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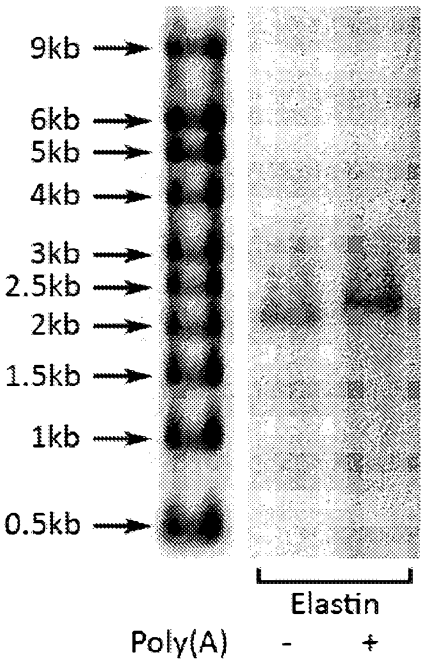
(54) Title: METHODS AND PRODUCTS FOR NUCLEIC ACID PRODUCTION AND DELIVERY

FIG. 1




(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. Methods and products for altering the DNA sequence of a cell are described, as are methods and products for inducing cells to express proteins using synthetic RNA molecules, including cells present in vivo. Therapeutics comprising nucleic acids encoding gene-editing proteins are also described.

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# METHODS AND PRODUCTS FOR NUCLEIC ACID PRODUCTION AND DELIVERY

## PRIORITY

The present application claims priority to U.S. Provisional Application No. 61/934,397, filed on January 31, 2014, U.S. Provisional Application No. 62/038,608, filed on August 18, 2014, and U.S. Provisional Application No. 62/069,667, filed on October 28, 2014, the entire contents of which are hereby incorporated by reference in their entireties.

The present application is related to U.S. Application No. 13/465,490, filed on May 7, 2012, International Application No. PCT/US2012/067966, filed on December 5, 2012, U.S. Application No. 13/931,251, filed on June 28, 2013, and International Application No. PCT/US2013/068118, filed on November 1, 2013, the entire contents of which are hereby incorporated by reference in their entireties.

## 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 contents of the text file submitted electronically herewith are incorporated herein by reference in their entirety: A computer readable format copy of the Sequence Listing (filename: FAB-008PC SequenceListing.txt; date recorded: January 30, 2015; file size: 929 KB).

## 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; 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 *in vivo* 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). However, current methods for gene editing cells are inefficient and carry a risk of uncontrolled mutagenesis, making them undesirable for both research and therapeutic 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.

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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.

Throughout this specification, 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 element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this specification

## SUMMARY OF THE INVENTION

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 do not involve exposing cells to exogenous DNA or to allogeneic or animal-derived materials, making products produced according to the methods of the present invention useful for therapeutic and cosmetic applications.

In one aspect, there is provided an *in vivo* method for treating a dystrophic epidermolysis bullosa patient comprising

delivering a synthetic RNA encoding collagen type VII to the patient's keratinocytes by injection to the epidermis, thereby resulting in the amelioration of one or more of the dystrophic epidermolysis bullosa patient's symptoms.

In another aspect, there is provided an *in vivo* method for treating epidermolysis bullosa, comprising

delivering a synthetic RNA encoding a gene-editing protein that targets a COL7 gene to a patient in need thereof and

inducing a single-strand or double-strand break in the COL7 gene of the patient's keratinocytes,

thereby eliminating a mutation that is at least partially responsible for a disease phenotype, wherein:

the synthetic RNA is delivered to the patient's keratinocytes by injection to the epidermis and

the gene-editing protein comprises a DNA-binding domain and a nuclease domain.

In another aspect, there is provided an *in vivo* method for treating dystrophic epidermolysis bullosa, comprising

delivering a synthetic RNA encoding a gene-editing protein that targets a COL7 gene to a patient in need thereof and

delivering a COL7 repair template to the patient, thereby editing the COL7 gene, wherein:

the synthetic RNA and repair template are delivered to the patient's keratinocytes by injection to the epidermis and

the gene-editing protein comprises a DNA-binding domain and a nuclease domain and causes a double-strand break in the COL7 gene of the patient's keratinocytes.

In some aspects, there is provided a method for expressing a protein in a cell population of a patient, comprising introducing an RNA into the cell population, the RNA comprising one or more non-canonical nucleotides that do not induce significant cellular immune response and do not substantially reduce protein expression. In some embodiments, at least 50%, or at least 75%, or at least 90% of the non-canonical nucleotides are selected from one or more of 5-hydroxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-hydroxyuridine, 5-hydroxymethyluridine, 5-carboxyuridine, and 5-formyluridine, or in some embodiments selected from one or more of 5-hydroxymethylcytidine, 5-carboxycytidine, and 5-formylcytidine. Further embodiments relate to additional elements of the RNA, *e.g.* a 5' cap structure, a 3' poly(A) tail, and 5'-UTR and/or 3'-UTR, which optionally comprises one or more of a Kozak consensus sequence, a sequence that increases RNA stability in vivo (such as, by way of illustration, an alpha-globin or beta-globin 5'-UTR).

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. Other aspects relate to nucleic acids comprising one or more non-

canonical nucleotides. In one aspect, the invention provides nucleic acids comprising, for example, one or more of 5-hydroxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-hydroxyuridine, 5-hydroxymethyluridine, 5-carboxyuridine, and 5-formyluridine, or in some embodiments selected from one or more of 5-hydroxymethylcytidine, 5-carboxycytidine, and/or 5-formylcytidine.

The compositions of the present invention may alter, modify and/or change the appearance of a member of the integumenary 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.

