
85 90 95

Leu Asp Lys Ala Glu Asp Ser Trp Pro Ser Asp Met Cys Lys Lys Met
100 105 110

Phe Glu Val Glu Lys Val Asn Cys Ile Cys Val Asp Trp Arg His Gly
115 120 125

Ser Arg Ala Met Tyr Thr Gln Ala Val Gln Asn Ile Arg Val Val Gly
130 135 140

Ala Glu Thr Ala Phe Leu Ile Gln Ala Leu Ser Thr Gln Leu Gly Tyr
145 150 155 160

Ser Leu Glu Asp Val His Val Ile Gly His Ser Leu Gly Ala His Thr
165 170 175

Ala Ala Glu Ala Gly Arg Arg Leu Gly Gly Arg Val Gly Arg Ile Thr
180 185 190

Gly Leu Asp Pro Ala Gly Pro Cys Phe Gln Asp Glu Pro Glu Glu Val
195 200 205

Arg Leu Asp Pro Ser Asp Ala Val Phe Val Asp Val Ile His Thr Asp
210 215 220

Ser Ser Pro Ile Val Pro Ser Leu Gly Phe Gly Met Ser Gln Lys Val

225 230 235 240

Gly His Leu Asp Phe Phe Pro Asn Gly Gly Lys Glu Met Pro Gly Cys
245 250 255

Lys Lys Asn Val Leu Ser Thr Ile Thr Asp Ile Asp Gly Ile Trp Glu
260 265 270

Gly Ile Gly Gly Phe Val Ser Cys Asn His Leu Arg Ser Phe Glu Tyr
275 280 285

Tyr Ser Ser Ser Val Leu Asn Pro Asp Gly Phe Leu Gly Tyr Pro Cys
290 295 300

Ala Ser Tyr Asp Glu Phe Gln Glu Ser Lys Cys Phe Pro Cys Pro Ala
305 310 315 320

Glu Gly Cys Pro Lys Met Gly His Tyr Ala Asp Gln Phe Lys Gly Lys
325 330 335

Thr Ser Ala Val Glu Gln Thr Phe Phe Leu Asn Thr Gly Glu Ser Gly
340 345 350

Asn Phe Thr Ser Trp Arg Tyr Lys Val Ser Val Thr Leu Ser Gly Lys
355 360 365

Glu Lys Val Asn Gly Tyr Ile Arg Ile Ala Leu Tyr Gly Ser Asn Glu
370 375 380

Asn Ser Lys Gln Tyr Glu Ile Phe Lys Gly Ser Leu Lys Pro Asp Ala
385 390 395 400

Ser His Thr Cys Ala Ile Asp Val Asp Phe Asn Val Gly Lys Ile Gln
405 410 415

Lys Val Lys Phe Leu Trp Asn Lys Arg Gly Ile Asn Leu Ser Glu Pro
420 425 430

Lys Leu Gly Ala Ser Gln Ile Thr Val Gln Ser Gly Glu Asp Gly Thr
435 440 445

Glu Tyr Asn Phe Cys Ser Ser Asp Thr Val Glu Glu Asn Val Leu Gln
450 455 460

Ser Leu Tyr Pro Cys
465

<210> 525
<211> 753
<212> PRT
<213> Homo sapiens

<400> 525

```
Met Gly Arg Leu Gln Leu Val Val Leu Gly Leu Thr Cys Cys Trp Ala
1               5                  10                  15

Val Ala Ser Ala Ala Lys Leu Gly Ala Val Tyr Thr Glu Gly Gly Phe
            20                  25                  30

Val Glu Gly Val Asn Lys Lys Leu Gly Leu Leu Gly Asp Ser Val Asp
        35                  40                  45

Ile Phe Lys Gly Ile Pro Phe Ala Ala Pro Thr Lys Ala Leu Glu Asn
    50                  55                  60

Pro Gln Pro His Pro Gly Trp Gln Gly Thr Leu Lys Ala Lys Asn Phe
65                  70                  75                  80

Lys Lys Arg Cys Leu Gln Ala Thr Ile Thr Gln Asp Ser Thr Tyr Gly
                85                  90                  95

Asp Glu Asp Cys Leu Tyr Leu Asn Ile Trp Val Pro Gln Gly Arg Lys
            100                 105                 110

Gln Val Ser Arg Asp Leu Pro Val Met Ile Trp Ile Tyr Gly Gly Ala
        115                 120                 125

Phe Leu Met Gly Ser Gly His Gly Ala Asn Phe Leu Asn Asn Tyr Leu
    130                 135                 140

Tyr Asp Gly Glu Glu Ile Ala Thr Arg Gly Asn Val Ile Val Val Thr
145                 150                 155                 160

Phe Asn Tyr Arg Val Gly Pro Leu Gly Phe Leu Ser Thr Gly Asp Ala
                165                 170                 175

Asn Leu Pro Gly Asn Tyr Gly Leu Arg Asp Gln His Met Ala Ile Ala
            180                 185                 190

Trp Val Lys Arg Asn Ile Ala Ala Phe Gly Gly Asp Pro Asn Asn Ile
        195                 200                 205

Thr Leu Phe Gly Glu Ser Ala Gly Gly Ala Ser Val Ser Leu Gln Thr
    210                 215                 220

Leu Ser Pro Tyr Asn Lys Gly Leu Ile Arg Arg Ala Ile Ser Gln Ser
225                 230                 235                 240

Gly Val Ala Leu Ser Pro Trp Val Ile Gln Lys Asn Pro Leu Phe Trp
                245                 250                 255

Ala Lys Lys Val Ala Glu Lys Val Gly Cys Pro Val Gly Asp Ala Ala
            260                 265                 270
```

```
Arg Met Ala Gln Cys Leu Lys Val Thr Asp Pro Arg Ala Leu Thr Leu
        275                 280                 285

Ala Tyr Lys Val Pro Leu Ala Gly Leu Glu Tyr Pro Met Leu His Tyr
    290                 295                 300

Val Gly Phe Val Pro Val Ile Asp Gly Asp Phe Ile Pro Ala Asp Pro
305                 310                 315                 320

Ile Asn Leu Tyr Ala Asn Ala Ala Asp Ile Asp Tyr Ile Ala Gly Thr
                325                 330                 335

Asn Asn Met Asp Gly His Ile Phe Ala Ser Ile Asp Met Pro Ala Ile
            340                 345                 350

Asn Lys Gly Asn Lys Lys Val Thr Glu Glu Asp Phe Tyr Lys Leu Val
        355                 360                 365

Ser Glu Phe Thr Ile Thr Lys Gly Leu Arg Gly Ala Lys Thr Thr Phe
    370                 375                 380

Asp Val Tyr Thr Glu Ser Trp Ala Gln Asp Pro Ser Gln Glu Asn Lys
385                 390                 395                 400

Lys Lys Thr Val Val Asp Phe Glu Thr Asp Val Leu Phe Leu Val Pro
                405                 410                 415

Thr Glu Ile Ala Leu Ala Gln His Arg Ala Asn Ala Lys Ser Ala Lys
            420                 425                 430

Thr Tyr Ala Tyr Leu Phe Ser His Pro Ser Arg Met Pro Val Tyr Pro
        435                 440                 445

Lys Trp Val Gly Ala Asp His Ala Asp Asp Ile Gln Tyr Val Phe Gly
    450                 455                 460

Lys Pro Phe Ala Thr Pro Thr Gly Tyr Arg Pro Gln Asp Arg Thr Val
465                 470                 475                 480

Ser Lys Ala Met Ile Ala Tyr Trp Thr Asn Phe Ala Lys Thr Gly Asp
                485                 490                 495

Pro Asn Met Gly Asp Ser Ala Val Pro Thr His Trp Glu Pro Tyr Thr
            500                 505                 510

Thr Glu Asn Ser Gly Tyr Leu Glu Ile Thr Lys Lys Met Gly Ser Ser
        515                 520                 525

Ser Met Lys Arg Ser Leu Arg Thr Asn Phe Leu Arg Tyr Trp Thr Leu
    530                 535                 540
```

```
Thr Tyr Leu Ala Leu Pro Thr Val Thr Asp Gln Glu Ala Thr Pro Val
545                 550                 555                 560


Pro Pro Thr Gly Asp Ser Glu Ala Thr Pro Val Pro Pro Thr Gly Asp
                565                 570                 575


Ser Glu Thr Ala Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro
            580                 585                 590


Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly
        595                 600                 605


Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro
    610                 615                 620


Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr
625                 630                 635                 640


Gly Asp Ser Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly Ala
                645                 650                 655


Pro Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Pro Pro
            660                 665                 670


Thr Gly Asp Ala Gly Pro Pro Pro Val Pro Pro Thr Gly Asp Ser Gly
        675                 680                 685


Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Gly Ala Pro Pro Val Thr
    690                 695                 700


Pro Thr Gly Asp Ser Glu Thr Ala Pro Val Pro Pro Thr Gly Asp Ser
705                 710                 715                 720


Gly Ala Pro Pro Val Pro Pro Thr Gly Asp Ser Glu Ala Ala Pro Val
                725                 730                 735


Pro Pro Thr Asp Asp Ser Lys Glu Ala Gln Met Pro Ala Val Ile Arg
            740                 745                 750


Phe
```

<210> 526
<211> 13
<212> PRT
<213> Homo sapiens

<400> 526

```
Ser Tyr Ser Met Glu His Phe Arg Trp Gly Lys Pro Val
1               5                   10
```

<210> 527
<211> 18
<212> PRT
<213> Homo sapiens

<400> 527

Asp Glu Gly Pro Tyr Arg Met Glu His Phe Arg Trp Gly Ser Pro Pro
1 5 10 15

Lys Asp

<210> 528
<211> 11
<212> PRT
<213> Homo sapiens

<400> 528

Tyr Val Met Gly His Phe Arg Trp Asp Arg Phe
1 5 10

<210> 529
<211> 267
<212> PRT
<213> Homo sapiens

<400> 529

Met Pro Arg Ser Cys Cys Ser Arg Ser Gly Ala Leu Leu Leu Ala Leu
1 5 10 15

Leu Leu Gln Ala Ser Met Glu Val Arg Gly Trp Cys Leu Glu Ser Ser
20 25 30

Gln Cys Gln Asp Leu Thr Thr Glu Ser Asn Leu Leu Glu Cys Ile Arg
35 40 45

Ala Cys Lys Pro Asp Leu Ser Ala Glu Thr Pro Met Phe Pro Gly Asn
50 55 60

Gly Asp Glu Gln Pro Leu Thr Glu Asn Pro Arg Lys Tyr Val Met Gly
65 70 75 80

His Phe Arg Trp Asp Arg Phe Gly Arg Arg Asn Ser Ser Ser Ser Gly
85 90 95

Ser Ser Gly Ala Gly Gln Lys Arg Glu Asp Val Ser Ala Gly Glu Asp
100 105 110

Cys Gly Pro Leu Pro Glu Gly Gly Pro Glu Pro Arg Ser Asp Gly Ala
115 120 125

Lys Pro Gly Pro Arg Glu Gly Lys Arg Ser Tyr Ser Met Glu His Phe
130 135 140

```
Arg Trp Gly Lys Pro Val Gly Lys Lys Arg Arg Pro Val Lys Val Tyr
145                 150                 155                 160

Pro Asn Gly Ala Glu Asp Glu Ser Ala Glu Ala Phe Pro Leu Glu Phe
                165                 170                 175

Lys Arg Glu Leu Thr Gly Gln Arg Leu Arg Glu Gly Asp Gly Pro Asp
            180                 185                 190

Gly Pro Ala Asp Asp Gly Ala Gly Ala Gln Ala Asp Leu Glu His Ser
        195                 200                 205

Leu Leu Val Ala Ala Glu Lys Lys Asp Glu Gly Pro Tyr Arg Met Glu
    210                 215                 220

His Phe Arg Trp Gly Ser Pro Pro Lys Asp Lys Arg Tyr Gly Gly Phe
225                 230                 235                 240

Met Thr Ser Glu Lys Ser Gln Thr Pro Leu Val Thr Leu Phe Lys Asn
                245                 250                 255

Ala Ile Ile Lys Asn Ala Tyr Lys Lys Gly Glu
            260                 265
```

<210> 530
<211> 189
<212> PRT
<213> Homo sapiens

<400> 530

```
Met Ala Ser Pro Phe Ala Leu Leu Met Val Leu Val Val Leu Ser Cys
1               5                   10                  15

Lys Ser Ser Cys Ser Leu Gly Cys Asp Leu Pro Glu Thr His Ser Leu
            20                  25                  30

Asp Asn Arg Arg Thr Leu Met Leu Leu Ala Gln Met Ser Arg Ile Ser
        35                  40                  45

Pro Ser Ser Cys Leu Met Asp Arg His Asp Phe Gly Phe Pro Gln Glu
    50                  55                  60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Pro Ala Ile Ser Val Leu
65                  70                  75                  80

His Glu Leu Ile Gln Gln Ile Phe Asn Leu Phe Thr Thr Lys Asp Ser
                85                  90                  95

Ser Ala Ala Trp Asp Glu Asp Leu Leu Asp Lys Phe Cys Thr Glu Leu
            100                 105                 110
```

```
Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Met Gln Glu Glu Arg
        115                 120                 125


Val Gly Glu Thr Pro Leu Met Asn Ala Asp Ser Ile Leu Ala Val Lys
    130                 135                 140


Lys Tyr Phe Arg Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
145                 150                 155                 160


Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Leu Ser
                165                 170                 175


Leu Ser Thr Asn Leu Gln Glu Arg Leu Arg Arg Lys Glu
            180                 185


<210>  531
<211>  188
<212>  PRT
<213>  Homo sapiens

<400>  531

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys
1               5                   10                  15


Lys Ser Ser Cys Ser Val Gly Cys Asp Leu Pro Gln Thr His Ser Leu
            20                  25                  30


Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Lys Ile Ser
        35                  40                  45


Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
    50                  55                  60


Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His
65                  70                  75                  80


Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser
                85                  90                  95


Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr
            100                 105                 110


Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val
        115                 120                 125


Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys
    130                 135                 140


Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro
145                 150                 155                 160
```

Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu
165 170 175

Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
180 185

<210> 532
<211> 189
<212> PRT
<213> Homo sapiens

<400> 532

Met Ala Leu Ser Phe Ser Leu Leu Met Ala Val Leu Val Leu Ser Tyr
1 5 10 15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
20 25 30

Gly Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Gly Arg Ile Ser
35 40 45

His Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Glu Glu
50 55 60

Glu Phe Asp Gly His Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
65 70 75 80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Glu Asp Ser
85 90 95

Ser Ala Ala Trp Glu Gln Ser Leu Leu Glu Lys Phe Ser Thr Glu Leu
100 105 110

Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Glu Val Gly
115 120 125

Val Glu Glu Thr Pro Leu Met Asn Glu Asp Ser Ile Leu Ala Val Arg
130 135 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
145 150 155 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Leu Ser
165 170 175

Phe Ser Thr Asn Leu Gln Lys Arg Leu Arg Arg Lys Asp
180 185

<210> 533
<211> 189
<212> PRT
<213> Homo sapiens

<400> 533

Met Ala Leu Pro Phe Val Leu Leu Met Ala Leu Val Val Leu Asn Cys
1 5 10 15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
20 25 30

Ser Asn Arg Arg Thr Leu Met Ile Met Ala Gln Met Gly Arg Ile Ser
35 40 45

Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
50 55 60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
65 70 75 80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser
85 90 95

Ser Ala Thr Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu
100 105 110

Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Met Met Gln Glu Val Gly
115 120 125

Val Glu Asp Thr Pro Leu Met Asn Val Asp Ser Ile Leu Thr Val Arg
130 135 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
145 150 155 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
165 170 175

Leu Ser Ala Asn Leu Gln Glu Arg Leu Arg Arg Lys Glu
180 185

<210> 534
<211> 189
<212> PRT
<213> Homo sapiens

<400> 534

Met Ala Leu Pro Phe Ala Leu Leu Met Ala Leu Val Val Leu Ser Cys
1 5 10 15

Lys Ser Ser Cys Ser Leu Asp Cys Asp Leu Pro Gln Thr His Ser Leu
20 25 30

Gly His Arg Arg Thr Met Met Leu Leu Ala Gln Met Arg Arg Ile Ser
35 40 45

```
Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Arg Phe Pro Gln Glu
    50                  55                  60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Glu Ala Ile Ser Val Leu
65                  70                  75                  80

His Glu Val Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser
                85                  90                  95

Ser Val Ala Trp Asp Glu Arg Leu Leu Asp Lys Leu Tyr Thr Glu Leu
            100                 105                 110

Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Met Gln Glu Val Trp
        115                 120                 125

Val Gly Gly Thr Pro Leu Met Asn Glu Asp Ser Ile Leu Ala Val Arg
    130                 135                 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
145                 150                 155                 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
                165                 170                 175

Ser Ser Arg Asn Leu Gln Glu Arg Leu Arg Arg Lys Glu
            180                 185
```

<210> 535
<211> 189
<212> PRT
<213> Homo sapiens

<400> 535

```
Met Ala Arg Ser Phe Ser Leu Leu Met Val Val Leu Val Leu Ser Tyr
1               5                   10                  15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
            20                  25                  30

Arg Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Gly Arg Ile Ser
        35                  40                  45

Pro Phe Ser Cys Leu Lys Asp Arg His Glu Phe Arg Phe Pro Glu Glu
    50                  55                  60

Glu Phe Asp Gly His Gln Phe Gln Lys Thr Gln Ala Ile Ser Val Leu
65                  70                  75                  80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Glu Asp Ser
                85                  90                  95
```

```
Ser Ala Ala Trp Glu Gln Ser Leu Leu Glu Lys Phe Ser Thr Glu Leu
            100                 105                 110

Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Glu Val Gly
        115                 120                 125

Val Glu Glu Thr Pro Leu Met Asn Glu Asp Phe Ile Leu Ala Val Arg
    130                 135                 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Met Glu Lys Lys Tyr Ser
145                 150                 155                 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
                165                 170                 175

Phe Ser Thr Asn Leu Lys Lys Gly Leu Arg Arg Lys Asp
            180                 185


<210>  536
<211>  189
<212>  PRT
<213>  Homo sapiens

<400>  536

Met Ala Leu Thr Phe Tyr Leu Leu Val Ala Leu Val Val Leu Ser Tyr
1               5                   10                  15

Lys Ser Phe Ser Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
            20                  25                  30

Gly Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Arg Arg Ile Ser
        35                  40                  45

Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Glu Phe Pro Gln Glu
    50                  55                  60

Glu Phe Asp Asp Lys Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
65                  70                  75                  80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser
                85                  90                  95

Ser Ala Ala Leu Asp Glu Thr Leu Leu Asp Glu Phe Tyr Ile Glu Leu
            100                 105                 110

Asp Gln Gln Leu Asn Asp Leu Glu Ser Cys Val Met Gln Glu Val Gly
        115                 120                 125

Val Ile Glu Ser Pro Leu Met Tyr Glu Asp Ser Ile Leu Ala Val Arg
    130                 135                 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
```

145 150 155 160

Ser Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
165 170 175

Leu Ser Ile Asn Leu Gln Lys Arg Leu Lys Ser Lys Glu
180 185

<210> 537
<211> 189
<212> PRT
<213> Homo sapiens

<400> 537

Met Ala Leu Ser Phe Ser Leu Leu Met Ala Val Leu Val Leu Ser Tyr
1 5 10 15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
20 25 30

Gly Asn Arg Arg Ala Leu Ile Leu Leu Gly Gln Met Gly Arg Ile Ser
35 40 45

Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Arg Ile Pro Gln Glu
50 55 60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
65 70 75 80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Glu Asp Ser
85 90 95

Ser Ala Ala Trp Glu Gln Ser Leu Leu Glu Lys Phe Ser Thr Glu Leu
100 105 110

Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Glu Val Gly
115 120 125

Val Glu Glu Thr Pro Leu Met Asn Glu Asp Ser Ile Leu Ala Val Arg
130 135 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Ile Glu Arg Lys Tyr Ser
145 150 155 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Leu Ser
165 170 175

Phe Ser Thr Asn Leu Gln Lys Arg Leu Arg Arg Lys Asp
180 185

<210> 538
<211> 189

<212> PRT
<213> Homo sapiens

<400> 538

```
Met Ala Leu Pro Phe Ala Leu Met Met Ala Leu Val Val Leu Ser Cys
1               5                  10                  15

Lys Ser Ser Cys Ser Leu Gly Cys Asn Leu Ser Gln Thr His Ser Leu
            20                  25                  30

Asn Asn Arg Arg Thr Leu Met Leu Met Ala Gln Met Arg Arg Ile Ser
        35                  40                  45

Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Glu Phe Pro Gln Glu
    50                  55                  60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
65                  70                  75                  80

His Glu Met Met Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asn Ser
                85                  90                  95

Ser Ala Ala Trp Asp Glu Thr Leu Leu Glu Lys Phe Tyr Ile Glu Leu
            100                 105                 110

Phe Gln Gln Met Asn Asp Leu Glu Ala Cys Val Ile Gln Glu Val Gly
        115                 120                 125

Val Glu Glu Thr Pro Leu Met Asn Glu Asp Ser Ile Leu Ala Val Lys
    130                 135                 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Met Glu Lys Lys Tyr Ser
145                 150                 155                 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Leu Ser
                165                 170                 175

Phe Ser Thr Asn Leu Gln Lys Arg Leu Arg Arg Lys Asp
            180                 185
```

<210> 539
<211> 189
<212> PRT
<213> Homo sapiens

<400> 539

```
Met Ala Leu Ser Phe Ser Leu Leu Met Ala Val Leu Val Leu Ser Tyr
1               5                  10                  15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
            20                  25                  30
```

Gly Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Gly Arg Ile Ser
        35   40   45

His Phe Ser Cys Leu Lys Asp Arg Tyr Asp Phe Gly Phe Pro Gln Glu
    50   55   60

Val Phe Asp Gly Asn Gln Phe Gln Lys Ala Gln Ala Ile Ser Ala Phe
65   70   75   80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser
                85   90   95

Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Ile Glu Leu
            100   105   110

Phe Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Thr Gln Glu Val Gly
        115   120   125

Val Glu Glu Ile Ala Leu Met Asn Glu Asp Ser Ile Leu Ala Val Arg
    130   135   140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Met Gly Lys Lys Tyr Ser
145   150   155   160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
                165   170   175

Phe Ser Thr Asn Leu Gln Lys Gly Leu Arg Arg Lys Asp
            180   185

<210> 540
<211> 189
<212> PRT
<213> Homo sapiens

<400> 540

Met Ala Leu Ser Phe Ser Leu Leu Met Ala Val Leu Val Leu Ser Tyr
1   5   10   15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
            20   25   30

Gly Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Gly Arg Ile Ser
        35   40   45

Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Leu Pro Gln Glu
    50   55   60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Thr Gln Ala Ile Ser Val Leu
65   70   75   80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Glu Asp Ser

85 90 95

Ser Ala Ala Trp Glu Gln Ser Leu Leu Glu Lys Phe Ser Thr Glu Leu
100 105 110

Tyr Gln Gln Leu Asn Asn Leu Glu Ala Cys Val Ile Gln Glu Val Gly
115 120 125

Met Glu Glu Thr Pro Leu Met Asn Glu Asp Ser Ile Leu Ala Val Arg
130 135 140

Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
145 150 155 160

Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Leu Ser
165 170 175

Phe Ser Thr Asn Leu Gln Lys Ile Leu Arg Arg Lys Asp
180 185

<210> 541
<211> 189
<212> PRT
<213> Homo sapiens

<400> 541

Met Ala Leu Ser Phe Ser Leu Leu Met Ala Val Leu Val Leu Ser Tyr
1 5 10 15

Lys Ser Ile Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Ser Leu
20 25 30

Gly Asn Arg Arg Ala Leu Ile Leu Leu Ala Gln Met Gly Arg Ile Ser
35 40 45

Pro Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
50 55 60

Glu Phe Asp Gly Asn Gln Phe Gln Lys Ala Gln Ala Ile Ser Val Leu
65 70 75 80

His Glu Met Ile Gln Gln Thr Phe Asn Leu Phe Ser Thr Lys Asp Ser
85 90 95

Ser Ala Thr Trp Glu Gln Ser Leu Leu Glu Lys Phe Ser Thr Glu Leu
100 105 110

Asn Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Glu Val Gly
115 120 125

Val Glu Glu Thr Pro Leu Met Asn Val Asp Ser Ile Leu Ala Val Lys
130 135 140

```
Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Thr Glu Lys Lys Tyr Ser
145                 150                 155                 160


Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser
                165                 170                 175


Leu Ser Lys Ile Phe Gln Glu Arg Leu Arg Arg Lys Glu
            180                 185


<210>  542
<211>  166
<212>  PRT
<213>  Homo sapiens

<400>  542

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1               5                   10                  15


Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu
            20                  25                  30


Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn
        35                  40                  45


Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp
    50                  55                  60


Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
65                  70                  75                  80


Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
                85                  90                  95


Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
            100                 105                 110


Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val
        115                 120                 125


Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser
    130                 135                 140


Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg
145                 150                 155                 160


Gly Arg Arg Ala Ser Gln
                165


<210>  543
<211>  187
<212>  PRT
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<213> Homo sapiens

<400> 543

```
Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
1               5                  10                  15

Thr Thr Ala Leu Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg
            20                  25                  30

Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg
        35                  40                  45

Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu
    50                  55                  60

Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile
65                  70                  75                  80

Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser
                85                  90                  95

Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val
            100                 105                 110

Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu
        115                 120                 125

Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys
    130                 135                 140

Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser
145                 150                 155                 160

His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr
                165                 170                 175

Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
            180                 185
```

<210> 544
<211> 207
<212> PRT
<213> Homo sapiens

<400> 544

```
Met Ser Thr Lys Pro Asp Met Ile Gln Lys Cys Leu Trp Leu Glu Ile
1               5                  10                  15

Leu Met Gly Ile Phe Ile Ala Gly Thr Leu Ser Leu Asp Cys Asn Leu
            20                  25                  30

Leu Asn Val His Leu Arg Arg Val Thr Trp Gln Asn Leu Arg His Leu
```

35 40 45

Ser Ser Met Ser Asn Ser Phe Pro Val Glu Cys Leu Arg Glu Asn Ile
50 55 60

Ala Phe Glu Leu Pro Gln Glu Phe Leu Gln Tyr Thr Gln Pro Met Lys
65 70 75 80

Arg Asp Ile Lys Lys Ala Phe Tyr Glu Met Ser Leu Gln Ala Phe Asn
85 90 95

Ile Phe Ser Gln His Thr Phe Lys Tyr Trp Lys Glu Arg His Leu Lys
100 105 110

Gln Ile Gln Ile Gly Leu Asp Gln Gln Ala Glu Tyr Leu Asn Gln Cys
115 120 125

Leu Glu Glu Asp Lys Asn Glu Asn Glu Asp Met Lys Glu Met Lys Glu
130 135 140

Asn Glu Met Lys Pro Ser Glu Ala Arg Val Pro Gln Leu Ser Ser Leu
145 150 155 160

Glu Leu Arg Arg Tyr Phe His Arg Ile Asp Asn Phe Leu Lys Glu Lys
165 170 175

Lys Tyr Ser Asp Cys Ala Trp Glu Ile Val Arg Val Glu Ile Arg Arg
180 185 190

Cys Leu Tyr Tyr Phe Tyr Lys Phe Thr Ala Leu Phe Arg Arg Lys
195 200 205

<210> 545
<211> 208
<212> PRT
<213> Homo sapiens

<400> 545

Met Ile Ile Lys His Phe Phe Gly Thr Val Leu Val Leu Leu Ala Ser
1 5 10 15

Thr Thr Ile Phe Ser Leu Asp Leu Lys Leu Ile Ile Phe Gln Gln Arg
20 25 30

Gln Val Asn Gln Glu Ser Leu Lys Leu Leu Asn Lys Leu Gln Thr Leu
35 40 45

Ser Ile Gln Gln Cys Leu Pro His Arg Lys Asn Phe Leu Leu Pro Gln
50 55 60

Lys Ser Leu Ser Pro Gln Gln Tyr Gln Lys Gly His Thr Leu Ala Ile
65 70 75 80

```
Leu His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe Arg Ala Asn Ile
                85                  90                  95

Ser Leu Asp Gly Trp Glu Glu Asn His Thr Glu Lys Phe Leu Ile Gln
            100                 105                 110

Leu His Gln Gln Leu Glu Tyr Leu Glu Ala Leu Met Gly Leu Glu Ala
        115                 120                 125

Glu Lys Leu Ser Gly Thr Leu Gly Ser Asp Asn Leu Arg Leu Gln Val
    130                 135                 140

Lys Met Tyr Phe Arg Arg Ile His Asp Tyr Leu Glu Asn Gln Asp Tyr
145                 150                 155                 160

Ser Thr Cys Ala Trp Ala Ile Val Gln Val Glu Ile Ser Arg Cys Leu
                165                 170                 175

Phe Phe Val Phe Ser Leu Thr Glu Lys Leu Ser Lys Gln Gly Arg Pro
            180                 185                 190

Leu Asn Asp Met Lys Gln Glu Leu Thr Thr Glu Phe Arg Ser Pro Arg
        195                 200                 205


<210>  546
<211>  4
<212>  PRT
<213>  Homo sapiens

<400>  546

Glu Tyr Phe Tyr
1


<210>  547
<211>  4
<212>  PRT
<213>  Homo sapiens

<400>  547

Gly His Gly Gly
1


<210>  548
<211>  153
<212>  PRT
<213>  Homo sapiens

<400>  548

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1               5                  10                  15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
```

20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr
145 150

<210> 549
<211> 136
<212> PRT
<213> Homo sapiens

<400> 549

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Ala Asn Trp Val Asn Val Ile Ser Asp Leu Lys
20 25 30

Lys Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu Tyr
35 40 45

Thr Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys
50 55 60

Phe Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser
65 70 75 80

Ile His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu
85 90 95

Ser Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu
100 105 110

```
Leu Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile
        115                 120                 125


Val Gln Met Phe Ile Asn Thr Ser
    130                 135


<210>  550
<211>  135
<212>  PRT
<213>  Homo sapiens

<400>  550

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1               5                   10                  15


Val Thr Asn Ser Ala Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys
            20                  25                  30


Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr
        35                  40                  45


Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe
    50                  55                  60


Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile
65                  70                  75                  80


His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser
                85                  90                  95


Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu
            100                 105                 110


Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile Val
        115                 120                 125


Gln Met Phe Ile Asn Thr Ser
    130                 135


<210>  551
<211>  153
<212>  PRT
<213>  Homo sapiens

<400>  551

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1               5                   10                  15


Val Thr Asn Ser Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser Ala
            20                  25                  30
```

Gly Leu Pro Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp Leu
35 40 45

Lys Lys Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu
50 55 60

Tyr Thr Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys
65 70 75 80

Cys Phe Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala
85 90 95

Ser Ile His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser
100 105 110

Leu Ser Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu
115 120 125

Glu Leu Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His
130 135 140

Ile Val Gln Met Phe Ile Asn Thr Ser
145 150

<210> 552
<211> 162
<212> PRT
<213> Homo sapiens

<400> 552

Met Asn Ser Phe Ser Thr Ser Ala Phe Gly Pro Val Ala Phe Ser Leu
1 5 10 15

Gly Leu Leu Leu Val Leu Pro Ala Ala Phe Pro Ala Pro Gly Ile His
20 25 30

Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala
35 40 45

Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
50 55 60

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
65 70 75 80

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
85 90 95

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
100 105 110

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val

115 120 125

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
130 135 140

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
145 150 155 160

Thr Ser

<210> 553
<211> 166
<212> PRT
<213> Homo sapiens

<400> 553

Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr Leu
1 5 10 15

Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala
20 25 30

Ala Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro
35 40 45

Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile
50 55 60

Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu
65 70 75 80

Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu
85 90 95

Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His
100 105 110

Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser
115 120 125

Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu
130 135 140

Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln
145 150 155 160

Met Phe Ile Asn Thr Ser
165

<210> 554
<211> 179

<212> PRT
<213> Homo sapiens

<400> 554

```
Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr Leu
1               5                  10                  15


Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala
            20                  25                  30


Ala Ala Pro Ile Ser Ser His Cys Arg Leu Asp Lys Ser Asn Phe Gln
        35                  40                  45


Gln Pro Tyr Ile Thr Asn Arg Thr Phe Met Leu Ala Lys Glu Ala Ser
    50                  55                  60


Leu Ala Asp Asn Asn Thr Asp Val Arg Leu Ile Gly Glu Lys Leu Phe
65                  70                  75                  80


His Gly Val Ser Met Ser Glu Arg Cys Tyr Leu Met Lys Gln Val Leu
                85                  90                  95


Asn Phe Thr Leu Glu Glu Val Leu Phe Pro Gln Ser Asp Arg Phe Gln
            100                 105                 110


Pro Tyr Met Gln Glu Val Val Pro Phe Leu Ala Arg Leu Ser Asn Arg
        115                 120                 125


Leu Ser Thr Cys His Ile Glu Gly Asp Asp Leu His Ile Gln Arg Asn
    130                 135                 140


Val Gln Lys Leu Lys Asp Thr Val Lys Lys Leu Gly Glu Ser Gly Glu
145                 150                 155                 160


Ile Lys Ala Ile Gly Glu Leu Asp Leu Leu Phe Met Ser Leu Arg Asn
                165                 170                 175


Ala Cys Ile
```

<210> 555
<211> 155
<212> PRT
<213> Homo sapiens

<400> 555

```
Met Ala Glu Gly Glu Ile Thr Thr Phe Thr Ala Leu Thr Glu Lys Phe
1               5                  10                  15


Asn Leu Pro Pro Gly Asn Tyr Lys Lys Pro Lys Leu Leu Tyr Cys Ser
            20                  25                  30
```

Asn Gly Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly
35 40 45

Thr Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu
50 55 60

Ser Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu
65 70 75 80

Ala Met Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu
85 90 95

Glu Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr
100 105 110

Ile Ser Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys
115 120 125

Asn Gly Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala
130 135 140

Ile Leu Phe Leu Pro Leu Pro Val Ser Ser Asp
145 150 155

<210> 556
<211> 135
<212> PRT
<213> Homo sapiens

<400> 556

Met Gly Asn Tyr Lys Pro Lys Leu Leu Tyr Cys Ser Asn Gly Gly His
1 5 10 15

Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly Thr Arg Asp Arg
20 25 30

Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu Ser Val Gly Glu
35 40 45

Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu Ala Met Asp Thr
50 55 60

Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu Glu Cys Leu Phe
65 70 75 80

Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr Ile Ser Lys Lys
85 90 95

His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys Asn Gly Ser Cys
100 105 110

Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala Ile Leu Phe Leu

115 120 125

Pro Leu Pro Val Ser Ser Asp
130 135

<210> 557
<211> 153
<212> PRT
<213> Homo sapiens

<400> 557

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
1 5 10 15

Thr Thr Ala Leu Ser Met Lys Pro Lys Leu Leu Tyr Cys Ser Asn Gly
20 25 30

Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly Thr Arg
35 40 45

Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu Ser Val
50 55 60

Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu Ala Met
65 70 75 80

Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu Glu Cys
85 90 95

Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr Ile Ser
100 105 110

Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys Asn Gly
115 120 125

Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala Ile Leu
130 135 140

Phe Leu Pro Leu Pro Val Ser Ser Asp
145 150

<210> 558
<211> 211
<212> PRT
<213> Homo sapiens

<400> 558

Met Arg Ser Gly Cys Val Val Val His Val Trp Ile Leu Ala Gly Leu
1 5 10 15

Trp Leu Ala Val Ala Gly Arg Asp Ser Ser Pro Leu Val His Tyr Gly
20 25 30

```
Trp Gly Asp Pro Ile Arg Leu Arg His Leu Tyr Thr Ser Gly Pro His
        35                  40                  45

Gly Leu Ser Ser Cys Phe Leu Arg Ile Arg Ala Asp Gly Val Val Asp
    50                  55                  60

Cys Ala Arg Gly Gln Ser Ala His Ser Leu Leu Glu Ile Lys Ala Val
65                  70                  75                  80

Ala Leu Arg Thr Val Ala Ile Lys Gly Val His Ser Val Arg Tyr Leu
                85                  90                  95

Cys Met Gly Ala Asp Gly Lys Met Gln Gly Leu Leu Gln Tyr Ser Glu
            100                 105                 110

Glu Asp Cys Ala Phe Glu Glu Glu Ile Arg Pro Asp Gly Tyr Asn Val
        115                 120                 125

Tyr Arg Ser Glu Lys His Arg Leu Pro Val Ser Leu Ser Ser Ala Lys
    130                 135                 140

Gln Arg Gln Leu Tyr Lys Asn Arg Gly Phe Leu Pro Leu Ser His Phe
145                 150                 155                 160

Leu Pro Met Leu Pro Met Val Pro Glu Glu Pro Glu Asp Leu Arg Gly
                165                 170                 175

His Leu Glu Ser Asp Met Phe Ser Ser Pro Leu Glu Thr Asp Ser Met
            180                 185                 190

Asp Pro Phe Gly Leu Val Thr Gly Leu Glu Ala Val Arg Ser Pro Ser
        195                 200                 205

Phe Glu Lys
    210


<210>  559
<211>  209
<212>  PRT
<213>  Homo sapiens

<400>  559

Met Asp Ser Asp Glu Thr Gly Phe Glu His Ser Gly Leu Trp Val Ser
1               5                   10                  15

Val Leu Ala Gly Leu Leu Leu Gly Ala Cys Gln Ala His Pro Ile Pro
            20                  25                  30

Asp Ser Ser Pro Leu Leu Gln Phe Gly Gly Gln Val Arg Gln Arg Tyr
        35                  40                  45
```

```
Leu Tyr Thr Asp Asp Ala Gln Gln Thr Glu Ala His Leu Glu Ile Arg
    50                  55                  60

Glu Asp Gly Thr Val Gly Gly Ala Ala Asp Gln Ser Pro Glu Ser Leu
65                  70                  75                  80

Leu Gln Leu Lys Ala Leu Lys Pro Gly Val Ile Gln Ile Leu Gly Val
                85                  90                  95

Lys Thr Ser Arg Phe Leu Cys Gln Arg Pro Asp Gly Ala Leu Tyr Gly
            100                 105                 110

Ser Leu His Phe Asp Pro Glu Ala Cys Ser Phe Arg Glu Leu Leu Leu
        115                 120                 125

Glu Asp Gly Tyr Asn Val Tyr Gln Ser Glu Ala His Gly Leu Pro Leu
    130                 135                 140

His Leu Pro Gly Asn Lys Ser Pro His Arg Asp Pro Ala Pro Arg Gly
145                 150                 155                 160

Pro Ala Arg Phe Leu Pro Leu Pro Gly Leu Pro Pro Ala Leu Pro Glu
                165                 170                 175

Pro Pro Gly Ile Leu Ala Pro Gln Pro Pro Asp Val Gly Ser Ser Asp
            180                 185                 190

Pro Leu Ser Met Val Gly Pro Ser Gln Gly Arg Ser Pro Ser Tyr Ala
        195                 200                 205

Ser
```

<210> 560
<211> 251
<212> PRT
<213> Homo sapiens

<400> 560

```
Met Leu Gly Ala Arg Leu Arg Leu Trp Val Cys Ala Leu Cys Ser Val
1               5                   10                  15

Cys Ser Met Ser Val Leu Arg Ala Tyr Pro Asn Ala Ser Pro Leu Leu
            20                  25                  30

Gly Ser Ser Trp Gly Gly Leu Ile His Leu Tyr Thr Ala Thr Ala Arg
        35                  40                  45

Asn Ser Tyr His Leu Gln Ile His Lys Asn Gly His Val Asp Gly Ala
    50                  55                  60

Pro His Gln Thr Ile Tyr Ser Ala Leu Met Ile Arg Ser Glu Asp Ala
```

65 70 75 80

Gly Phe Val Val Ile Thr Gly Val Met Ser Arg Arg Tyr Leu Cys Met
85 90 95

Asp Phe Arg Gly Asn Ile Phe Gly Ser His Tyr Phe Asp Pro Glu Asn
100 105 110

Cys Arg Phe Gln His Gln Thr Leu Glu Asn Gly Tyr Asp Val Tyr His
115 120 125

Ser Pro Gln Tyr His Phe Leu Val Ser Leu Gly Arg Ala Lys Arg Ala
130 135 140

Phe Leu Pro Gly Met Asn Pro Pro Pro Tyr Ser Gln Phe Leu Ser Arg
145 150 155 160

Arg Asn Glu Ile Pro Leu Ile His Phe Asn Thr Pro Ile Pro Arg Arg
165 170 175

His Thr Arg Ser Ala Glu Asp Asp Ser Glu Arg Asp Pro Leu Asn Val
180 185 190

Leu Lys Pro Arg Ala Arg Met Thr Pro Ala Pro Ala Ser Cys Ser Gln
195 200 205

Glu Leu Pro Ser Ala Glu Asp Asn Ser Pro Met Ala Ser Asp Pro Leu
210 215 220

Gly Val Val Arg Gly Gly Arg Val Asn Thr His Ala Gly Gly Thr Gly
225 230 235 240

Pro Glu Gly Cys Arg Pro Phe Ala Lys Phe Ile
245 250

<210> 561
<211> 247
<212> PRT
<213> Homo sapiens

<400> 561

Met Thr Ile Leu Phe Leu Thr Met Val Ile Ser Tyr Phe Gly Cys Met
1 5 10 15

Lys Ala Ala Pro Met Lys Glu Ala Asn Ile Arg Gly Gln Gly Gly Leu
20 25 30

Ala Tyr Pro Gly Val Arg Thr His Gly Thr Leu Glu Ser Val Asn Gly
35 40 45

Pro Lys Ala Gly Ser Arg Gly Leu Thr Ser Leu Ala Asp Thr Phe Glu
50 55 60

```
His Val Ile Glu Glu Leu Leu Asp Glu Asp Gln Lys Val Arg Pro Asn
65                  70                  75                  80

Glu Glu Asn Asn Lys Asp Ala Asp Leu Tyr Thr Ser Arg Val Met Leu
                85                  90                  95

Ser Ser Gln Val Pro Leu Glu Pro Pro Leu Leu Phe Leu Leu Glu Glu
            100                 105                 110

Tyr Lys Asn Tyr Leu Asp Ala Ala Asn Met Ser Met Arg Val Arg Arg
        115                 120                 125

His Ser Asp Pro Ala Arg Arg Gly Glu Leu Ser Val Cys Asp Ser Ile
    130                 135                 140

Ser Glu Trp Val Thr Ala Ala Asp Lys Lys Thr Ala Val Asp Met Ser
145                 150                 155                 160

Gly Gly Thr Val Thr Val Leu Glu Lys Val Pro Val Ser Lys Gly Gln
                165                 170                 175

Leu Lys Gln Tyr Phe Tyr Glu Thr Lys Cys Asn Pro Met Gly Tyr Thr
            180                 185                 190

Lys Glu Gly Cys Arg Gly Ile Asp Lys Arg His Trp Asn Ser Gln Cys
        195                 200                 205

Arg Thr Thr Gln Ser Tyr Val Arg Ala Leu Thr Met Asp Ser Lys Lys
    210                 215                 220

Arg Ile Gly Trp Arg Phe Ile Arg Ile Asp Thr Ser Cys Val Cys Thr
225                 230                 235                 240

Leu Thr Ile Lys Arg Gly Arg
                245
```

<210> 562
<211> 379
<212> PRT
<213> Homo sapiens

<400> 562

```
Met Glu Gln Leu Ser Ser Ala Asn Thr Arg Phe Ala Leu Asp Leu Phe
1               5                   10                  15

Leu Ala Leu Ser Glu Asn Asn Pro Ala Gly Asn Ile Phe Ile Ser Pro
            20                  25                  30

Phe Ser Ile Ser Ser Ala Met Ala Met Val Phe Leu Gly Thr Arg Gly
        35                  40                  45
```

```
Asn Thr Ala Ala Gln Leu Ser Lys Thr Phe His Phe Asn Thr Val Glu
    50                  55                  60

Glu Val His Ser Arg Phe Gln Ser Leu Asn Ala Asp Ile Asn Lys Arg
65                  70                  75                  80

Gly Ala Ser Tyr Ile Leu Lys Leu Ala Asn Arg Leu Tyr Gly Glu Lys
                85                  90                  95

Thr Tyr Asn Phe Leu Pro Glu Phe Leu Val Ser Thr Gln Lys Thr Tyr
            100                 105                 110

Gly Ala Asp Leu Ala Ser Val Asp Phe Gln His Ala Ser Glu Asp Ala
        115                 120                 125

Arg Lys Thr Ile Asn Gln Trp Val Lys Gly Gln Thr Glu Gly Lys Ile
    130                 135                 140

Pro Glu Leu Leu Ala Ser Gly Met Val Asp Asn Met Thr Lys Leu Val
145                 150                 155                 160

Leu Val Asn Ala Ile Tyr Phe Lys Gly Asn Trp Lys Asp Lys Phe Met
                165                 170                 175

Lys Glu Ala Thr Thr Asn Ala Pro Phe Arg Leu Asn Lys Lys Asp Arg
            180                 185                 190

Lys Thr Val Lys Met Met Tyr Gln Lys Lys Lys Phe Ala Tyr Gly Tyr
        195                 200                 205

Ile Glu Asp Leu Lys Cys Arg Val Leu Glu Leu Pro Tyr Gln Gly Glu
    210                 215                 220

Glu Leu Ser Met Val Ile Leu Leu Pro Asp Asp Ile Glu Asp Glu Ser
225                 230                 235                 240

Thr Gly Leu Lys Lys Ile Glu Glu Gln Leu Thr Leu Glu Lys Leu His
                245                 250                 255

Glu Trp Thr Lys Pro Glu Asn Leu Asp Phe Ile Glu Val Asn Val Ser
            260                 265                 270

Leu Pro Arg Phe Lys Leu Glu Glu Ser Tyr Thr Leu Asn Ser Asp Leu
        275                 280                 285

Ala Arg Leu Gly Val Gln Asp Leu Phe Asn Ser Ser Lys Ala Asp Leu
    290                 295                 300

Ser Gly Met Ser Gly Ala Arg Asp Ile Phe Ile Ser Lys Ile Val His
305                 310                 315                 320
```

```
Lys Ser Phe Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala
                325                 330                 335


Thr Ala Gly Ile Ala Thr Phe Cys Met Leu Met Pro Glu Glu Asn Phe
            340                 345                 350


Thr Ala Asp His Pro Phe Leu Phe Phe Ile Arg His Asn Ser Ser Gly
        355                 360                 365


Ser Ile Leu Phe Leu Gly Arg Phe Ser Ser Pro
    370                 375


<210>  563
<211>  404
<212>  PRT
<213>  Homo sapiens

<400>  563

Met Ala Asp Lys Val Leu Lys Glu Lys Arg Lys Leu Phe Ile Arg Ser
1               5                   10                  15


Met Gly Glu Gly Thr Ile Asn Gly Leu Leu Asp Glu Leu Leu Gln Thr
            20                  25                  30


Arg Val Leu Asn Lys Glu Glu Met Glu Lys Val Lys Arg Glu Asn Ala
        35                  40                  45


Thr Val Met Asp Lys Thr Arg Ala Leu Ile Asp Ser Val Ile Pro Lys
    50                  55                  60


Gly Ala Gln Ala Cys Gln Ile Cys Ile Thr Tyr Ile Cys Glu Glu Asp
65                  70                  75                  80


Ser Tyr Leu Ala Gly Thr Leu Gly Leu Ser Ala Asp Gln Thr Ser Gly
                85                  90                  95


Asn Tyr Leu Asn Met Gln Asp Ser Gln Gly Val Leu Ser Ser Phe Pro
            100                 105                 110


Ala Pro Gln Ala Val Gln Asp Asn Pro Ala Met Pro Thr Ser Ser Gly
        115                 120                 125


Ser Glu Gly Asn Val Lys Leu Cys Ser Leu Glu Glu Ala Gln Arg Ile
    130                 135                 140


Trp Lys Gln Lys Ser Ala Glu Ile Tyr Pro Ile Met Asp Lys Ser Ser
145                 150                 155                 160


Arg Thr Arg Leu Ala Leu Ile Ile Cys Asn Glu Glu Phe Asp Ser Ile
                165                 170                 175
```

```
Pro Arg Arg Thr Gly Ala Glu Val Asp Ile Thr Gly Met Thr Met Leu
            180                 185                 190

Leu Gln Asn Leu Gly Tyr Ser Val Asp Val Lys Lys Asn Leu Thr Ala
        195                 200                 205

Ser Asp Met Thr Thr Glu Leu Glu Ala Phe Ala His Arg Pro Glu His
    210                 215                 220

Lys Thr Ser Asp Ser Thr Phe Leu Val Phe Met Ser His Gly Ile Arg
225                 230                 235                 240

Glu Gly Ile Cys Gly Lys Lys His Ser Glu Gln Val Pro Asp Ile Leu
                245                 250                 255

Gln Leu Asn Ala Ile Phe Asn Met Leu Asn Thr Lys Asn Cys Pro Ser
            260                 265                 270

Leu Lys Asp Lys Pro Lys Val Ile Ile Ile Gln Ala Cys Arg Gly Asp
        275                 280                 285

Ser Pro Gly Val Val Trp Phe Lys Asp Ser Val Gly Val Ser Gly Asn
    290                 295                 300

Leu Ser Leu Pro Thr Thr Glu Glu Phe Glu Asp Asp Ala Ile Lys Lys
305                 310                 315                 320

Ala His Ile Glu Lys Asp Phe Ile Ala Phe Cys Ser Ser Thr Pro Asp
                325                 330                 335

Asn Val Ser Trp Arg His Pro Thr Met Gly Ser Val Phe Ile Gly Arg
            340                 345                 350

Leu Ile Glu His Met Gln Glu Tyr Ala Cys Ser Cys Asp Val Glu Glu
        355                 360                 365

Ile Phe Arg Lys Val Arg Phe Ser Phe Glu Gln Pro Asp Gly Arg Ala
    370                 375                 380

Gln Met Pro Thr Thr Glu Arg Val Thr Leu Thr Arg Cys Phe Tyr Leu
385                 390                 395                 400

Phe Pro Gly His


<210>  564
<211>  202
<212>  PRT
<213>  Homo sapiens

<400>  564

Met Lys Val Leu Ala Ala Gly Val Val Pro Leu Leu Leu Val Leu His
```

1 5 10 15

Trp Lys His Gly Ala Gly Ser Pro Leu Pro Ile Thr Pro Val Asn Ala
20 25 30

Thr Cys Ala Ile Arg His Pro Cys His Asn Asn Leu Met Asn Gln Ile
35 40 45

Arg Ser Gln Leu Ala Gln Leu Asn Gly Ser Ala Asn Ala Leu Phe Ile
50 55 60

Leu Tyr Tyr Thr Ala Gln Gly Glu Pro Phe Pro Asn Asn Leu Asp Lys
65 70 75 80

Leu Cys Gly Pro Asn Val Thr Asp Phe Pro Pro Phe His Ala Asn Gly
85 90 95

Thr Glu Lys Ala Lys Leu Val Glu Leu Tyr Arg Ile Val Val Tyr Leu
100 105 110

Gly Thr Ser Leu Gly Asn Ile Thr Arg Asp Gln Lys Ile Leu Asn Pro
115 120 125

Ser Ala Leu Ser Leu His Ser Lys Leu Asn Ala Thr Ala Asp Ile Leu
130 135 140

Arg Gly Leu Leu Ser Asn Val Leu Cys Arg Leu Cys Ser Lys Tyr His
145 150 155 160

Val Gly His Val Asp Val Thr Tyr Gly Pro Asp Thr Ser Gly Lys Asp
165 170 175

Val Phe Gln Lys Lys Lys Leu Gly Cys Gln Leu Leu Gly Lys Tyr Lys
180 185 190

Gln Ile Ile Ala Val Leu Ala Gln Ala Phe
195 200

<210> 565
<211> 161
<212> PRT
<213> Homo sapiens

<400> 565

Met Asp Ser Asp Glu Thr Gly Phe Glu His Ser Gly Leu Trp Val Ser
1 5 10 15

Val Leu Ala Gly Leu Leu Leu Gly Ala Cys Gln Ala Gly Ile His Val
20 25 30

Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala Asn
35 40 45

```
Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile Gln
    50                  55                  60

Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His Pro
65                  70                  75                  80

Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln Val
                85                  90                  95

Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu Asn
            100                 105                 110

Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val Thr
        115                 120                 125

Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile Lys
    130                 135                 140

Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn Thr
145                 150                 155                 160

Ser
```

<210> 566
<211> 154
<212> PRT
<213> Homo sapiens

<400> 566

```
Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
1               5                   10                  15

Thr Thr Ala Leu Ser Met Lys Lys Pro Lys Leu Leu Tyr Cys Ser Asn
            20                  25                  30

Gly Gly His Phe Leu Arg Ile Leu Pro Asp Gly Thr Val Asp Gly Thr
        35                  40                  45

Arg Asp Arg Ser Asp Gln His Ile Gln Leu Gln Leu Ser Ala Glu Ser
    50                  55                  60

Val Gly Glu Val Tyr Ile Lys Ser Thr Glu Thr Gly Gln Tyr Leu Ala
65                  70                  75                  80

Met Asp Thr Asp Gly Leu Leu Tyr Gly Ser Gln Thr Pro Asn Glu Glu
                85                  90                  95

Cys Leu Phe Leu Glu Arg Leu Glu Glu Asn His Tyr Asn Thr Tyr Ile
            100                 105                 110
```

```
Ser Lys Lys His Ala Glu Lys Asn Trp Phe Val Gly Leu Lys Lys Asn
        115                 120                 125


Gly Ser Cys Lys Arg Gly Pro Arg Thr His Tyr Gly Gln Lys Ala Ile
    130                 135                 140


Leu Phe Leu Pro Leu Pro Val Ser Ser Asp
145                 150


<210>  567
<211>  753
<212>  PRT
<213>  Homo sapiens

<400>  567

Met Glu Arg Arg Ala Trp Ser Leu Gln Cys Thr Ala Phe Val Leu Phe
1               5                   10                  15


Cys Ala Trp Cys Ala Leu Asn Ser Ala Lys Ala Lys Arg Gln Phe Val
            20                  25                  30


Asn Glu Trp Ala Ala Glu Ile Pro Gly Gly Pro Glu Ala Ala Ser Ala
        35                  40                  45


Ile Ala Glu Glu Leu Gly Tyr Asp Leu Leu Gly Gln Ile Gly Ser Leu
    50                  55                  60


Glu Asn His Tyr Leu Phe Lys His Lys Asn His Pro Arg Arg Ser Arg
65                  70                  75                  80


Arg Ser Ala Phe His Ile Thr Lys Arg Leu Ser Asp Asp Asp Arg Val
                85                  90                  95


Ile Trp Ala Glu Gln Gln Tyr Glu Lys Glu Arg Ser Lys Arg Ser Ala
            100                 105                 110


Leu Arg Asp Ser Ala Leu Asn Leu Phe Asn Asp Pro Met Trp Asn Gln
        115                 120                 125


Gln Trp Tyr Leu Gln Asp Thr Arg Met Thr Ala Ala Leu Pro Lys Leu
    130                 135                 140


Asp Leu His Val Ile Pro Val Trp Gln Lys Gly Ile Thr Gly Lys Gly
145                 150                 155                 160


Val Val Ile Thr Val Leu Asp Asp Gly Leu Glu Trp Asn His Thr Asp
                165                 170                 175


Ile Tyr Ala Asn Tyr Asp Pro Glu Ala Ser Tyr Asp Phe Asn Asp Asn
            180                 185                 190
```

```
Asp His Asp Pro Phe Pro Arg Tyr Asp Pro Thr Asn Glu Asn Lys His
        195                 200                 205

Gly Thr Arg Cys Ala Gly Glu Ile Ala Met Gln Ala Asn Asn His Lys
    210                 215                 220

Cys Gly Val Gly Val Ala Tyr Asn Ser Lys Val Gly Gly Ile Arg Met
225                 230                 235                 240

Leu Asp Gly Ile Val Thr Asp Ala Ile Glu Ala Ser Ser Ile Gly Phe
                245                 250                 255

Asn Pro Gly His Val Asp Ile Tyr Ser Ala Ser Trp Gly Pro Asn Asp
            260                 265                 270

Asp Gly Lys Thr Val Glu Gly Pro Gly Arg Leu Ala Gln Lys Ala Phe
        275                 280                 285

Glu Tyr Gly Val Lys Gln Gly Arg Gln Gly Lys Gly Ser Ile Phe Val
    290                 295                 300

Trp Ala Ser Gly Asn Gly Gly Arg Gln Gly Asp Asn Cys Asp Cys Asp
305                 310                 315                 320

Gly Tyr Thr Asp Ser Ile Tyr Thr Ile Ser Ile Ser Ser Ala Ser Gln
                325                 330                 335

Gln Gly Leu Ser Pro Trp Tyr Ala Glu Lys Cys Ser Ser Thr Leu Ala
            340                 345                 350

Thr Ser Tyr Ser Ser Gly Asp Tyr Thr Asp Gln Arg Ile Thr Ser Ala
        355                 360                 365

Asp Leu His Asn Asp Cys Thr Glu Thr His Thr Gly Thr Ser Ala Ser
    370                 375                 380

Ala Pro Leu Ala Ala Gly Ile Phe Ala Leu Ala Leu Glu Ala Asn Pro
385                 390                 395                 400

Asn Leu Thr Trp Arg Asp Met Gln His Leu Val Val Trp Thr Ser Glu
                405                 410                 415

Tyr Asp Pro Leu Ala Asn Asn Pro Gly Trp Lys Lys Asn Gly Ala Gly
            420                 425                 430

Leu Met Val Asn Ser Arg Phe Gly Phe Gly Leu Leu Asn Ala Lys Ala
        435                 440                 445

Leu Val Asp Leu Ala Asp Pro Arg Thr Trp Arg Ser Val Pro Glu Lys
    450                 455                 460
```

```
Lys Glu Cys Val Val Lys Asp Asn Asp Phe Glu Pro Arg Ala Leu Lys
465                 470                 475                 480

Ala Asn Gly Glu Val Ile Ile Glu Ile Pro Thr Arg Ala Cys Glu Gly
                485                 490                 495

Gln Glu Asn Ala Ile Lys Ser Leu Glu His Val Gln Phe Glu Ala Thr
            500                 505                 510

Ile Glu Tyr Ser Arg Arg Gly Asp Leu His Val Thr Leu Thr Ser Ala
        515                 520                 525

Ala Gly Thr Ser Thr Val Leu Leu Ala Glu Arg Glu Arg Asp Thr Ser
    530                 535                 540

Pro Asn Gly Phe Lys Asn Trp Asp Phe Met Ser Val His Thr Trp Gly
545                 550                 555                 560

Glu Asn Pro Ile Gly Thr Trp Thr Leu Arg Ile Thr Asp Met Ser Gly
                565                 570                 575

Arg Ile Gln Asn Glu Gly Arg Ile Val Asn Trp Lys Leu Ile Leu His
            580                 585                 590

Gly Thr Ser Ser Gln Pro Glu His Met Lys Gln Pro Arg Val Tyr Thr
        595                 600                 605

Ser Tyr Asn Thr Val Gln Asn Asp Arg Arg Gly Val Glu Lys Met Val
    610                 615                 620

Asp Pro Gly Glu Glu Gln Pro Thr Gln Glu Asn Pro Lys Glu Asn Thr
625                 630                 635                 640

Leu Val Ser Lys Ser Pro Ser Ser Ser Ser Val Gly Gly Arg Arg Asp
                645                 650                 655

Glu Leu Glu Glu Gly Ala Pro Ser Gln Ala Met Leu Arg Leu Leu Gln
            660                 665                 670

Ser Ala Phe Ser Lys Asn Ser Pro Pro Lys Gln Ser Pro Lys Lys Ser
        675                 680                 685

Pro Ser Ala Lys Leu Asn Ile Pro Tyr Glu Asn Phe Tyr Glu Ala Leu
    690                 695                 700

Glu Lys Leu Asn Lys Pro Ser Gln Leu Lys Asp Ser Glu Asp Ser Leu
705                 710                 715                 720

Tyr Asn Asp Tyr Val Asp Val Phe Tyr Asn Thr Lys Pro Tyr Lys His
                725                 730                 735
```

Arg Asp Asp Arg Leu Leu Gln Ala Leu Val Asp Ile Leu Asn Glu Glu
740 745 750

Asn

<210> 568
<211> 638
<212> PRT
<213> Homo sapiens

<400> 568

Met Lys Gly Gly Cys Val Ser Gln Trp Lys Ala Ala Ala Gly Phe Leu
1 5 10 15

Phe Cys Val Met Val Phe Ala Ser Ala Glu Arg Pro Val Phe Thr Asn
20 25 30

His Phe Leu Val Glu Leu His Lys Gly Gly Glu Asp Lys Ala Arg Gln
35 40 45

Val Ala Ala Glu His Gly Phe Gly Val Arg Lys Leu Pro Phe Ala Glu
50 55 60

Gly Leu Tyr His Phe Tyr His Asn Gly Leu Ala Lys Ala Lys Arg Arg
65 70 75 80

Arg Ser Leu His His Lys Gln Gln Leu Glu Arg Asp Pro Arg Val Lys
85 90 95

Met Ala Leu Gln Gln Glu Gly Phe Asp Arg Lys Lys Arg Gly Tyr Arg
100 105 110

Asp Ile Asn Glu Ile Asp Ile Asn Met Asn Asp Pro Leu Phe Thr Lys
115 120 125

Gln Trp Tyr Leu Ile Asn Thr Gly Gln Ala Asp Gly Thr Pro Gly Leu
130 135 140

Asp Leu Asn Val Ala Glu Ala Trp Glu Leu Gly Tyr Thr Gly Lys Gly
145 150 155 160

Val Thr Ile Gly Ile Met Asp Asp Gly Ile Asp Tyr Leu His Pro Asp
165 170 175

Leu Ala Ser Asn Tyr Asn Ala Glu Ala Ser Tyr Asp Phe Ser Ser Asn
180 185 190

Asp Pro Tyr Pro Tyr Pro Arg Tyr Thr Asp Asp Trp Phe Asn Ser His
195 200 205

Gly Thr Arg Cys Ala Gly Glu Val Ser Ala Ala Ala Asn Asn Asn Ile

210 215 220

Cys Gly Val Gly Val Ala Tyr Asn Ser Lys Val Ala Gly Ile Arg Met
225 230 235 240

Leu Asp Gln Pro Phe Met Thr Asp Ile Ile Glu Ala Ser Ser Ile Ser
245 250 255

His Met Pro Gln Leu Ile Asp Ile Tyr Ser Ala Ser Trp Gly Pro Thr
260 265 270

Asp Asn Gly Lys Thr Val Asp Gly Pro Arg Glu Leu Thr Leu Gln Ala
275 280 285

Met Ala Asp Gly Val Asn Lys Gly Arg Gly Gly Lys Gly Ser Ile Tyr
290 295 300

Val Trp Ala Ser Gly Asp Gly Gly Ser Tyr Asp Asp Cys Asn Cys Asp
305 310 315 320

Gly Tyr Ala Ser Ser Met Trp Thr Ile Ser Ile Asn Ser Ala Ile Asn
325 330 335

Asp Gly Arg Thr Ala Leu Tyr Asp Glu Ser Cys Ser Ser Thr Leu Ala
340 345 350

Ser Thr Phe Ser Asn Gly Arg Lys Arg Asn Pro Glu Ala Gly Val Ala
355 360 365

Thr Thr Asp Leu Tyr Gly Asn Cys Thr Leu Arg His Ser Gly Thr Ser
370 375 380

Ala Ala Ala Pro Glu Ala Ala Gly Val Phe Ala Leu Ala Leu Glu Ala
385 390 395 400

Asn Leu Gly Leu Thr Trp Arg Asp Met Gln His Leu Thr Val Leu Thr
405 410 415

Ser Lys Arg Asn Gln Leu His Asp Glu Val His Gln Trp Arg Arg Asn
420 425 430

Gly Val Gly Leu Glu Phe Asn His Leu Phe Gly Tyr Gly Val Leu Asp
435 440 445

Ala Gly Ala Met Val Lys Met Ala Lys Asp Trp Lys Thr Val Pro Glu
450 455 460

Arg Phe His Cys Val Gly Gly Ser Val Gln Asp Pro Glu Lys Ile Pro
465 470 475 480

Ser Thr Gly Lys Leu Val Leu Thr Leu Thr Thr Asp Ala Cys Glu Gly

485 490 495

Lys Glu Asn Phe Val Arg Tyr Leu Glu His Val Gln Ala Val Ile Thr
500 505 510

Val Asn Ala Thr Arg Arg Gly Asp Leu Asn Ile Asn Met Thr Ser Pro
515 520 525

Met Gly Thr Lys Ser Ile Leu Leu Ser Arg Arg Pro Arg Asp Asp Asp
530 535 540

Ser Lys Val Gly Phe Asp Lys Trp Pro Phe Met Thr Thr His Thr Trp
545 550 555 560

Gly Glu Asp Ala Arg Gly Thr Trp Thr Leu Glu Leu Gly Phe Val Gly
565 570 575

Ser Ala Pro Gln Lys Gly Val Leu Lys Glu Trp Thr Leu Met Leu His
580 585 590

Gly Thr Gln Ser Ala Pro Tyr Ile Asp Gln Val Val Arg Asp Tyr Gln
595 600 605

Ser Lys Leu Ala Met Ser Lys Lys Glu Glu Leu Glu Glu Glu Leu Asp
610 615 620

Glu Ala Val Glu Arg Ser Leu Lys Ser Ile Leu Asn Lys Asn
625 630 635

<210> 569
<211> 794
<212> PRT
<213> Homo sapiens

<400> 569

Met Glu Leu Arg Pro Trp Leu Leu Trp Val Val Ala Ala Thr Gly Thr
1 5 10 15

Leu Val Leu Leu Ala Ala Asp Ala Gln Gly Gln Lys Val Phe Thr Asn
20 25 30

Thr Trp Ala Val Arg Ile Pro Gly Gly Pro Ala Val Ala Asn Ser Val
35 40 45

Ala Arg Lys His Gly Phe Leu Asn Leu Gly Gln Ile Phe Gly Asp Tyr
50 55 60

Tyr His Phe Trp His Arg Gly Val Thr Lys Arg Ser Leu Ser Pro His
65 70 75 80

Arg Pro Arg His Ser Arg Leu Gln Arg Glu Pro Gln Val Gln Trp Leu
85 90 95

```
Glu Gln Gln Val Ala Lys Arg Arg Thr Lys Arg Asp Val Tyr Gln Glu
            100                 105                 110

Pro Thr Asp Pro Lys Phe Pro Gln Gln Trp Tyr Leu Ser Gly Val Thr
        115                 120                 125

Gln Arg Asp Leu Asn Val Lys Ala Ala Trp Ala Gln Gly Tyr Thr Gly
    130                 135                 140

His Gly Ile Val Val Ser Ile Leu Asp Asp Gly Ile Glu Lys Asn His
145                 150                 155                 160

Pro Asp Leu Ala Gly Asn Tyr Asp Pro Gly Ala Ser Phe Asp Val Asn
                165                 170                 175

Asp Gln Asp Pro Asp Pro Gln Pro Arg Tyr Thr Gln Met Asn Asp Asn
            180                 185                 190

Arg His Gly Thr Arg Cys Ala Gly Glu Val Ala Ala Val Ala Asn Asn
        195                 200                 205

Gly Val Cys Gly Val Gly Val Ala Tyr Asn Ala Arg Ile Gly Gly Val
    210                 215                 220

Arg Met Leu Asp Gly Glu Val Thr Asp Ala Val Glu Ala Arg Ser Leu
225                 230                 235                 240

Gly Leu Asn Pro Asn His Ile His Ile Tyr Ser Ala Ser Trp Gly Pro
                245                 250                 255

Glu Asp Asp Gly Lys Thr Val Asp Gly Pro Ala Arg Leu Ala Glu Glu
            260                 265                 270

Ala Phe Phe Arg Gly Val Ser Gln Gly Arg Gly Gly Leu Gly Ser Ile
        275                 280                 285

Phe Val Trp Ala Ser Gly Asn Gly Gly Arg Glu His Asp Ser Cys Asn
    290                 295                 300

Cys Asp Gly Tyr Thr Asn Ser Ile Tyr Thr Leu Ser Ile Ser Ser Ala
305                 310                 315                 320

Thr Gln Phe Gly Asn Val Pro Trp Tyr Ser Glu Ala Cys Ser Ser Thr
                325                 330                 335

Leu Ala Thr Thr Tyr Ser Ser Gly Asn Gln Asn Glu Lys Gln Ile Val
            340                 345                 350

Thr Thr Asp Leu Arg Gln Lys Cys Thr Glu Ser His Thr Gly Thr Ser
        355                 360                 365
```

```
Ala Ser Ala Pro Leu Ala Ala Gly Ile Ile Ala Leu Thr Leu Glu Ala
    370                 375                 380

Asn Lys Asn Leu Thr Trp Arg Asp Met Gln His Leu Val Val Gln Thr
385                 390                 395                 400

Ser Lys Pro Ala His Leu Asn Ala Asn Asp Trp Ala Thr Asn Gly Val
                405                 410                 415

Gly Arg Lys Val Ser His Ser Tyr Gly Tyr Gly Leu Leu Asp Ala Gly
            420                 425                 430

Ala Met Val Ala Leu Ala Gln Asn Trp Thr Thr Val Ala Pro Gln Arg
        435                 440                 445

Lys Cys Ile Ile Asp Ile Leu Thr Glu Pro Lys Asp Ile Gly Lys Arg
    450                 455                 460

Leu Glu Val Arg Lys Thr Val Thr Ala Cys Leu Gly Glu Pro Asn His
465                 470                 475                 480

Ile Thr Arg Leu Glu His Ala Gln Ala Arg Leu Thr Leu Ser Tyr Asn
                485                 490                 495

Arg Arg Gly Asp Leu Ala Ile His Leu Val Ser Pro Met Gly Thr Arg
            500                 505                 510

Ser Thr Leu Leu Ala Ala Arg Pro His Asp Tyr Ser Ala Asp Gly Phe
        515                 520                 525

Asn Asp Trp Ala Phe Met Thr Thr His Ser Trp Asp Glu Asp Pro Ser
    530                 535                 540

Gly Glu Trp Val Leu Glu Ile Glu Asn Thr Ser Glu Ala Asn Asn Tyr
545                 550                 555                 560

Gly Thr Leu Thr Lys Phe Thr Leu Val Leu Tyr Gly Thr Ala Pro Glu
                565                 570                 575

Gly Leu Pro Val Pro Pro Glu Ser Ser Gly Cys Lys Thr Leu Thr Ser
            580                 585                 590

Ser Gln Ala Cys Val Val Cys Glu Glu Gly Phe Ser Leu His Gln Lys
        595                 600                 605

Ser Cys Val Gln His Cys Pro Pro Gly Phe Ala Pro Gln Val Leu Asp
    610                 615                 620

Thr His Tyr Ser Thr Glu Asn Asp Val Glu Thr Ile Arg Ala Ser Val
625                 630                 635                 640
```

```
Cys Ala Pro Cys His Ala Ser Cys Ala Thr Cys Gln Gly Pro Ala Leu
                645                 650                 655

Thr Asp Cys Leu Ser Cys Pro Ser His Ala Ser Leu Asp Pro Val Glu
            660                 665                 670

Gln Thr Cys Ser Arg Gln Ser Gln Ser Ser Arg Glu Ser Pro Pro Gln
        675                 680                 685

Gln Gln Pro Pro Arg Leu Pro Pro Glu Val Glu Ala Gly Gln Arg Leu
    690                 695                 700

Arg Ala Gly Leu Leu Pro Ser His Leu Pro Glu Val Val Ala Gly Leu
705                 710                 715                 720

Ser Cys Ala Phe Ile Val Leu Val Phe Val Thr Val Phe Leu Val Leu
                725                 730                 735

Gln Leu Arg Ser Gly Phe Ser Phe Arg Gly Val Lys Val Tyr Thr Met
            740                 745                 750

Asp Arg Gly Leu Ile Ser Tyr Lys Gly Leu Pro Pro Glu Ala Trp Gln
        755                 760                 765

Glu Glu Cys Pro Ser Asp Ser Glu Glu Asp Glu Gly Arg Gly Glu Arg
    770                 775                 780

Thr Ala Phe Ile Lys Asp Gln Ser Ala Leu
785                 790


<210>  570
<211>  715
<212>  PRT
<213>  Homo sapiens

<400>  570

Met Glu Leu Arg Pro Trp Leu Leu Trp Val Val Ala Ala Thr Gly Thr
1               5                   10                  15

Leu Val Leu Leu Ala Ala Asp Ala Gln Gly Gln Lys Val Phe Thr Asn
            20                  25                  30

Thr Trp Ala Val Arg Ile Pro Gly Gly Pro Ala Val Ala Asn Ser Val
        35                  40                  45

Ala Arg Lys His Gly Phe Leu Asn Leu Gly Gln Ile Phe Gly Asp Tyr
    50                  55                  60

Tyr His Phe Trp His Arg Gly Val Thr Lys Arg Ser Leu Ser Pro His
65                  70                  75                  80
```

```
Arg Pro Arg His Ser Arg Leu Gln Arg Glu Pro Gln Val Gln Trp Leu
                85                  90                  95

Glu Gln Gln Val Ala Lys Arg Arg Thr Lys Arg Asp Val Tyr Gln Glu
            100                 105                 110

Pro Thr Asp Pro Lys Phe Pro Gln Gln Trp Tyr Leu Ser Gly Val Thr
        115                 120                 125

Gln Arg Asp Leu Asn Val Lys Ala Ala Trp Ala Gln Gly Tyr Thr Gly
    130                 135                 140

His Gly Ile Val Val Ser Ile Leu Asp Asp Gly Ile Glu Lys Asn His
145                 150                 155                 160

Pro Asp Leu Ala Gly Asn Tyr Asp Pro Gly Ala Ser Phe Asp Val Asn
                165                 170                 175

Asp Gln Asp Pro Asp Pro Gln Pro Arg Tyr Thr Gln Met Asn Asp Asn
            180                 185                 190

Arg His Gly Thr Arg Cys Ala Gly Glu Val Ala Ala Val Ala Asn Asn
        195                 200                 205

Gly Val Cys Gly Val Gly Val Ala Tyr Asn Ala Arg Ile Gly Gly Val
    210                 215                 220

Arg Met Leu Asp Gly Glu Val Thr Asp Ala Val Glu Ala Arg Ser Leu
225                 230                 235                 240

Gly Leu Asn Pro Asn His Ile His Ile Tyr Ser Ala Ser Trp Gly Pro
                245                 250                 255

Glu Asp Asp Gly Lys Thr Val Asp Gly Pro Ala Arg Leu Ala Glu Glu
            260                 265                 270

Ala Phe Phe Arg Gly Val Ser Gln Gly Arg Gly Gly Leu Gly Ser Ile
        275                 280                 285

Phe Val Trp Ala Ser Gly Asn Gly Gly Arg Glu His Asp Ser Cys Asn
    290                 295                 300

Cys Asp Gly Tyr Thr Asn Ser Ile Tyr Thr Leu Ser Ile Ser Ser Ala
305                 310                 315                 320

Thr Gln Phe Gly Asn Val Pro Trp Tyr Ser Glu Ala Cys Ser Ser Thr
                325                 330                 335

Leu Ala Thr Thr Tyr Ser Ser Gly Asn Gln Asn Glu Lys Gln Ile Val
            340                 345                 350
```

```
Thr Thr Asp Leu Arg Gln Lys Cys Thr Glu Ser His Thr Gly Thr Ser
        355                 360                 365

Ala Ser Ala Pro Leu Ala Ala Gly Ile Ile Ala Leu Thr Leu Glu Ala
    370                 375                 380

Asn Lys Asn Leu Thr Trp Arg Asp Met Gln His Leu Val Val Gln Thr
385                 390                 395                 400

Ser Lys Pro Ala His Leu Asn Ala Asn Asp Trp Ala Thr Asn Gly Val
                405                 410                 415

Gly Arg Lys Val Ser His Ser Tyr Gly Tyr Gly Leu Leu Asp Ala Gly
            420                 425                 430

Ala Met Val Ala Leu Ala Gln Asn Trp Thr Thr Val Ala Pro Gln Arg
        435                 440                 445

Lys Cys Ile Ile Asp Ile Leu Thr Glu Pro Lys Asp Ile Gly Lys Arg
    450                 455                 460

Leu Glu Val Arg Lys Thr Val Thr Ala Cys Leu Gly Glu Pro Asn His
465                 470                 475                 480

Ile Thr Arg Leu Glu His Ala Gln Ala Arg Leu Thr Leu Ser Tyr Asn
                485                 490                 495

Arg Arg Gly Asp Leu Ala Ile His Leu Val Ser Pro Met Gly Thr Arg
            500                 505                 510

Ser Thr Leu Leu Ala Ala Arg Pro His Asp Tyr Ser Ala Asp Gly Phe
        515                 520                 525

Asn Asp Trp Ala Phe Met Thr Thr His Ser Trp Asp Glu Asp Pro Ser
    530                 535                 540

Gly Glu Trp Val Leu Glu Ile Glu Asn Thr Ser Glu Ala Asn Asn Tyr
545                 550                 555                 560

Gly Thr Leu Thr Lys Phe Thr Leu Val Leu Tyr Gly Thr Ala Pro Glu
                565                 570                 575

Gly Leu Pro Val Pro Pro Glu Ser Ser Gly Cys Lys Thr Leu Thr Ser
            580                 585                 590

Ser Gln Ala Cys Val Val Cys Glu Glu Gly Phe Ser Leu His Gln Lys
        595                 600                 605

Ser Cys Val Gln His Cys Pro Pro Gly Phe Ala Pro Gln Val Leu Asp
    610                 615                 620
```

```
Thr His Tyr Ser Thr Glu Asn Asp Val Glu Thr Ile Arg Ala Ser Val
625                 630                 635                 640


Cys Ala Pro Cys His Ala Ser Cys Ala Thr Cys Gln Gly Pro Ala Leu
                645                 650                 655


Thr Asp Cys Leu Ser Cys Pro Ser His Ala Ser Leu Asp Pro Val Glu
            660                 665                 670


Gln Thr Cys Ser Arg Gln Ser Gln Ser Ser Arg Glu Ser Pro Pro Gln
        675                 680                 685


Gln Gln Pro Pro Arg Leu Pro Pro Glu Val Glu Ala Gly Gln Arg Leu
    690                 695                 700


Arg Ala Gly Leu Leu Pro Ser His Leu Pro Glu
705                 710                 715


<210>  571
<211>  755
<212>  PRT
<213>  Homo sapiens

<400>  571

Met Arg Pro Ala Pro Ile Ala Leu Trp Leu Arg Leu Val Leu Ala Leu
1               5                   10                  15


Ala Leu Val Arg Pro Arg Ala Val Gly Trp Ala Pro Val Arg Ala Pro
            20                  25                  30


Ile Tyr Val Ser Ser Trp Ala Val Gln Val Ser Gln Gly Asn Arg Glu
        35                  40                  45


Val Glu Arg Leu Ala Arg Lys Phe Gly Phe Val Asn Leu Gly Pro Ile
    50                  55                  60


Phe Pro Asp Gly Gln Tyr Phe His Leu Arg His Arg Gly Val Val Gln
65                  70                  75                  80


Gln Ser Leu Thr Pro His Trp Gly His Arg Leu His Leu Lys Lys Asn
                85                  90                  95


Pro Lys Val Gln Trp Phe Gln Gln Gln Thr Leu Gln Arg Arg Val Lys
            100                 105                 110


Arg Ser Val Val Val Pro Thr Asp Pro Trp Phe Ser Lys Gln Trp Tyr
        115                 120                 125


Met Asn Ser Glu Ala Gln Pro Asp Leu Ser Ile Leu Gln Ala Trp Ser
    130                 135                 140
```

```
Gln Gly Leu Ser Gly Gln Gly Ile Val Val Ser Val Leu Asp Asp Gly
145                 150                 155                 160

Ile Glu Lys Asp His Pro Asp Leu Trp Ala Asn Tyr Asp Pro Leu Ala
                165                 170                 175

Ser Tyr Asp Phe Asn Asp Tyr Asp Pro Asp Pro Gln Pro Arg Tyr Thr
            180                 185                 190

Pro Ser Lys Glu Asn Arg His Gly Thr Arg Cys Ala Gly Glu Val Ala
        195                 200                 205

Ala Met Ala Asn Asn Gly Phe Cys Gly Val Gly Val Ala Phe Asn Ala
    210                 215                 220

Arg Ile Gly Gly Val Arg Met Leu Asp Gly Thr Ile Thr Asp Val Ile
225                 230                 235                 240

Glu Ala Gln Ser Leu Ser Leu Gln Pro Gln His Ile His Ile Tyr Ser
                245                 250                 255

Ala Ser Trp Gly Pro Glu Asp Asp Gly Arg Thr Val Asp Gly Pro Gly
            260                 265                 270

Ile Leu Thr Arg Glu Ala Phe Arg Arg Gly Val Thr Lys Gly Arg Gly
        275                 280                 285

Gly Leu Gly Thr Leu Phe Ile Trp Ala Ser Gly Asn Gly Gly Leu His
    290                 295                 300

Tyr Asp Asn Cys Asn Cys Asp Gly Tyr Thr Asn Ser Ile His Thr Leu
305                 310                 315                 320

Ser Val Gly Ser Thr Thr Gln Gln Gly Arg Val Pro Trp Tyr Ser Glu
                325                 330                 335

Ala Cys Ala Ser Thr Leu Thr Thr Thr Tyr Ser Ser Gly Val Ala Thr
            340                 345                 350

Asp Pro Gln Ile Val Thr Thr Asp Leu His His Gly Cys Thr Asp Gln
        355                 360                 365

His Thr Gly Thr Ser Ala Ser Ala Pro Leu Ala Ala Gly Met Ile Ala
    370                 375                 380

Leu Ala Leu Glu Ala Asn Pro Phe Leu Thr Trp Arg Asp Met Gln His
385                 390                 395                 400

Leu Val Val Arg Ala Ser Lys Pro Ala His Leu Gln Ala Glu Asp Trp
                405                 410                 415
```

```
Arg Thr Asn Gly Val Gly Arg Gln Val Ser His His Tyr Gly Tyr Gly
            420                 425                 430

Leu Leu Asp Ala Gly Leu Leu Val Asp Thr Ala Arg Thr Trp Leu Pro
        435                 440                 445

Thr Gln Pro Gln Arg Lys Cys Ala Val Arg Val Gln Ser Arg Pro Thr
    450                 455                 460

Pro Ile Leu Pro Leu Ile Tyr Ile Arg Glu Asn Val Ser Ala Cys Ala
465                 470                 475                 480

Gly Leu His Asn Ser Ile Arg Ser Leu Glu His Val Gln Ala Gln Leu
                485                 490                 495

Thr Leu Ser Tyr Ser Arg Arg Gly Asp Leu Glu Ile Ser Leu Thr Ser
            500                 505                 510

Pro Met Gly Thr Arg Ser Thr Leu Val Ala Ile Arg Pro Leu Asp Val
        515                 520                 525

Ser Thr Glu Gly Tyr Asn Asn Trp Val Phe Met Ser Thr His Phe Trp
    530                 535                 540

Asp Glu Asn Pro Gln Gly Val Trp Thr Leu Gly Leu Glu Asn Lys Gly
545                 550                 555                 560

Tyr Tyr Phe Asn Thr Gly Thr Leu Tyr Arg Tyr Thr Leu Leu Leu Tyr
                565                 570                 575

Gly Thr Ala Glu Asp Met Thr Ala Arg Pro Thr Gly Pro Gln Val Thr
            580                 585                 590

Ser Ser Ala Cys Val Gln Arg Asp Thr Glu Gly Leu Cys Gln Ala Cys
        595                 600                 605

Asp Gly Pro Ala Tyr Ile Leu Gly Gln Leu Cys Leu Ala Tyr Cys Pro
    610                 615                 620

Pro Arg Phe Phe Asn His Thr Arg Leu Val Thr Ala Gly Pro Gly His
625                 630                 635                 640

Thr Ala Ala Pro Ala Leu Arg Val Cys Ser Ser Cys His Ala Ser Cys
                645                 650                 655

Tyr Thr Cys Arg Gly Gly Ser Pro Arg Asp Cys Thr Ser Cys Pro Pro
            660                 665                 670

Ser Ser Thr Leu Asp Gln Gln Gln Gly Ser Cys Met Gly Pro Thr Thr
        675                 680                 685
```

Pro Asp Ser Arg Pro Arg Leu Arg Ala Ala Ala Cys Pro His His Arg
690 695 700

Cys Pro Ala Ser Ala Met Val Leu Ser Leu Leu Ala Val Thr Leu Gly
705 710 715 720

Gly Pro Val Leu Cys Gly Met Ser Met Asp Leu Pro Leu Tyr Ala Trp
725 730 735

Leu Ser Arg Ala Arg Ala Thr Pro Thr Lys Pro Gln Val Trp Leu Pro
740 745 750

Ala Gly Thr
755

<210> 572
<211> 1860
<212> PRT
<213> Homo sapiens

<400> 572

Met Gly Trp Gly Ser Arg Cys Cys Cys Pro Gly Arg Leu Asp Leu Leu
1 5 10 15

Cys Val Leu Ala Leu Leu Gly Gly Cys Leu Leu Pro Val Cys Arg Thr
20 25 30

Arg Val Tyr Thr Asn His Trp Ala Val Lys Ile Ala Gly Gly Phe Pro
35 40 45

Glu Ala Asn Arg Ile Ala Ser Lys Tyr Gly Phe Ile Asn Ile Gly Gln
50 55 60

Ile Gly Ala Leu Lys Asp Tyr Tyr His Phe Tyr His Ser Arg Thr Ile
65 70 75 80

Lys Arg Ser Val Ile Ser Ser Arg Gly Thr His Ser Phe Ile Ser Met
85 90 95

Glu Pro Lys Val Glu Trp Ile Gln Gln Gln Val Val Lys Lys Arg Thr
100 105 110

Lys Arg Asp Tyr Asp Phe Ser Arg Ala Gln Ser Thr Tyr Phe Asn Asp
115 120 125

Pro Lys Trp Pro Ser Met Trp Tyr Met His Cys Ser Asp Asn Thr His
130 135 140

Pro Cys Gln Ser Asp Met Asn Ile Glu Gly Ala Trp Lys Arg Gly Tyr
145 150 155 160

Thr Gly Lys Asn Ile Val Val Thr Ile Leu Asp Asp Gly Ile Glu Arg

165 170 175

Thr His Pro Asp Leu Met Gln Asn Tyr Asp Ala Leu Ala Ser Cys Asp
180 185 190

Val Asn Gly Asn Asp Leu Asp Pro Met Pro Arg Tyr Asp Ala Ser Asn
195 200 205

Glu Asn Lys His Gly Thr Arg Cys Ala Gly Glu Val Ala Ala Ala Ala
210 215 220

Asn Asn Ser His Cys Thr Val Gly Ile Ala Phe Asn Ala Lys Ile Gly
225 230 235 240

Gly Val Arg Met Leu Asp Gly Asp Val Thr Asp Met Val Glu Ala Lys
245 250 255

Ser Val Ser Phe Asn Pro Gln His Val His Ile Tyr Ser Ala Ser Trp
260 265 270

Gly Pro Asp Asp Asp Gly Lys Thr Val Asp Gly Pro Ala Pro Leu Thr
275 280 285

Arg Gln Ala Phe Glu Asn Gly Val Arg Met Gly Arg Arg Gly Leu Gly
290 295 300

Ser Val Phe Val Trp Ala Ser Gly Asn Gly Gly Arg Ser Lys Asp His
305 310 315 320

Cys Ser Cys Asp Gly Tyr Thr Asn Ser Ile Tyr Thr Ile Ser Ile Ser
325 330 335

Ser Thr Ala Glu Ser Gly Lys Lys Pro Trp Tyr Leu Glu Glu Cys Ser
340 345 350

Ser Thr Leu Ala Thr Thr Tyr Ser Ser Gly Glu Ser Tyr Asp Lys Lys
355 360 365

Ile Ile Thr Thr Asp Leu Arg Gln Arg Cys Thr Asp Asn His Thr Gly
370 375 380

Thr Ser Ala Ser Ala Pro Met Ala Ala Gly Ile Ile Ala Leu Ala Leu
385 390 395 400

Glu Ala Asn Pro Phe Leu Thr Trp Arg Asp Val Gln His Val Ile Val
405 410 415

Arg Thr Ser Arg Ala Gly His Leu Asn Ala Asn Asp Trp Lys Thr Asn
420 425 430

Ala Ala Gly Phe Lys Val Ser His Leu Tyr Gly Phe Gly Leu Met Asp

```
        435                 440                 445

Ala Glu Ala Met Val Met Glu Ala Glu Lys Trp Thr Thr Val Pro Arg
    450                 455                 460

Gln His Val Cys Val Glu Ser Thr Asp Arg Gln Ile Lys Thr Ile Arg
465                 470                 475                 480

Pro Asn Ser Ala Val Arg Ser Ile Tyr Lys Ala Ser Gly Cys Ser Asp
                485                 490                 495

Asn Pro Asn Arg His Val Asn Tyr Leu Glu His Val Val Val Arg Ile
            500                 505                 510

Thr Ile Thr His Pro Arg Arg Gly Asp Leu Ala Ile Tyr Leu Thr Ser
        515                 520                 525

Pro Ser Gly Thr Arg Ser Gln Leu Leu Ala Asn Arg Leu Phe Asp His
    530                 535                 540

Ser Met Glu Gly Phe Lys Asn Trp Glu Phe Met Thr Ile His Cys Trp
545                 550                 555                 560

Gly Glu Arg Ala Ala Gly Asp Trp Val Leu Glu Val Tyr Asp Thr Pro
                565                 570                 575

Ser Gln Leu Arg Asn Phe Lys Thr Pro Gly Lys Leu Lys Glu Trp Ser
            580                 585                 590

Leu Val Leu Tyr Gly Thr Ser Val Gln Pro Tyr Ser Pro Thr Asn Glu
        595                 600                 605

Phe Pro Lys Val Glu Arg Phe Arg Tyr Ser Arg Val Glu Asp Pro Thr
    610                 615                 620

Asp Asp Tyr Gly Thr Glu Asp Tyr Ala Gly Pro Cys Asp Pro Glu Cys
625                 630                 635                 640

Ser Glu Val Gly Cys Asp Gly Pro Gly Pro Asp His Cys Asn Asp Cys
                645                 650                 655

Leu His Tyr Tyr Tyr Lys Leu Lys Asn Asn Thr Arg Ile Cys Val Ser
            660                 665                 670

Ser Cys Pro Pro Gly His Tyr His Ala Asp Lys Lys Arg Cys Arg Lys
        675                 680                 685

Cys Ala Pro Asn Cys Glu Ser Cys Phe Gly Ser His Gly Asp Gln Cys
    690                 695                 700

Met Ser Cys Lys Tyr Gly Tyr Phe Leu Asn Glu Glu Thr Asn Ser Cys
```

705 710 715 720

Val Thr His Cys Pro Asp Gly Ser Tyr Gln Asp Thr Lys Lys Asn Leu
725 730 735

Cys Arg Lys Cys Ser Glu Asn Cys Lys Thr Cys Thr Glu Phe His Asn
740 745 750

Cys Thr Glu Cys Arg Asp Gly Leu Ser Leu Gln Gly Ser Arg Cys Ser
755 760 765

Val Ser Cys Glu Asp Gly Arg Tyr Phe Asn Gly Gln Asp Cys Gln Pro
770 775 780

Cys His Arg Phe Cys Ala Thr Cys Ala Gly Ala Gly Ala Asp Gly Cys
785 790 795 800

Ile Asn Cys Thr Glu Gly Tyr Phe Met Glu Asp Gly Arg Cys Val Gln
805 810 815

Ser Cys Ser Ile Ser Tyr Tyr Phe Asp His Ser Ser Glu Asn Gly Tyr
820 825 830

Lys Ser Cys Lys Lys Cys Asp Ile Ser Cys Leu Thr Cys Asn Gly Pro
835 840 845

Gly Phe Lys Asn Cys Thr Ser Cys Pro Ser Gly Tyr Leu Leu Asp Leu
850 855 860

Gly Met Cys Gln Met Gly Ala Ile Cys Lys Asp Gly Glu Tyr Val Asp
865 870 875 880

Glu His Gly His Cys Gln Thr Cys Glu Ala Ser Cys Ala Lys Cys Gln
885 890 895

Gly Pro Thr Gln Glu Asp Cys Thr Thr Cys Pro Met Thr Arg Ile Phe
900 905 910

Asp Asp Gly Arg Cys Val Ser Asn Cys Pro Ser Trp Lys Phe Glu Phe
915 920 925

Glu Asn Gln Cys His Pro Cys His His Thr Cys Gln Arg Cys Gln Gly
930 935 940

Ser Gly Pro Thr His Cys Thr Ser Cys Gly Ala Asp Asn Tyr Gly Arg
945 950 955 960

Glu His Phe Leu Tyr Gln Gly Glu Cys Gly Asp Ser Cys Pro Glu Gly
965 970 975

His Tyr Ala Thr Glu Gly Asn Thr Cys Leu Pro Cys Pro Asp Asn Cys

980 985 990

Glu Leu Cys His Ser Val His Val Cys Thr Arg Cys Met Lys Gly Tyr
995 1000 1005

Phe Ile Ala Pro Thr Asn His Thr Cys Gln Lys Leu Glu Cys Gly
1010 1015 1020

Gln Gly Glu Val Gln Asp Pro Asp Tyr Glu Glu Cys Val Pro Cys
1025 1030 1035

Glu Glu Gly Cys Leu Gly Cys Ser Leu Asp Asp Pro Gly Thr Cys
1040 1045 1050

Thr Ser Cys Ala Met Gly Tyr Tyr Arg Phe Asp His His Cys Tyr
1055 1060 1065

Lys Thr Cys Pro Glu Lys Thr Tyr Ser Glu Glu Val Glu Cys Lys
1070 1075 1080

Ala Cys Asp Ser Asn Cys Gly Ser Cys Asp Gln Asn Gly Cys Tyr
1085 1090 1095

Trp Cys Glu Glu Gly Phe Phe Leu Leu Gly Gly Ser Cys Val Arg
1100 1105 1110

Lys Cys Gly Pro Gly Phe Tyr Gly Asp Gln Glu Met Gly Glu Cys
1115 1120 1125

Glu Ser Cys His Arg Ala Cys Glu Thr Cys Thr Gly Pro Gly His
1130 1135 1140

Asp Glu Cys Ser Ser Cys Gln Glu Gly Leu Gln Leu Leu Arg Gly
1145 1150 1155

Met Cys Val His Ala Thr Lys Thr Gln Glu Glu Gly Lys Phe Trp
1160 1165 1170

Asn Asp Ile Leu Arg Lys Leu Gln Pro Cys His Ser Ser Cys Lys
1175 1180 1185

Thr Cys Asn Gly Ser Ala Thr Leu Cys Thr Ser Cys Pro Lys Gly
1190 1195 1200

Ala Tyr Leu Leu Ala Gln Ala Cys Val Ser Ser Cys Pro Gln Gly
1205 1210 1215

Thr Trp Pro Ser Val Arg Ser Gly Ser Cys Glu Asn Cys Thr Glu
1220 1225 1230

Ala Cys Ala Ile Cys Ser Gly Ala Asp Leu Cys Lys Lys Cys Gln

1235 1240 1245

Met Gln Pro Gly His Pro Leu Phe Leu His Glu Gly Arg Cys Tyr
1250 1255 1260

Ser Lys Cys Pro Glu Gly Ser Tyr Ala Glu Asp Gly Ile Cys Glu
1265 1270 1275

Arg Cys Ser Ser Pro Cys Arg Thr Cys Glu Gly Asn Ala Thr Asn
1280 1285 1290

Cys His Ser Cys Glu Gly Gly His Val Leu His His Gly Val Cys
1295 1300 1305

Gln Glu Asn Cys Pro Glu Arg His Val Ala Val Lys Gly Val Cys
1310 1315 1320

Lys His Cys Pro Glu Met Cys Gln Asp Cys Ile His Glu Lys Thr
1325 1330 1335

Cys Lys Glu Cys Thr Pro Glu Phe Phe Leu His Asp Asp Met Cys
1340 1345 1350

His Gln Ser Cys Pro Arg Gly Phe Tyr Ala Asp Ser Arg His Cys
1355 1360 1365

Val Pro Cys His Lys Asp Cys Leu Glu Cys Ser Gly Pro Lys Ala
1370 1375 1380

Asp Asp Cys Glu Leu Cys Leu Glu Ser Ser Trp Val Leu Tyr Asp
1385 1390 1395

Gly Leu Cys Leu Glu Glu Cys Pro Ala Gly Thr Tyr Tyr Glu Lys
1400 1405 1410

Glu Thr Lys Glu Cys Arg Asp Cys His Lys Ser Cys Leu Thr Cys
1415 1420 1425

Ser Ser Ser Gly Thr Cys Thr Thr Cys Gln Lys Gly Leu Ile Met
1430 1435 1440

Asn Pro Arg Gly Ser Cys Met Ala Asn Glu Lys Cys Ser Pro Ser
1445 1450 1455

Glu Tyr Trp Asp Glu Asp Ala Pro Gly Cys Lys Pro Cys His Val
1460 1465 1470

Lys Cys Phe His Cys Met Gly Pro Ala Glu Asp Gln Cys Gln Thr
1475 1480 1485

Cys Pro Met Asn Ser Leu Leu Leu Asn Thr Thr Cys Val Lys Asp

1490 1495 1500

Cys Pro Glu Gly Tyr Tyr Ala Asp Glu Asp Ser Asn Arg Cys Ala
1505 1510 1515

His Cys His Ser Ser Cys Arg Thr Cys Glu Gly Arg His Ser Arg
1520 1525 1530

Gln Cys His Ser Cys Arg Pro Gly Trp Phe Gln Leu Gly Lys Glu
1535 1540 1545

Cys Leu Leu Gln Cys Arg Glu Gly Tyr Tyr Ala Asp Asn Ser Thr
1550 1555 1560

Gly Arg Cys Glu Arg Cys Asn Arg Ser Cys Lys Gly Cys Gln Gly
1565 1570 1575

Pro Arg Pro Thr Asp Cys Leu Ser Cys Asp Arg Phe Phe Phe Leu
1580 1585 1590

Leu Arg Ser Lys Gly Glu Cys His Arg Ser Cys Pro Asp His Tyr
1595 1600 1605

Tyr Val Glu Gln Ser Thr Gln Thr Cys Glu Arg Cys His Pro Thr
1610 1615 1620

Cys Asp Gln Cys Lys Gly Lys Gly Ala Leu Asn Cys Leu Ser Cys
1625 1630 1635

Val Trp Ser Tyr His Leu Met Gly Gly Ile Cys Thr Ser Asp Cys
1640 1645 1650

Leu Val Gly Glu Tyr Arg Val Gly Glu Gly Glu Lys Phe Asn Cys
1655 1660 1665

Glu Lys Cys His Glu Ser Cys Met Glu Cys Lys Gly Pro Gly Ala
1670 1675 1680

Lys Asn Cys Thr Leu Cys Pro Ala Asn Leu Val Leu His Met Asp
1685 1690 1695

Asp Ser His Cys Leu His Cys Cys Asn Thr Ser Asp Pro Pro Ser
1700 1705 1710

Ala Gln Glu Cys Cys Asp Cys Gln Asp Thr Thr Asp Glu Cys Ile
1715 1720 1725

Leu Arg Thr Ser Lys Val Arg Pro Ala Thr Glu His Phe Lys Thr
1730 1735 1740

Ala Leu Phe Ile Thr Ser Ser Met Met Leu Val Leu Leu Leu Gly

1745 1750 1755

Ala Ala Val Val Val Trp Lys Lys Ser Arg Gly Arg Val Gln Pro
1760 1765 1770

Ala Ala Lys Ala Gly Tyr Glu Lys Leu Ala Asp Pro Asn Lys Ser
1775 1780 1785

Tyr Ser Ser Tyr Lys Ser Ser Tyr Arg Glu Ser Thr Ser Phe Glu
1790 1795 1800

Glu Asp Gln Val Ile Glu Tyr Arg Asp Arg Asp Tyr Asp Glu Asp
1805 1810 1815

Asp Asp Asp Asp Ile Val Tyr Met Gly Gln Asp Gly Thr Val Tyr
1820 1825 1830

Arg Lys Phe Lys Tyr Gly Leu Leu Asp Asp Asp Asp Ile Asp Glu
1835 1840 1845

Leu Glu Tyr Asp Asp Glu Ser Tyr Ser Tyr Tyr Gln
1850 1855 1860

<210> 573
<211> 969
<212> PRT
<213> Homo sapiens

<400> 573

Met Pro Pro Arg Ala Pro Pro Ala Pro Gly Pro Arg Pro Pro Pro Arg
1 5 10 15

Ala Ala Ala Ala Thr Asp Thr Ala Ala Gly Ala Gly Gly Ala Gly Gly
20 25 30

Ala Gly Gly Ala Gly Gly Pro Gly Phe Arg Pro Leu Ala Pro Arg Pro
35 40 45

Trp Arg Trp Leu Leu Leu Leu Ala Leu Pro Ala Ala Cys Ser Ala Pro
50 55 60

Pro Pro Arg Pro Val Tyr Thr Asn His Trp Ala Val Gln Val Leu Gly
65 70 75 80

Gly Pro Ala Glu Ala Asp Arg Val Ala Ala Ala His Gly Tyr Leu Asn
85 90 95

Leu Gly Gln Ile Gly Asn Leu Glu Asp Tyr Tyr His Phe Tyr His Ser
100 105 110

Lys Thr Phe Lys Arg Ser Thr Leu Ser Ser Arg Gly Pro His Thr Phe
115 120 125

```
Leu Arg Met Asp Pro Gln Val Lys Trp Leu Gln Gln Gln Glu Val Lys
    130                 135                 140

Arg Arg Val Lys Arg Gln Val Arg Ser Asp Pro Gln Ala Leu Tyr Phe
145                 150                 155                 160

Asn Asp Pro Ile Trp Ser Asn Met Trp Tyr Leu His Cys Gly Asp Lys
                165                 170                 175

Asn Ser Arg Cys Arg Ser Glu Met Asn Val Gln Ala Ala Trp Lys Arg
            180                 185                 190

Gly Tyr Thr Gly Lys Asn Val Val Val Thr Ile Leu Asp Asp Gly Ile
        195                 200                 205

Glu Arg Asn His Pro Asp Leu Ala Pro Asn Tyr Asp Ser Tyr Ala Ser
    210                 215                 220

Tyr Asp Val Asn Gly Asn Asp Tyr Asp Pro Ser Pro Arg Tyr Asp Ala
225                 230                 235                 240

Ser Asn Glu Asn Lys His Gly Thr Arg Cys Ala Gly Glu Val Ala Ala
                245                 250                 255

Ser Ala Asn Asn Ser Tyr Cys Ile Val Gly Ile Ala Tyr Asn Ala Lys
            260                 265                 270

Ile Gly Gly Ile Arg Met Leu Asp Gly Asp Val Thr Asp Val Val Glu
        275                 280                 285

Ala Lys Ser Leu Gly Ile Arg Pro Asn Tyr Ile Asp Ile Tyr Ser Ala
    290                 295                 300

Ser Trp Gly Pro Asp Asp Asp Gly Lys Thr Val Asp Gly Pro Gly Arg
305                 310                 315                 320

Leu Ala Lys Gln Ala Phe Glu Tyr Gly Ile Lys Lys Gly Arg Gln Gly
                325                 330                 335

Leu Gly Ser Ile Phe Val Trp Ala Ser Gly Asn Gly Gly Arg Glu Gly
            340                 345                 350

Asp Tyr Cys Ser Cys Asp Gly Tyr Thr Asn Ser Ile Tyr Thr Ile Ser
        355                 360                 365

Val Ser Ser Ala Thr Glu Asn Gly Tyr Lys Pro Trp Tyr Leu Glu Glu
    370                 375                 380

Cys Ala Ser Thr Leu Ala Thr Thr Tyr Ser Ser Gly Ala Phe Tyr Glu
385                 390                 395                 400
```

```
Arg Lys Ile Val Thr Thr Asp Leu Arg Gln Arg Cys Thr Asp Gly His
                405                 410                 415

Thr Gly Thr Ser Val Ser Ala Pro Met Val Ala Gly Ile Ile Ala Leu
            420                 425                 430

Ala Leu Glu Ala Asn Ser Gln Leu Thr Trp Arg Asp Val Gln His Leu
        435                 440                 445

Leu Val Lys Thr Ser Arg Pro Ala His Leu Lys Ala Ser Asp Trp Lys
    450                 455                 460

Val Asn Gly Ala Gly His Lys Val Ser His Phe Tyr Gly Phe Gly Leu
465                 470                 475                 480

Val Asp Ala Glu Ala Leu Val Val Glu Ala Lys Lys Trp Thr Ala Val
                485                 490                 495

Pro Ser Gln His Met Cys Val Ala Ala Ser Asp Lys Arg Pro Arg Ser
            500                 505                 510

Ile Pro Leu Val Gln Val Leu Arg Thr Thr Ala Leu Thr Ser Ala Cys
        515                 520                 525

Ala Glu His Ser Asp Gln Arg Val Val Tyr Leu Glu His Val Val Val
    530                 535                 540

Arg Thr Ser Ile Ser His Pro Arg Arg Gly Asp Leu Gln Ile Tyr Leu
545                 550                 555                 560

Val Ser Pro Ser Gly Thr Lys Ser Gln Leu Leu Ala Lys Arg Leu Leu
                565                 570                 575

Asp Leu Ser Asn Glu Gly Phe Thr Asn Trp Glu Phe Met Thr Val His
            580                 585                 590

Cys Trp Gly Glu Lys Ala Glu Gly Gln Trp Thr Leu Glu Ile Gln Asp
        595                 600                 605

Leu Pro Ser Gln Val Arg Asn Pro Glu Lys Gln Gly Lys Leu Lys Glu
    610                 615                 620

Trp Ser Leu Ile Leu Tyr Gly Thr Ala Glu His Pro Tyr His Thr Phe
625                 630                 635                 640

Ser Ala His Gln Ser Arg Ser Arg Met Leu Glu Leu Ser Ala Pro Glu
                645                 650                 655

Leu Glu Pro Pro Lys Ala Ala Leu Ser Pro Ser Gln Val Glu Val Pro
            660                 665                 670
```

```
Glu Asp Glu Glu Asp Tyr Thr Ala Gln Ser Thr Pro Gly Ser Ala Asn
        675                 680                 685

Ile Leu Gln Thr Ser Val Cys His Pro Glu Cys Gly Asp Lys Gly Cys
    690                 695                 700

Asp Gly Pro Asn Ala Asp Gln Cys Leu Asn Cys Val His Phe Ser Leu
705                 710                 715                 720

Gly Ser Val Lys Thr Ser Arg Lys Cys Val Ser Val Cys Pro Leu Gly
                725                 730                 735

Tyr Phe Gly Asp Thr Ala Ala Arg Arg Cys Arg Arg Cys His Lys Gly
            740                 745                 750

Cys Glu Thr Cys Ser Ser Arg Ala Ala Thr Gln Cys Leu Ser Cys Arg
        755                 760                 765

Arg Gly Phe Tyr His His Gln Glu Met Asn Thr Cys Val Thr Leu Cys
    770                 775                 780

Pro Ala Gly Phe Tyr Ala Asp Glu Ser Gln Lys Asn Cys Leu Lys Cys
785                 790                 795                 800

His Pro Ser Cys Lys Lys Cys Val Asp Glu Pro Glu Lys Cys Thr Val
                805                 810                 815

Cys Lys Glu Gly Phe Ser Leu Ala Arg Gly Ser Cys Ile Pro Asp Cys
            820                 825                 830

Glu Pro Gly Thr Tyr Phe Asp Ser Glu Leu Ile Arg Cys Gly Glu Cys
        835                 840                 845

His His Thr Cys Gly Thr Cys Val Gly Pro Gly Arg Glu Glu Cys Ile
    850                 855                 860

His Cys Ala Lys Asn Phe His Phe His Asp Trp Lys Cys Val Pro Ala
865                 870                 875                 880

Cys Gly Glu Gly Phe Tyr Pro Glu Glu Met Pro Gly Leu Pro His Lys
                885                 890                 895

Val Cys Arg Arg Cys Asp Glu Asn Cys Leu Ser Cys Ala Gly Ser Ser
            900                 905                 910

Arg Asn Cys Ser Arg Cys Lys Thr Gly Phe Thr Gln Leu Gly Thr Ser
        915                 920                 925

Cys Ile Thr Asn His Thr Cys Ser Asn Ala Asp Glu Thr Phe Cys Glu
    930                 935                 940
```

```
Met Val Lys Ser Asn Arg Leu Cys Glu Arg Lys Leu Phe Ile Gln Phe
945                 950                 955                 960


Cys Cys Arg Thr Cys Leu Leu Ala Gly
                965


<210>  574
<211>  785
<212>  PRT
<213>  Homo sapiens

<400>  574

Met Pro Lys Gly Arg Gln Lys Val Pro His Leu Asp Ala Pro Leu Gly
1               5                   10                  15


Leu Pro Thr Cys Leu Trp Leu Glu Leu Ala Gly Leu Phe Leu Leu Val
            20                  25                  30


Pro Trp Val Met Gly Leu Ala Gly Thr Gly Gly Pro Asp Gly Gln Gly
        35                  40                  45


Thr Gly Gly Pro Ser Trp Ala Val His Leu Glu Ser Leu Glu Gly Asp
    50                  55                  60


Gly Glu Glu Glu Thr Leu Glu Gln Gln Ala Asp Ala Leu Ala Gln Ala
65                  70                  75                  80


Ala Gly Leu Val Asn Ala Gly Arg Ile Gly Glu Leu Gln Gly His Tyr
                85                  90                  95


Leu Phe Val Gln Pro Ala Gly His Arg Pro Ala Leu Glu Val Glu Ala
            100                 105                 110


Ile Arg Gln Gln Val Glu Ala Val Leu Ala Gly His Glu Ala Val Arg
        115                 120                 125


Trp His Ser Glu Gln Arg Leu Leu Arg Arg Ala Lys Arg Ser Val His
    130                 135                 140


Phe Asn Asp Pro Lys Tyr Pro Gln Gln Trp His Leu Asn Asn Arg Arg
145                 150                 155                 160


Ser Pro Gly Arg Asp Ile Asn Val Thr Gly Val Trp Glu Arg Asn Val
                165                 170                 175


Thr Gly Arg Gly Val Thr Val Val Val Val Asp Asp Gly Val Glu His
            180                 185                 190


Thr Ile Gln Asp Ile Ala Pro Asn Tyr Ser Pro Glu Gly Ser Tyr Asp
        195                 200                 205
```

```
Leu Asn Ser Asn Asp Pro Asp Pro Met Pro His Pro Asp Val Glu Asn
    210                 215                 220

Gly Asn His His Gly Thr Arg Cys Ala Gly Glu Ile Ala Ala Val Pro
225                 230                 235                 240

Asn Asn Ser Phe Cys Ala Val Gly Val Ala Tyr Gly Ser Arg Ile Ala
                245                 250                 255

Gly Ile Arg Val Leu Asp Gly Pro Leu Thr Asp Ser Met Glu Ala Val
            260                 265                 270

Ala Phe Asn Lys His Tyr Gln Ile Asn Asp Ile Tyr Ser Cys Ser Trp
        275                 280                 285

Gly Pro Asp Asp Asp Gly Lys Thr Val Asp Gly Pro His Gln Leu Gly
    290                 295                 300

Lys Ala Ala Leu Gln His Gly Val Ile Ala Gly Arg Gln Gly Phe Gly
305                 310                 315                 320

Ser Ile Phe Val Val Ala Ser Gly Asn Gly Gly Gln His Asn Asp Asn
                325                 330                 335

Cys Asn Tyr Asp Gly Tyr Ala Asn Ser Ile Tyr Thr Val Thr Ile Gly
            340                 345                 350

Ala Val Asp Glu Glu Gly Arg Met Pro Phe Tyr Ala Glu Glu Cys Ala
        355                 360                 365

Ser Met Leu Ala Val Thr Phe Ser Gly Gly Asp Lys Met Leu Arg Ser
    370                 375                 380

Ile Val Thr Thr Asp Trp Asp Leu Gln Lys Gly Thr Gly Cys Thr Glu
385                 390                 395                 400

Gly His Thr Gly Thr Ser Ala Ala Ala Pro Leu Ala Ala Gly Met Ile
                405                 410                 415

Ala Leu Met Leu Gln Val Arg Pro Cys Leu Thr Trp Arg Asp Val Gln
            420                 425                 430

His Ile Ile Val Phe Thr Ala Thr Arg Tyr Glu Asp Arg Arg Ala Glu
        435                 440                 445

Trp Val Thr Asn Glu Ala Gly Phe Ser His Ser His Gln His Gly Phe
    450                 455                 460

Gly Leu Leu Asn Ala Trp Arg Leu Val Asn Ala Ala Lys Ile Trp Thr
465                 470                 475                 480
```

```
Ser Val Pro Tyr Leu Ala Ser Tyr Val Ser Pro Val Leu Lys Glu Asn
                485                 490                 495

Lys Ala Ile Pro Gln Ser Pro Arg Ser Leu Glu Val Leu Trp Asn Val
            500                 505                 510

Ser Arg Met Asp Leu Glu Met Ser Gly Leu Lys Thr Leu Glu His Val
        515                 520                 525

Ala Val Thr Val Ser Ile Thr His Pro Arg Arg Gly Ser Leu Glu Leu
    530                 535                 540

Lys Leu Phe Cys Pro Ser Gly Met Met Ser Leu Ile Gly Ala Pro Arg
545                 550                 555                 560

Ser Met Asp Ser Asp Pro Asn Gly Phe Asn Asp Trp Thr Phe Ser Thr
                565                 570                 575

Val Arg Cys Trp Gly Glu Arg Ala Arg Gly Thr Tyr Arg Leu Val Ile
            580                 585                 590

Arg Asp Val Gly Asp Glu Ser Phe Gln Val Gly Ile Leu Arg Gln Trp
        595                 600                 605

Gln Leu Thr Leu Tyr Gly Ser Val Trp Ser Ala Val Asp Ile Arg Asp
    610                 615                 620

Arg Gln Arg Leu Leu Glu Ser Ala Met Ser Gly Lys Tyr Leu His Asp
625                 630                 635                 640

Asp Phe Ala Leu Pro Cys Pro Pro Gly Leu Lys Ile Pro Glu Glu Asp
                645                 650                 655

Gly Tyr Thr Ile Thr Pro Asn Thr Leu Lys Thr Leu Val Leu Val Gly
            660                 665                 670

Cys Phe Thr Val Phe Trp Thr Val Tyr Tyr Met Leu Glu Val Tyr Leu
        675                 680                 685

Ser Gln Arg Asn Val Ala Ser Asn Gln Val Cys Arg Ser Gly Pro Cys
    690                 695                 700

His Trp Pro His Arg Ser Arg Lys Ala Lys Glu Glu Gly Thr Glu Leu
705                 710                 715                 720

Glu Ser Val Pro Leu Cys Ser Ser Lys Asp Pro Asp Glu Val Glu Thr
                725                 730                 735

Glu Ser Arg Gly Pro Pro Thr Thr Ser Asp Leu Leu Ala Pro Asp Leu
            740                 745                 750
```

```
Leu Glu Gln Gly Asp Trp Ser Leu Ser Gln Asn Lys Ser Ala Leu Asp
        755                 760                 765


Cys Pro His Gln His Leu Asp Val Pro His Gly Lys Glu Glu Gln Ile
    770                 775                 780


Cys
785


<210>  575
<211>  1052
<212>  PRT
<213>  Homo sapiens

<400>  575

Met Lys Leu Val Asn Ile Trp Leu Leu Leu Val Val Leu Leu Cys
1               5                   10                  15


Gly Lys Lys His Leu Gly Asp Arg Leu Glu Lys Lys Ser Phe Glu Lys
            20                  25                  30


Ala Pro Cys Pro Gly Cys Ser His Leu Thr Leu Lys Val Glu Phe Ser
        35                  40                  45


Ser Thr Val Val Glu Tyr Glu Tyr Ile Val Ala Phe Asn Gly Tyr Phe
    50                  55                  60


Thr Ala Lys Ala Arg Asn Ser Phe Ile Ser Ser Ala Leu Lys Ser Ser
65                  70                  75                  80


Glu Val Asp Asn Trp Arg Ile Ile Pro Arg Asn Asn Pro Ser Ser Asp
                85                  90                  95


Tyr Pro Ser Asp Phe Glu Val Ile Gln Ile Lys Glu Lys Gln Lys Ala
            100                 105                 110


Gly Leu Leu Thr Leu Glu Asp His Pro Asn Ile Lys Arg Val Thr Pro
        115                 120                 125


Gln Arg Lys Val Phe Arg Ser Leu Lys Tyr Ala Glu Ser Asp Pro Thr
    130                 135                 140


Val Pro Cys Asn Glu Thr Arg Trp Ser Gln Lys Trp Gln Ser Ser Arg
145                 150                 155                 160


Pro Leu Arg Arg Ala Ser Leu Ser Leu Gly Ser Gly Phe Trp His Ala
                165                 170                 175


Thr Gly Arg His Ser Ser Arg Arg Leu Leu Arg Ala Ile Pro Arg Gln
            180                 185                 190
```

```
Val Ala Gln Thr Leu Gln Ala Asp Val Leu Trp Gln Met Gly Tyr Thr
        195                 200                 205

Gly Ala Asn Val Arg Val Ala Val Phe Asp Thr Gly Leu Ser Glu Lys
    210                 215                 220

His Pro His Phe Lys Asn Val Lys Glu Arg Thr Asn Trp Thr Asn Glu
225                 230                 235                 240

Arg Thr Leu Asp Asp Gly Leu Gly His Gly Thr Phe Val Ala Gly Val
                245                 250                 255

Ile Ala Ser Met Arg Glu Cys Gln Gly Phe Ala Pro Asp Ala Glu Leu
            260                 265                 270

His Ile Phe Arg Val Phe Thr Asn Asn Gln Val Ser Tyr Thr Ser Trp
        275                 280                 285

Phe Leu Asp Ala Phe Asn Tyr Ala Ile Leu Lys Lys Ile Asp Val Leu
    290                 295                 300

Asn Leu Ser Ile Gly Gly Pro Asp Phe Met Asp His Pro Phe Val Asp
305                 310                 315                 320

Lys Val Trp Glu Leu Thr Ala Asn Asn Val Ile Met Val Ser Ala Ile
                325                 330                 335

Gly Asn Asp Gly Pro Leu Tyr Gly Thr Leu Asn Asn Pro Ala Asp Gln
            340                 345                 350

Met Asp Val Ile Gly Val Gly Gly Ile Asp Phe Glu Asp Asn Ile Ala
        355                 360                 365

Arg Phe Ser Ser Arg Gly Met Thr Thr Trp Glu Leu Pro Gly Gly Tyr
    370                 375                 380

Gly Arg Met Lys Pro Asp Ile Val Thr Tyr Gly Ala Gly Val Arg Gly
385                 390                 395                 400

Ser Gly Val Lys Gly Gly Cys Arg Ala Leu Ser Gly Thr Ser Val Ala
                405                 410                 415

Ser Pro Val Val Ala Gly Ala Val Thr Leu Leu Val Ser Thr Val Gln
            420                 425                 430

Lys Arg Glu Leu Val Asn Pro Ala Ser Met Lys Gln Ala Leu Ile Ala
        435                 440                 445

Ser Ala Arg Arg Leu Pro Gly Val Asn Met Phe Glu Gln Gly His Gly
    450                 455                 460
```

```
Lys Leu Asp Leu Leu Arg Ala Tyr Gln Ile Leu Asn Ser Tyr Lys Pro
465                 470                 475                 480

Gln Ala Ser Leu Ser Pro Ser Tyr Ile Asp Leu Thr Glu Cys Pro Tyr
                485                 490                 495

Met Trp Pro Tyr Cys Ser Gln Pro Ile Tyr Tyr Gly Gly Met Pro Thr
            500                 505                 510

Val Val Asn Val Thr Ile Leu Asn Gly Met Gly Val Thr Gly Arg Ile
        515                 520                 525

Val Asp Lys Pro Asp Trp Gln Pro Tyr Leu Pro Gln Asn Gly Asp Asn
    530                 535                 540

Ile Glu Val Ala Phe Ser Tyr Ser Ser Val Leu Trp Pro Trp Ser Gly
545                 550                 555                 560

Tyr Leu Ala Ile Ser Ile Ser Val Thr Lys Lys Ala Ala Ser Trp Glu
                565                 570                 575

Gly Ile Ala Gln Gly His Val Met Ile Thr Val Ala Ser Pro Ala Glu
            580                 585                 590

Thr Glu Ser Lys Asn Gly Ala Glu Gln Thr Ser Thr Val Lys Leu Pro
        595                 600                 605

Ile Lys Val Lys Ile Ile Pro Thr Pro Pro Arg Ser Lys Arg Val Leu
    610                 615                 620

Trp Asp Gln Tyr His Asn Leu Arg Tyr Pro Pro Gly Tyr Phe Pro Arg
625                 630                 635                 640

Asp Asn Leu Arg Met Lys Asn Asp Pro Leu Asp Trp Asn Gly Asp His
                645                 650                 655

Ile His Thr Asn Phe Arg Asp Met Tyr Gln His Leu Arg Ser Met Gly
            660                 665                 670

Tyr Phe Val Glu Val Leu Gly Ala Pro Phe Thr Cys Phe Asp Ala Ser
        675                 680                 685

Gln Tyr Gly Thr Leu Leu Met Val Asp Ser Glu Glu Glu Tyr Phe Pro
    690                 695                 700

Glu Glu Ile Ala Lys Leu Arg Arg Asp Val Asp Asn Gly Leu Ser Leu
705                 710                 715                 720

Val Ile Phe Ser Asp Trp Tyr Asn Thr Ser Val Met Arg Lys Val Lys
                725                 730                 735
```

```
Phe Tyr Asp Glu Asn Thr Arg Gln Trp Trp Met Pro Asp Thr Gly Gly
            740                 745                 750

Ala Asn Ile Pro Ala Leu Asn Glu Leu Leu Ser Val Trp Asn Met Gly
        755                 760                 765

Phe Ser Asp Gly Leu Tyr Glu Gly Glu Phe Thr Leu Ala Asn His Asp
    770                 775                 780

Met Tyr Tyr Ala Ser Gly Cys Ser Ile Ala Lys Phe Pro Glu Asp Gly
785                 790                 795                 800

Val Val Ile Thr Gln Thr Phe Lys Asp Gln Gly Leu Glu Val Leu Lys
                805                 810                 815

Gln Glu Thr Ala Val Val Glu Asn Val Pro Ile Leu Gly Leu Tyr Gln
            820                 825                 830

Ile Pro Ala Glu Gly Gly Gly Arg Ile Val Leu Tyr Gly Asp Ser Asn
        835                 840                 845

Cys Leu Asp Asp Ser His Arg Gln Lys Asp Cys Phe Trp Leu Leu Asp
    850                 855                 860

Ala Leu Leu Gln Tyr Thr Ser Tyr Gly Val Thr Pro Pro Ser Leu Ser
865                 870                 875                 880

His Ser Gly Asn Arg Gln Arg Pro Pro Ser Gly Ala Gly Ser Val Thr
                885                 890                 895

Pro Glu Arg Met Glu Gly Asn His Leu His Arg Tyr Ser Lys Val Leu
            900                 905                 910

Glu Ala His Leu Gly Asp Pro Lys Pro Arg Pro Leu Pro Ala Cys Pro
        915                 920                 925

Arg Leu Ser Trp Ala Lys Pro Gln Pro Leu Asn Glu Thr Ala Pro Ser
    930                 935                 940

Asn Leu Trp Lys His Gln Lys Leu Leu Ser Ile Asp Leu Asp Lys Val
945                 950                 955                 960

Val Leu Pro Asn Phe Arg Ser Asn Arg Pro Gln Val Arg Pro Leu Ser
                965                 970                 975

Pro Gly Glu Ser Gly Ala Trp Asp Ile Pro Gly Gly Ile Met Pro Gly
            980                 985                 990

Arg Tyr Asn Gln Glu Val Gly Gln  Thr Ile Pro Val Phe  Ala Phe Leu
        995                 1000                1005
```

Gly Ala Met Val Val Leu Ala Phe Phe Val Val Gln Ile Asn Lys
1010 1015 1020

Ala Lys Ser Arg Pro Lys Arg Arg Lys Pro Arg Val Lys Arg Pro
1025 1030 1035

Gln Leu Met Gln Gln Val His Pro Pro Lys Thr Pro Ser Val
1040 1045 1050

<210> 576
<211> 692
<212> PRT
<213> Homo sapiens

<400> 576

Met Gly Thr Val Ser Ser Arg Arg Ser Trp Trp Pro Leu Pro Leu Leu
1 5 10 15

Leu Leu Leu Leu Leu Leu Leu Gly Pro Ala Gly Ala Arg Ala Gln Glu
20 25 30

Asp Glu Asp Gly Asp Tyr Glu Glu Leu Val Leu Ala Leu Arg Ser Glu
35 40 45

Glu Asp Gly Leu Ala Glu Ala Pro Glu His Gly Thr Thr Ala Thr Phe
50 55 60

His Arg Cys Ala Lys Asp Pro Trp Arg Leu Pro Gly Thr Tyr Val Val
65 70 75 80

Val Leu Lys Glu Glu Thr His Leu Ser Gln Ser Glu Arg Thr Ala Arg
85 90 95

Arg Leu Gln Ala Gln Ala Ala Arg Arg Gly Tyr Leu Thr Lys Ile Leu
100 105 110

His Val Phe His Gly Leu Leu Pro Gly Phe Leu Val Lys Met Ser Gly
115 120 125

Asp Leu Leu Glu Leu Ala Leu Lys Leu Pro His Val Asp Tyr Ile Glu
130 135 140

Glu Asp Ser Ser Val Phe Ala Gln Ser Ile Pro Trp Asn Leu Glu Arg
145 150 155 160

Ile Thr Pro Pro Arg Tyr Arg Ala Asp Glu Tyr Gln Pro Pro Asp Gly
165 170 175

Gly Ser Leu Val Glu Val Tyr Leu Leu Asp Thr Ser Ile Gln Ser Asp
180 185 190

His Arg Glu Ile Glu Gly Arg Val Met Val Thr Asp Phe Glu Asn Val

```
        195                 200                 205

Pro Glu Glu Asp Gly Thr Arg Phe His Arg Gln Ala Ser Lys Cys Asp
    210                 215                 220

Ser His Gly Thr His Leu Ala Gly Val Val Ser Gly Arg Asp Ala Gly
225                 230                 235                 240

Val Ala Lys Gly Ala Ser Met Arg Ser Leu Arg Val Leu Asn Cys Gln
                245                 250                 255

Gly Lys Gly Thr Val Ser Gly Thr Leu Ile Gly Leu Glu Phe Ile Arg
            260                 265                 270

Lys Ser Gln Leu Val Gln Pro Val Gly Pro Leu Val Val Leu Leu Pro
        275                 280                 285

Leu Ala Gly Gly Tyr Ser Arg Val Leu Asn Ala Ala Cys Gln Arg Leu
    290                 295                 300

Ala Arg Ala Gly Val Val Leu Val Thr Ala Ala Gly Asn Phe Arg Asp
305                 310                 315                 320

Asp Ala Cys Leu Tyr Ser Pro Ala Ser Ala Pro Glu Val Ile Thr Val
                325                 330                 335

Gly Ala Thr Asn Ala Gln Asp Gln Pro Val Thr Leu Gly Thr Leu Gly
            340                 345                 350

Thr Asn Phe Gly Arg Cys Val Asp Leu Phe Ala Pro Gly Glu Asp Ile
        355                 360                 365

Ile Gly Ala Ser Ser Asp Cys Ser Thr Cys Phe Val Ser Gln Ser Gly
    370                 375                 380

Thr Ser Gln Ala Ala Ala His Val Ala Gly Ile Ala Ala Met Met Leu
385                 390                 395                 400

Ser Ala Glu Pro Glu Leu Thr Leu Ala Glu Leu Arg Gln Arg Leu Ile
                405                 410                 415

His Phe Ser Ala Lys Asp Val Ile Asn Glu Ala Trp Phe Pro Glu Asp
            420                 425                 430

Gln Arg Val Leu Thr Pro Asn Leu Val Ala Ala Leu Pro Pro Ser Thr
        435                 440                 445

His Gly Ala Gly Trp Gln Leu Phe Cys Arg Thr Val Trp Ser Ala His
    450                 455                 460

Ser Gly Pro Thr Arg Met Ala Thr Ala Val Ala Arg Cys Ala Pro Asp
```

```
465                 470                 475                 480

Glu Glu Leu Leu Ser Cys Ser Ser Phe Ser Arg Ser Gly Lys Arg Arg
                485                 490                 495

Gly Glu Arg Met Glu Ala Gln Gly Gly Lys Leu Val Cys Arg Ala His
            500                 505                 510

Asn Ala Phe Gly Gly Glu Gly Val Tyr Ala Ile Ala Arg Cys Cys Leu
        515                 520                 525

Leu Pro Gln Ala Asn Cys Ser Val His Thr Ala Pro Pro Ala Glu Ala
    530                 535                 540

Ser Met Gly Thr Arg Val His Cys His Gln Gln Gly His Val Leu Thr
545                 550                 555                 560

Gly Cys Ser Ser His Trp Glu Val Glu Asp Leu Gly Thr His Lys Pro
                565                 570                 575

Pro Val Leu Arg Pro Arg Gly Gln Pro Asn Gln Cys Val Gly His Arg
            580                 585                 590

Glu Ala Ser Ile His Ala Ser Cys Cys His Ala Pro Gly Leu Glu Cys
        595                 600                 605

Lys Val Lys Glu His Gly Ile Pro Ala Pro Gln Glu Gln Val Thr Val
    610                 615                 620

Ala Cys Glu Glu Gly Trp Thr Leu Thr Gly Cys Ser Ala Leu Pro Gly
625                 630                 635                 640

Thr Ser His Val Leu Gly Ala Tyr Ala Val Asp Asn Thr Cys Val Val
                645                 650                 655

Arg Ser Arg Asp Val Ser Thr Thr Gly Ser Thr Ser Glu Gly Ala Val
            660                 665                 670

Thr Ala Val Ala Ile Cys Cys Arg Ser Arg His Leu Ala Gln Ala Ser
        675                 680                 685

Gln Glu Leu Gln
    690


<210>  577
<211>  519
<212>  PRT
<213>  Homo sapiens

<400>  577

Met Ile Pro Val Ser Leu Val Val Val Val Val Gly Gly Trp Thr Val
1               5                   10                  15
```

```
Val Tyr Leu Thr Asp Leu Val Leu Lys Ser Ser Val Tyr Phe Lys His
            20                  25                  30

Ser Tyr Glu Asp Trp Leu Glu Asn Asn Gly Leu Ser Ile Ser Pro Phe
        35                  40                  45

His Ile Arg Trp Gln Thr Ala Val Phe Asn Arg Ala Phe Tyr Ser Trp
    50                  55                  60

Gly Arg Arg Lys Ala Arg Met Leu Tyr Gln Trp Phe Asn Phe Gly Met
65                  70                  75                  80

Val Phe Gly Val Ile Ala Met Phe Ser Ser Phe Phe Leu Leu Gly Lys
                85                  90                  95

Thr Leu Met Gln Thr Leu Ala Gln Met Met Ala Asp Ser Pro Ser Ser
            100                 105                 110

Tyr Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
        115                 120                 125

Ser Ser Ser Ser Ser Ser Ser Ser Leu His Asn Glu Gln Val Leu Gln
    130                 135                 140

Val Val Val Pro Gly Ile Asn Leu Pro Val Asn Gln Leu Thr Tyr Phe
145                 150                 155                 160

Phe Thr Ala Val Leu Ile Ser Gly Val Val His Glu Ile Gly His Gly
                165                 170                 175

Ile Ala Ala Ile Arg Glu Gln Val Arg Phe Asn Gly Phe Gly Ile Phe
            180                 185                 190

Leu Phe Ile Ile Tyr Pro Gly Ala Phe Val Asp Leu Phe Thr Thr His
        195                 200                 205

Leu Gln Leu Ile Ser Pro Val Gln Gln Leu Arg Ile Phe Cys Ala Gly
    210                 215                 220

Ile Trp His Asn Phe Val Leu Ala Leu Leu Gly Ile Leu Ala Leu Val
225                 230                 235                 240

Leu Leu Pro Val Ile Leu Leu Pro Phe Tyr Tyr Thr Gly Val Gly Val
                245                 250                 255

Leu Ile Thr Glu Val Ala Glu Asp Ser Pro Ala Ile Gly Pro Arg Gly
            260                 265                 270

Leu Phe Val Gly Asp Leu Val Thr His Leu Gln Asp Cys Pro Val Thr
        275                 280                 285
```

```
Asn Val Gln Asp Trp Asn Glu Cys Leu Asp Thr Ile Ala Tyr Glu Pro
    290                 295                 300

Gln Ile Gly Tyr Cys Ile Ser Ala Ser Thr Leu Gln Gln Leu Ser Phe
305                 310                 315                 320

Pro Val Arg Ala Tyr Lys Arg Leu Asp Gly Ser Thr Glu Cys Cys Asn
                325                 330                 335

Asn His Ser Leu Thr Asp Val Cys Phe Ser Tyr Arg Asn Asn Phe Asn
            340                 345                 350

Lys Arg Leu His Thr Cys Leu Pro Ala Arg Lys Ala Val Glu Ala Thr
        355                 360                 365

Gln Val Cys Arg Thr Asn Lys Asp Cys Lys Lys Ser Ser Ser Ser Ser
    370                 375                 380

Phe Cys Ile Ile Pro Ser Leu Glu Thr His Thr Arg Leu Ile Lys Val
385                 390                 395                 400

Lys His Pro Pro Gln Ile Asp Met Leu Tyr Val Gly His Pro Leu His
                405                 410                 415

Leu His Tyr Thr Val Ser Ile Thr Ser Phe Ile Pro Arg Phe Asn Phe
            420                 425                 430

Leu Ser Ile Asp Leu Pro Val Val Val Glu Thr Phe Val Lys Tyr Leu
        435                 440                 445

Ile Ser Leu Ser Gly Ala Leu Ala Ile Val Asn Ala Val Pro Cys Phe
    450                 455                 460

Ala Leu Asp Gly Gln Trp Ile Leu Asn Ser Phe Leu Asp Ala Thr Leu
465                 470                 475                 480

Thr Ser Val Ile Gly Asp Asn Asp Val Lys Asp Leu Ile Gly Phe Phe
                485                 490                 495

Ile Leu Leu Gly Gly Ser Val Leu Leu Ala Ala Asn Val Thr Leu Gly
            500                 505                 510

Leu Trp Met Val Thr Ala Arg
        515


<210>  578
<211>  476
<212>  PRT
<213>  Homo sapiens

<400>  578
```

```
Met Ala Gly Arg Gly Gly Ser Ala Leu Leu Ala Leu Cys Gly Ala Leu
1               5                  10                  15

Ala Ala Cys Gly Trp Leu Leu Gly Ala Glu Ala Gln Glu Pro Gly Ala
            20                  25                  30

Pro Ala Ala Gly Met Arg Arg Arg Arg Leu Gln Gln Glu Asp Gly
        35                  40                  45

Ile Ser Phe Glu Tyr His Arg Tyr Pro Glu Leu Arg Glu Ala Leu Val
    50                  55                  60

Ser Val Trp Leu Gln Cys Thr Ala Ile Ser Arg Ile Tyr Thr Val Gly
65                  70                  75                  80

Arg Ser Phe Glu Gly Arg Glu Leu Leu Val Ile Glu Leu Ser Asp Asn
                85                  90                  95

Pro Gly Val His Glu Pro Gly Glu Pro Glu Phe Lys Tyr Ile Gly Asn
            100                 105                 110

Met His Gly Asn Glu Ala Val Gly Arg Glu Leu Leu Ile Phe Leu Ala
        115                 120                 125

Gln Tyr Leu Cys Asn Glu Tyr Gln Lys Gly Asn Glu Thr Ile Val Asn
    130                 135                 140

Leu Ile His Ser Thr Arg Ile His Ile Met Pro Ser Leu Asn Pro Asp
145                 150                 155                 160

Gly Phe Glu Lys Ala Ala Ser Gln Pro Gly Glu Leu Lys Asp Trp Phe
                165                 170                 175

Val Gly Arg Ser Asn Ala Gln Gly Ile Asp Leu Asn Arg Asn Phe Pro
            180                 185                 190

Asp Leu Asp Arg Ile Val Tyr Val Asn Glu Lys Glu Gly Gly Pro Asn
        195                 200                 205

Asn His Leu Leu Lys Asn Met Lys Lys Ile Val Asp Gln Asn Thr Lys
    210                 215                 220

Leu Ala Pro Glu Thr Lys Ala Val Ile His Trp Ile Met Asp Ile Pro
225                 230                 235                 240

Phe Val Leu Ser Ala Asn Leu His Gly Gly Asp Leu Val Ala Asn Tyr
                245                 250                 255

Pro Tyr Asp Glu Thr Arg Ser Gly Ser Ala His Glu Tyr Ser Ser Ser
            260                 265                 270
```

```
Pro Asp Asp Ala Ile Phe Gln Ser Leu Ala Arg Ala Tyr Ser Ser Phe
        275                 280                 285

Asn Pro Ala Met Ser Asp Pro Asn Arg Pro Pro Cys Arg Lys Asn Asp
    290                 295                 300

Asp Asp Ser Ser Phe Val Asp Gly Thr Thr Asn Gly Gly Ala Trp Tyr
305                 310                 315                 320

Ser Val Pro Gly Gly Met Gln Asp Phe Asn Tyr Leu Ser Ser Asn Cys
                325                 330                 335

Phe Glu Ile Thr Val Glu Leu Ser Cys Glu Lys Phe Pro Pro Glu Glu
            340                 345                 350

Thr Leu Lys Thr Tyr Trp Glu Asp Asn Lys Asn Ser Leu Ile Ser Tyr
        355                 360                 365

Leu Glu Gln Ile His Arg Gly Val Lys Gly Phe Val Arg Asp Leu Gln
    370                 375                 380

Gly Asn Pro Ile Ala Asn Ala Thr Ile Ser Val Glu Gly Ile Asp His
385                 390                 395                 400

Asp Val Thr Ser Ala Lys Asp Gly Asp Tyr Trp Arg Leu Leu Ile Pro
                405                 410                 415

Gly Asn Tyr Lys Leu Thr Ala Ser Ala Pro Gly Tyr Leu Ala Ile Thr
            420                 425                 430

Lys Lys Val Ala Val Pro Tyr Ser Pro Ala Ala Gly Val Asp Phe Glu
        435                 440                 445

Leu Glu Ser Phe Ser Glu Arg Lys Glu Glu Glu Lys Glu Glu Leu Met
    450                 455                 460

Glu Trp Trp Lys Met Met Ser Glu Thr Leu Asn Phe
465                 470                 475


<210>  579
<211>  431
<212>  PRT
<213>  Homo sapiens

<400>  579

Met His Val Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala
1               5                   10                  15

Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser
            20                  25                  30
```

```
Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser
        35                  40                  45

Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu
    50                  55                  60

Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro
65                  70                  75                  80

Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly
                85                  90                  95

Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser
            100                 105                 110

Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr
        115                 120                 125

Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys
    130                 135                 140

Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu
145                 150                 155                 160

Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile
                165                 170                 175

Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile
            180                 185                 190

Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu
        195                 200                 205

Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu
    210                 215                 220

Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg
225                 230                 235                 240

His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser
                245                 250                 255

Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn
            260                 265                 270

Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe
        275                 280                 285

Arg Ser Ile Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser
    290                 295                 300
```

Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu
305 310 315 320

Asn Ser Ser Ser Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr
325 330 335

Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu
340 345 350

Gly Tyr Ala Ala Asn Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn
355 360 365

Ser His Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His
370 375 380

Phe Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln
385 390 395 400

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile
405 410 415

Leu Lys Lys Tyr Arg Asn Met Val Val Glu Ala Cys Gly Cys His
420 425 430

<210> 580
<211> 431
<212> PRT
<213> Homo sapiens

<400> 580

Met His Val Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala
1 5 10 15

Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser
20 25 30

Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser
35 40 45

Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu
50 55 60

Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro
65 70 75 80

Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly
85 90 95

Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser
100 105 110

Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr

```
        115                 120                 125

Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys
    130                 135                 140

Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu
145                 150                 155                 160

Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile
                165                 170                 175

Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile
            180                 185                 190

Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu
        195                 200                 205

Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu
    210                 215                 220

Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg
225                 230                 235                 240

His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser
                245                 250                 255

Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn
            260                 265                 270

Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe
        275                 280                 285

Arg Ser Ile Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser
    290                 295                 300

Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu
305                 310                 315                 320

Asn Ser Ser Ser Asp Gln Arg Gln Ala Cys Ser Lys His Glu Leu Tyr
                325                 330                 335

Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu
            340                 345                 350

Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn
        355                 360                 365

Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His
    370                 375                 380

Phe Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln
```

385 390 395 400

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Asp Ser Asn Val Ile
405 410 415

Leu Lys Lys Tyr Arg Asn Met Val Val Glu Ala Cys Gly Cys His
420 425 430

<210> 581
<211> 431
<212> PRT
<213> Homo sapiens

<400> 581

Met His Val Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala
1 5 10 15

Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser
20 25 30

Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser
35 40 45

Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu
50 55 60

Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro
65 70 75 80

Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly
85 90 95

Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser
100 105 110

Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr
115 120 125

Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys
130 135 140

Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu
145 150 155 160

Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile
165 170 175

Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile
180 185 190

Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu
195 200 205

```
Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu
    210                 215                 220

Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg
225                 230                 235                 240

His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser
                245                 250                 255

Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn
            260                 265                 270

Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe
        275                 280                 285

Arg Ser Ile Arg Ser Thr Gly Ser Lys Gln Arg Ser Gln Asn Arg Ser
    290                 295                 300

Lys Thr Pro Lys Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu
305                 310                 315                 320

Asn Ser Ser Ser Asp Gln Arg Gln Ala Cys Ser Lys His Glu Leu Tyr
                325                 330                 335

Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu
            340                 345                 350

Gly Tyr Ala Ala Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn
        355                 360                 365

Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His
    370                 375                 380

Ser Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln
385                 390                 395                 400

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Asp Ser Asn Val Ile
                405                 410                 415

Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys His
            420                 425                 430


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<211>  1314
<212>  DNA
<213>  Artificial sequence

<220>
<223>  Synthetic sequence

<400>  582
gtaagtatcc gcgccgggaa cagccgcggg ccgcacgccg cgggccgcac gccgcacgcc       60
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tgcgcaggga ggcgccgcgc acgccggggt cgctccgggt acgcgcgctg gactagctca 120

ccccgctcct tctcagggcg gcccggcgga agcggccttg caactccctt ctctggttct 180

cccggttgca tttacactgg cttctgcttt ccgaaggaaa aggggacatt ttgtcctgcg 240

gtgcgactgc gggtcaaggc acgggcgaag gcagggcagg ctggtggagg ggaccggttc 300

cgaggggtgt gcggctgtct ccatgcttgt cacttctctg cgataacttg tttcagtaat 360

attaatagat ggtatctgct agtatataca tacacataat gtgtgtgtct gtgtgtatct 420

gtatatagcg tgtgtgttgt gtgtgtgtgt ttgcgcgcac gggcgcgcgc acacctaata 480

ttttcaaggc tggatttttt tgaacgaaat gctttcctgg aacgaggtga aactttcaga 540

gctgcagaat agctagagca gcaggggccc tggcttttgg aaactgaccc gacctttatt 600

ccagattctg ccccactccg cagagctgtg tgaccttggg ggattcccct aacctctctg 660

agacgtggct ttgttttctg tagggagaag ataaaggtga cgcccatttt gcggacctgg 720

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Thr Ala Lys Asp Ser Ile Phe Glu Pro Ala Lys Gly Gly Glu Lys Leu
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Gln Ile Lys Lys Thr Val Ser Phe His Leu Tyr Ile Ser Thr Ala Pro
65                  70                  75                  80

Cys Gly Asp Gly Ala Leu Phe Asp Lys Ser Cys Ser Asp Arg Ala Met
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Glu Ser Thr Glu Ser Arg His Tyr Pro Val Phe Glu Asn Pro Lys Gln
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Gly Lys Leu Arg Thr Lys Val Glu Asn Gly Glu Gly Thr Ile Pro Val
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Glu Ser Ser Asp Ile Val Pro Thr Trp Asp Gly Ile Arg Leu Gly Glu
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Arg Leu Arg Thr Met Ser Cys Ser Asp Lys Ile Leu Arg Trp Asn Val
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Leu Gly Leu Gln Gly Ala Leu Leu Thr His Phe Leu Gln Pro Ile Tyr
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Leu Lys Ser Val Thr Leu Gly Tyr Leu Phe Ser Gln Gly His Leu Thr
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Arg Ala Ile Cys Cys Arg Val Thr Arg Asp Gly Ser Ala Phe Glu Asp
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Gly Leu Arg His Pro Phe Ile Val Asn His Pro Lys Val Gly Arg Val
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Pro Cys Gly Asp Ala Arg Ile Phe Ser Pro His Glu Pro Ile Leu Glu
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Glu Pro Ile Tyr Phe Ser Ser Ile Ile Leu Gly Ser Leu Tyr His Gly
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Asn Ala Glu Ala Arg Gln Pro Gly Lys Ala Pro Asn Phe Ser Val Asn
            260                 265                 270

Trp Thr Val Gly Asp Ser Ala Ile Glu Val Ile Asn Ala Thr Thr Gly
        275                 280                 285

Lys Asp Glu Leu Gly Arg Ala Ser Arg Leu Cys Lys His Ala Leu Tyr
    290                 295                 300

Cys Arg Trp Met Arg Val His Gly Lys Val Pro Ser His Leu Leu Arg
305                 310                 315                 320

Ser Lys Ile Thr Lys Pro Asn Val Tyr His Glu Ser Lys Leu Ala Ala
                325                 330                 335

Lys Glu Tyr Gln Ala Ala Lys Ala Arg Leu Phe Thr Ala Phe Ile Lys
            340                 345                 350

Ala Gly Leu Gly Ala Trp Val Glu Lys Pro Thr Glu Gln Asp Gln Phe
        355                 360                 365


<210>  590
<211>  326
<212>  PRT
<213>  Artificial sequence

<220>
<223>  Synthetic sequence

<400>  590

Ala Ile Gly Thr Gly Glu Tyr Asn Tyr Ser Gln Asp Ile Lys Pro Asp
1               5                   10                  15
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Gly Arg Val Leu His Asp Thr His Ala Val Val Thr Ala Arg Arg Ser
            20                  25                  30

Leu Leu Arg Tyr Phe Tyr Arg Gln Leu Leu Leu Phe Tyr Ser Lys Asn
        35                  40                  45

Pro Ala Met Met Glu Lys Ser Ile Phe Cys Thr Glu Pro Thr Ser Asn
    50                  55                  60

Leu Leu Thr Leu Lys Gln Asn Ile Asn Ile Cys Leu Tyr Met Asn Gln
65                  70                  75                  80

Leu Pro Lys Gly Ser Ala Gln Ile Lys Ser Gln Leu Arg Leu Asn Pro
                85                  90                  95

His Ser Ile Ser Ala Phe Glu Ala Asn Glu Glu Leu Cys Leu His Val
            100                 105                 110

Ala Val Glu Gly Lys Ile Tyr Leu Thr Val Tyr Cys Pro Lys Asp Gly
        115                 120                 125

Val Asn Arg Ile Ser Ser Met Ser Ser Ser Asp Lys Leu Thr Arg Trp
    130                 135                 140

Glu Val Leu Gly Val Gln Gly Ala Leu Leu Ser His Phe Ile Gln Pro
145                 150                 155                 160

Val Tyr Ile Ser Ser Ile Leu Ile Gly Asp Gly Asn Cys Ser Asp Thr
                165                 170                 175

Arg Gly Leu Glu Ile Ala Ile Lys Gln Arg Val Asp Asp Ala Leu Thr
            180                 185                 190

Ser Lys Leu Pro Met Phe Tyr Leu Val Asn Arg Pro His Ile Ser Leu
        195                 200                 205

Val Pro Ser Ala Tyr Pro Leu Gln Met Asn Leu Glu Tyr Lys Phe Leu
    210                 215                 220

Ser Leu Asn Trp Ala Gln Gly Asp Val Ser Leu Glu Ile Val Asp Gly
225                 230                 235                 240

Leu Ser Gly Lys Ile Thr Glu Ser Ser Pro Phe Lys Ser Gly Met Ser
                245                 250                 255

Met Ala Ser Arg Leu Cys Lys Ala Ala Met Leu Ser Arg Phe Asn Leu
            260                 265                 270

Leu Ala Lys Glu Ala Lys Lys Glu Leu Leu Glu Ala Gly Thr Tyr His
        275                 280                 285
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Ala Ala Lys Cys Met Ser Ala Ser Tyr Gln Glu Ala Lys Cys Lys Leu
290 295 300

Lys Ser Tyr Leu Gln Gln His Gly Tyr Gly Ser Trp Ile Val Lys Ser
305 310 315 320

Pro Cys Ile Glu Gln Phe
325

<210> 591
<211> 322
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 591

Ala Leu Gly Thr Gly Ser Ser Cys Cys Ala Gly Trp Leu Glu Phe Ser
1 5 10 15

Gly Gln Gln Leu His Asp Cys His Gly Leu Val Ile Ala Arg Arg Ala
20 25 30

Leu Leu Arg Phe Leu Phe Arg Gln Leu Leu Leu Ala Thr Gln Gly Gly
35 40 45

Pro Lys Gly Lys Glu Gln Ser Val Leu Ala Pro Gln Pro Gly Pro Gly
50 55 60

Pro Pro Phe Thr Leu Lys Pro Arg Val Phe Leu His Leu Tyr Ile Ser
65 70 75 80

Asn Thr Pro Lys Gly Ala Ala Arg Asp Ile Tyr Leu Pro Pro Thr Ser
85 90 95

Glu Gly Gly Leu Pro His Ser Pro Pro Met Arg Leu Gln Ala His Val
100 105 110

Leu Gly Gln Leu Lys Pro Val Cys Tyr Val Ala Pro Ser Leu Cys Asp
115 120 125

Thr His Val Gly Cys Leu Ser Ala Ser Asp Lys Leu Ala Arg Trp Ala
130 135 140

Val Leu Gly Leu Gly Gly Ala Leu Leu Ala His Leu Val Ser Pro Leu
145 150 155 160

Tyr Ser Thr Ser Leu Ile Leu Ala Asp Ser Cys His Asp Pro Pro Thr
165 170 175

Leu Ser Arg Ala Ile His Thr Arg Pro Cys Leu Asp Ser Val Leu Gly
180 185 190

```
Pro Cys Leu Pro Pro Pro Tyr Val Arg Thr Ala Leu His Leu Phe Ala
        195                 200                 205

Gly Pro Pro Val Ala Pro Ser Glu Pro Thr Pro Asp Thr Cys Arg Gly
    210                 215                 220

Leu Ser Leu Asn Trp Ser Leu Gly Asp Pro Gly Ile Glu Val Val Asp
225                 230                 235                 240

Val Ala Thr Gly Arg Val Lys Ala Asn Ala Ala Leu Gly Pro Pro Ser
                245                 250                 255

Arg Leu Cys Lys Ala Ser Phe Leu Arg Ala Phe His Gln Ala Ala Arg
            260                 265                 270

Ala Val Gly Lys Pro Tyr Leu Leu Ala Leu Lys Thr Tyr Glu Ala Ala
        275                 280                 285

Lys Ala Gly Pro Tyr Gln Glu Ala Arg Arg Gln Leu Ser Leu Leu Leu
    290                 295                 300

Asp Gln Gln Gly Leu Gly Ala Trp Pro Ser Lys Pro Leu Val Gly Lys
305                 310                 315                 320

Phe Arg
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<210> 592
<211> 125
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 592

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Gly Asp Pro Thr Leu Arg Arg Arg Ile Glu Pro Trp Glu Phe Asp Val
1               5                   10                  15

Phe Tyr Asp Pro Arg Glu Leu Arg Lys Glu Ala Cys Leu Leu Tyr Glu
            20                  25                  30

Ile Lys Trp Gly Met Ser Arg Lys Ile Trp Arg Ser Ser Gly Lys Asn
        35                  40                  45

Thr Thr Asn His Val Glu Val Asn Phe Ile Lys Lys Phe Thr Ser Glu
    50                  55                  60

Arg Asp Phe His Pro Ser Met Ser Cys Ser Ile Thr Trp Phe Leu Ser
65                  70                  75                  80
```

Trp Ser Pro Cys Trp Glu Cys Ser Gln Ala Ile Arg Glu Phe Leu Ser
85 90 95

Arg His Pro Gly Val Thr Leu Val Ile Tyr Val Ala Arg Leu Phe Trp
100 105 110

His Met Asp Gln Gln Asn Arg Gln Gly Leu Arg Asp Leu
115 120 125

<210> 593
<211> 106
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic sequence

<400> 593

Gly Arg Asn Lys Thr Phe Leu Cys Tyr Val Val Glu Ala Gln Gly Lys
1 5 10 15

Gly Gly Gln Val Gln Ala Ser Arg Gly Tyr Leu Glu Asp Glu His Ala
20 25 30

Ala Ala His Ala Glu Glu Ala Phe Phe Asn Thr Ile Leu Pro Ala Phe
35 40 45

Asp Pro Ala Leu Arg Tyr Asn Val Thr Trp Tyr Val Ser Ser Ser Pro
50 55 60

Cys Ala Ala Cys Ala Asp Arg Ile Ile Lys Thr Leu Ser Lys Thr Lys
65 70 75 80

Asn Leu Arg Leu Leu Ile Leu Val Gly Arg Leu Phe Met Trp Glu Glu
85 90 95

Pro Glu Ile Gln Ala Ala Leu Lys Lys Leu
100 105

<210> 594
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 594
tcctctgtct ccctgtctct gtctctctct c 31

<210> 595
<211> 21
<212> DNA
<213> Artificial Sequence

<220>

<223> Synthetic sequence

<400> 595
ggacttgggc caggggagga g 21

<210> 596
<211> 17
<212> PRT
<213> Gaussia princeps

<400> 596

Met Gly Val Lys Val Leu Phe Ala Leu Ile Cys Ile Ala Val Ala Glu
1 5 10 15

Ala

<210> 597
<211> 29
<212> PRT
<213> Homo Sapiens

<400> 597

Met His Val Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala
1 5 10 15

Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala
20 25

<210> 598
<211> 18
<212> PRT
<213> Homo Sapiens

<400> 598

Met Ala Phe Leu Trp Leu Leu Ser Cys Trp Ala Leu Leu Gly Thr Thr
1 5 10 15

Phe Gly

<210> 599
<211> 16
<212> PRT
<213> Homo Sapiens

<400> 599

Met Leu Gly Ile Thr Val Leu Ala Ala Leu Leu Ala Cys Ala Ser Ser
1 5 10 15

<210> 600
<211> 27
<212> PRT
<213> Homo Sapiens

<400> 600

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Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
1               5                   10                  15


Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly
            20                  25


<210>  601
<211>  24
<212>  PRT
<213>  Homo Sapiens

<400>  601

Met Arg Ser Gly Cys Val Val Val His Val Trp Ile Leu Ala Gly Leu
1               5                   10                  15


Trp Leu Ala Val Ala Gly Arg Pro
            20


<210>  602
<211>  28
<212>  PRT
<213>  Homo Sapiens

<400>  602

Met Asp Ser Asp Glu Thr Gly Phe Glu His Ser Gly Leu Trp Val Ser
1               5                   10                  15


Val Leu Ala Gly Leu Leu Leu Gly Ala Cys Gln Ala
            20                  25


<210>  603
<211>  24
<212>  PRT
<213>  Homo Sapiens

<400>  603

Met Leu Gly Ala Arg Leu Arg Leu Trp Val Cys Ala Leu Cys Ser Val
1               5                   10                  15


Cys Ser Met Ser Val Leu Arg Ala
            20


<210>  604
<211>  20
<212>  PRT
<213>  Homo Sapiens

<400>  604

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1               5                   10                  15


Val Thr Asn Ser
            20
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<210> 605
<211> 33
<212> PRT
<213> Homo Sapiens

<400> 605

Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr Leu
1 5 10 15

Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala
20 25 30

Ala

<210> 606
<211> 29
<212> PRT
<213> Homo Sapiens

<400> 606

Met Asn Ser Phe Ser Thr Ser Ala Phe Gly Pro Val Ala Phe Ser Leu
1 5 10 15

Gly Leu Leu Leu Val Leu Pro Ala Ala Phe Pro Ala Pro
20 25

<210> 607
<211> 23
<212> PRT
<213> Homo Sapiens

<400> 607

Met Ala Leu Thr Phe Ala Leu Leu Val Ala Leu Leu Val Leu Ser Cys
1 5 10 15

Lys Ser Ser Cys Ser Val Gly
20

<210> 608
<211> 21
<212> PRT
<213> Homo Sapiens

<400> 608

Met Thr Asn Lys Cys Leu Leu Gln Ile Ala Leu Leu Leu Cys Phe Ser
1 5 10 15

Thr Thr Ala Leu Ser
20

<210> 609
<211> 23
<212> PRT

<213> Homo Sapiens

<400> 609

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1 5 10 15

Gly Ser Leu Gly Cys Tyr Cys
20

<210> 610
<211> 15
<212> PRT
<213> Homo Sapiens

<400> 610

Met Asn Pro Leu Leu Ile Leu Thr Phe Val Ala Ala Ala Leu Ala
1 5 10 15

<210> 611
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 611
taaggctgtg ctgaccatcg 20

<210> 612
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 612
taaaaacatg gccccagcag 20

<210> 613
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 613
tctaaaaaca tggccccagc 20

<210> 614
<211> 81
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 614

cccctccagg ccgtgcataa ggctgtgctg accatcgacg tcaaagggac tgaagctgct 60

ggggccatgt ttttagaggc c 81

<210> 615
<211> 20
<212> DNA
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<220>
<223> Synthetic sequence

<400> 615
tgcctggtcc ctgtctccct 20

<210> 616
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 616
tgtcttctgg gcagcatctc 20

<210> 617
<211> 81
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 617
cccctccagg ccgtgcataa ggctgtgctg accatcgacg agaaagggac tgaagctgct 60

ggggccatgt ttttagaggc c 81

<210> 618
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 618
tcccacacgt gttatttggc 20

<210> 619
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 619
tggcaaccaa tcccaaagtt 20

<210> 620

<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 620
taataaataa aaataaaaaa 20

<210> 621
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 621
ttgcctattt ttccagagat 20

<210> 622
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 622
tattcccggg ctcccaggca 20

<210> 623
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 623
tggtgcatct gactcctgag 20

<210> 624
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 624
tcaccttgcc ccacagggca 20

<210> 625
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 625

tccaggcatg cagatcccac 20

<210> 626
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 626
ttgtagcacc gcccagacga 20

<210> 627
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 627
gccaaggaca ggtacggctg tcatc 25

<210> 628
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 628
cttgccatga gccttcacct tagggttg 28

<210> 629
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<220>
<221> misc_feature
<222> (12)..(12)
<223> Xaa can be any naturally occurring amino acid

<400> 629

Leu Thr Pro Val Gln Val Val Ala Ile Ala Trp Xaa Tyr Glx Gly His
1 5 10 15

Gly Gly

<210> 630
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 630

Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu
1 5 10 15

Cys Gln Asp

<210> 631
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 631

Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu
1 5 10 15

Cys Gln Ala

<210> 632
<211> 196
<212> PRT
<213> Homo sapiens

<400> 632

Gln Leu Val Lys Ser Glu Leu Glu Glu Lys Lys Ser Glu Leu Arg His
1 5 10 15

Lys Leu Lys Tyr Val Pro His Glu Tyr Ile Glu Leu Ile Glu Ile Ala
20 25 30

Arg Asn Ser Thr Gln Asp Arg Ile Leu Glu Met Lys Val Met Glu Phe
35 40 45

Phe Met Lys Val Tyr Gly Tyr Arg Gly Lys His Leu Gly Gly Ser Arg
50 55 60

Lys Pro Asp Gly Ala Ile Tyr Thr Val Gly Ser Pro Ile Asp Tyr Gly
65 70 75 80

Val Ile Val Asp Thr Lys Ala Tyr Ser Gly Gly Tyr Asn Leu Pro Ile
85 90 95

Gly Gln Ala Asp Glu Met Gln Arg Tyr Val Glu Glu Asn Gln Thr Arg
100 105 110

Asn Lys His Ile Asn Pro Asn Glu Trp Trp Lys Val Tyr Pro Ser Ser
115 120 125

Val Thr Glu Phe Lys Phe Leu Phe Val Ser Gly His Phe Lys Gly Asn
130 135 140

Tyr Lys Ala Gln Leu Thr Arg Leu Asn His Ile Thr Asn Cys Asn Gly
145 150 155 160

Ala Val Leu Ser Val Glu Glu Leu Leu Ile Gly Gly Glu Met Ile Lys
165 170 175

Ala Gly Thr Leu Thr Leu Glu Glu Val Arg Arg Lys Phe Asn Asn Gly
180 185 190

Glu Ile Asn Phe
195

<210> 633
<211> 555
<212> DNA
<213> Homo sapiens

<400> 633
atgaagagcg tcttgctgct gaccacgctc ctcgtgcctg cacacctggt ggccgcctgg 60

agcaataatt atgcggtgga ctgccctcaa cactgtgaca gcagtgagtg caaaagcagc 120

ccgcgctgca agaggacagt gctcgacgac tgtggctgct gccgagtgtg cgctgcaggg 180

cggggagaaa cttgctaccg cacagtctca ggcatggatg gcatgaagtg tggcccgggg 240

ctgaggtgtc agccttctaa tggggaggat ccttttggtg aagagtttgg tatctgcaaa 300

gactgtccct acggcacctt cgggatggat tgcagagaga cctgcaactg ccagtcaggc 360

atctgtgaca gggggacggg aaaatgcctg aaattcccct tcttccaata ttcagtaacc 420

aagtcttcca acagatttgt ttctctcacg gagcatgaca tggcatctgg agatggcaat 480

attgtgagag aagaagttgt gaaagagaat gctgccgggt ctcccgtaat gaggaaatgg 540

ttaaatccac gctga 555

<210> 634
<211> 184
<212> PRT
<213> Homo sapiens

<400> 634

Met Lys Ser Val Leu Leu Leu Thr Thr Leu Leu Val Pro Ala His Leu
1 5 10 15

Val Ala Ala Trp Ser Asn Asn Tyr Ala Val Asp Cys Pro Gln His Cys
20 25 30

Asp Ser Ser Glu Cys Lys Ser Ser Pro Arg Cys Lys Arg Thr Val Leu
35 40 45

```
Asp Asp Cys Gly Cys Cys Arg Val Cys Ala Ala Gly Arg Gly Glu Thr
    50                  55                  60

Cys Tyr Arg Thr Val Ser Gly Met Asp Gly Met Lys Cys Gly Pro Gly
65                  70                  75                  80

Leu Arg Cys Gln Pro Ser Asn Gly Glu Asp Pro Phe Gly Glu Glu Phe
                85                  90                  95

Gly Ile Cys Lys Asp Cys Pro Tyr Gly Thr Phe Gly Met Asp Cys Arg
            100                 105                 110

Glu Thr Cys Asn Cys Gln Ser Gly Ile Cys Asp Arg Gly Thr Gly Lys
        115                 120                 125

Cys Leu Lys Phe Pro Phe Phe Gln Tyr Ser Val Thr Lys Ser Ser Asn
    130                 135                 140

Arg Phe Val Ser Leu Thr Glu His Asp Met Ala Ser Gly Asp Gly Asn
145                 150                 155                 160

Ile Val Arg Glu Glu Val Val Lys Glu Asn Ala Ala Gly Ser Pro Val
                165                 170                 175

Met Arg Lys Trp Leu Asn Pro Arg
            180
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<210> 635
<211> 405
<212> DNA
<213> Homo sapiens

<400> 635

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atgaagagcg tcttgctgct gaccacgctc ctcgtgcctg cacacctggt ggccgcctgg       60

agcaataatt atgcggtgga ctgccctcaa cactgtgaca gcagtgagtg caaaagcagc      120

ccgcgctgca agaggacagt gctcgacgac tgtggctgct gccgagtgtg cgctgcaggg      180

cggggagaaa cttgctaccg cacagtctca ggcatggatg gcatgaagtg tggcccgggg      240

ctgaggtgtc agccttctaa tggggaggat ccttttggtg aagagtttgg tatctgcaaa      300

gagcatgaca tggcatctgg agatggcaat attgtgagag aagaagttgt gaaagagaat      360

gctgccgggt ctcccgtaat gaggaaatgg ttaaatccac gctga                      405
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<210> 636
<211> 134
<212> PRT
<213> Homo sapiens

<400> 636

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Met Lys Ser Val Leu Leu Leu Thr Thr Leu Leu Val Pro Ala His Leu
1               5                   10                  15
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Val Ala Ala Trp Ser Asn Asn Tyr Ala Val Asp Cys Pro Gln His Cys
20 25 30

Asp Ser Ser Glu Cys Lys Ser Ser Pro Arg Cys Lys Arg Thr Val Leu
35 40 45

Asp Asp Cys Gly Cys Cys Arg Val Cys Ala Ala Gly Arg Gly Glu Thr
50 55 60

Cys Tyr Arg Thr Val Ser Gly Met Asp Gly Met Lys Cys Gly Pro Gly
65 70 75 80

Leu Arg Cys Gln Pro Ser Asn Gly Glu Asp Pro Phe Gly Glu Glu Phe
85 90 95

Gly Ile Cys Lys Glu His Asp Met Ala Ser Gly Asp Gly Asn Ile Val
100 105 110

Arg Glu Glu Val Val Lys Glu Asn Ala Ala Gly Ser Pro Val Met Arg
115 120 125

Lys Trp Leu Asn Pro Arg
130

<210> 637
<211> 444
<212> DNA
<213> Homo sapiens

<400> 637
atggcttctc atcgtctgct cctcctctgc cttgctggac tggtatttgt gtctgaggct 60

ggccctacgg gcaccggtga atccaagtgt cctctgatgg tcaaagttct agatgctgtc 120

cgaggcagtc ctgccatcaa tgtggccgtg catgtgttca gaaaggctgc tgatgacacc 180

tgggagccat ttgcctctgg gaaaaccagt gagtctggag agctgcatgg gctcacaact 240

gaggaggaat ttgtagaagg gatatacaaa gtggaaatag acaccaaatc ttactggaag 300

gcacttggca tctccccatt ccatgagcat gcagaggtgg tattcacagc caacgactcc 360

ggcccccgcc gctacaccat tgccgccctg ctgagcccct actcctattc caccacggct 420

gtcgtcacca atcccaagga atga 444

<210> 638
<211> 147
<212> PRT
<213> Homo sapiens

<400> 638

Met Ala Ser His Arg Leu Leu Leu Leu Cys Leu Ala Gly Leu Val Phe
1 5 10 15

Val Ser Glu Ala Gly Pro Thr Gly Thr Gly Glu Ser Lys Cys Pro Leu
20 25 30

Met Val Lys Val Leu Asp Ala Val Arg Gly Ser Pro Ala Ile Asn Val
35 40 45

Ala Val His Val Phe Arg Lys Ala Ala Asp Asp Thr Trp Glu Pro Phe
50 55 60

Ala Ser Gly Lys Thr Ser Glu Ser Gly Glu Leu His Gly Leu Thr Thr
65 70 75 80

Glu Glu Glu Phe Val Glu Gly Ile Tyr Lys Val Glu Ile Asp Thr Lys
85 90 95

Ser Tyr Trp Lys Ala Leu Gly Ile Ser Pro Phe His Glu His Ala Glu
100 105 110

Val Val Phe Thr Ala Asn Asp Ser Gly Pro Arg Arg Tyr Thr Ile Ala
115 120 125

Ala Leu Leu Ser Pro Tyr Ser Tyr Ser Thr Thr Ala Val Val Thr Asn
130 135 140

Pro Lys Glu
145

<210> 639
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 639
tgctgtccga ggcagtcctg 20

<210> 640
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 640
tcagcagcct ttctgaacac 20

<210> 641
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 641
tgtccgaggc agtcctgcca 20

<210> 642
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 642
tcagcagcct ttctgaacac 20

<210> 643
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 643
tccgaggcag tcctgccatc 20

<210> 644
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 644
tcagcagcct ttctgaacac 20

<210> 645
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 645
tgtccgaggc agtcctgcca 20

<210> 646
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 646
tcatcagcag cctttctgaa 20

<210> 647
<211> 20
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<213> Artificial Sequence

<220>

<223> Synthetic sequence

<400> 647
tccgaggcag tcctgccatc 20

<210> 648
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 648
tcatcagcag cctttctgaa 20

<210> 649
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 649
tccgaggcag tcctgccatc 20

<210> 650
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic sequence

<400> 650
tgtcatcagc agcctttctg 20