In some aspects, synthetic 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 synthetic RNA molecules encoding reprogramming proteins. Still further aspects pertain to methods for producing synthetic 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. 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. 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 synthetic RNA. In 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.

## DETAILED DESCRIPTION OF THE FIGURES

**FIG. 1** depicts RNA encoding human elastin protein and containing adenosine, 50% guanosine, 50% 7-deazaguanosine, 60% uridine, 40% 5-methyluridine, and 5-methylcytidine, resolved on a denaturing formaldehyde-agarose gel.

**FIG. 2** depicts primary adult human dermal fibroblasts transfected with the RNA of **FIG. 1**.

**FIG. 3** depicts the result of an immunocytochemical analysis of the primary adult human dermal fibroblasts of **FIG. 2** using an antibody targeting human elastin protein.

**FIG. 4** depicts primary human dermal fibroblasts transfected with synthetic RNA comprising cytidine, 5-methylcytidine ("5mC"), 5-hydroxymethylcytidine ("5hmC"), 5-carboxycytidine ("5cC") or 5-formylcytidine ("5fC") and encoding Oct4 protein. Cells were fixed and stained for Oct4 protein 24 hours after transfection.

**FIG. 5** depicts primary human dermal fibroblasts transfected with synthetic RNA comprising 5-hydroxymethylcytidine and encoding green fluorescent protein ("GFP"). Cells were imaged 24 hours after transfection.

**FIG. 6** depicts a region of the ventral forearm of a healthy, 33 year-old, male human subject treated with synthetic RNA comprising 5-hydroxymethylcytidine ("5hmC") and encoding GFP. Arrows indicate fluorescent cells.

**FIG. 7** depicts a region of the ventral forearm of a healthy, 33 year-old, male patient treated with synthetic RNA comprising 5-hydroxymethylcytidine ("5hmC") and encoding GFP. The top panel shows an untreated area on the same forearm, while the bottom panels show two fields within the treatment area. Fluorescent cells (indicated with arrows) are clearly visible in the bottom panels.

**FIG. 8** depicts primary human dermal fibroblasts transfected with synthetic RNA comprising 5-methyluridine and 5-hydroxymethylcytidine and encoding the indicated protein. Cells were fixed and stained using antibodies targeting the indicated protein 48 hours after transfection.

**FIG. 9** depicts primary human dermal fibroblasts transfected with synthetic RNA comprising 5-methyluridine and 5-hydroxymethylcytidine and encoding human tyrosinase. Cells were fixed and stained using an antibody targeting human tyrosinase 24 hours after transfection.

**FIG. 10** depicts primary human epidermal melanocytes.

**FIG. 11** depicts primary human dermal fibroblasts transfected with synthetic RNA comprising 5-hydroxymethylcytidine and encoding the indicated proteins.

**FIG. 12** depicts primary human dermal fibroblasts transfected daily with synthetic RNA comprising 5-hydroxymethylcytidine and encoding human tyrosinase. The number of transfections are shown above each sample. The cells were imaged 48 hours after the final transfection.

**FIG. 13** depicts primary human dermal fibroblasts transfected daily with synthetic RNA comprising the indicated nucleotides and encoding human tyrosinase. The cells were imaged 48 hours after transfection.

**FIG. 14** depicts IFNB1 expression and pigment production in primary human dermal fibroblasts transfected with synthetic RNA comprising the indicated nucleotides and encoding human tyrosinase. Values are normalized to the sample transfected with synthetic RNA comprising only canonical nucleotides ("A,G,U,C"). GAPDH was used as a loading control. Error bars indicate standard error (n=2).

**FIG. 15** depicts expression of the indicated genes, measured as in **FIG. 14**.

**FIG. 16** depicts a region of the ventral forearm of a healthy, 33 year-old, male human subject treated with synthetic RNA comprising 5-methyluridine and 5-hydroxymethylcytidine and encoding human tyrosinase (top panel), and an ephelis on the ventral forearm of the same subject (bottom panel). The same magnification was used for both images.

**FIG. 17** depicts primary human dermal fibroblasts transfected with synthetic RNA comprising 5-hydroxymethylcytidine and encoding collagen I (A1) ("+ COL1 RNA"). Cells were fixed and stained using an antibody targeting collagen I between 24 and 72 hours after transfection. Two representative fields are shown for each of: the transfected cells and un-transfected cells ("Neg."). Arrows indicate extracellular deposits of collagen I.

**FIG. 18** depicts primary human dermal fibroblasts transfected with synthetic RNA comprising 5-hydroxymethylcytidine and encoding collagen VII (A1) ("+ COL7 RNA"). Cells were fixed and stained using an antibody targeting collagen I between 24 and 72 hours after transfection. A representative field is shown for each of: the transfected cells and un-transfected cells ("Neg.").

## DETAILED DESCRIPTION OF THE INVENTION

*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 "cell-culture medium" is meant a medium that can be used for cell culture, by way of non-limiting example, Dulbecco's Modified Eagle's Medium (DMEM) or DMEM + 10% fetal bovine serum (FBS), whether or not the medium is used *in vitro* or *in vivo*.

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, whether or not the medium is used *in vitro* or *in vivo*.

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 "lipid carrier" is meant a substance that can increase the solubility of a lipid or lipid-soluble molecule in an aqueous solution, by way of non-limiting example, human serum albumin or methyl-beta-cyclodextrin.

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 “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.

By “feeder” is meant a cell that can be used to condition medium or to otherwise support the growth of other cells in culture.

By “conditioning” is meant contacting one or more feeders with a medium.

By “fatty acid” is meant a molecule that comprises an aliphatic chain of at least two carbon atoms, by way of non-limiting example, linoleic acid, α-linolenic acid, octanoic acid, a leukotriene, a prostaglandin, cholesterol, a glucocorticoid, a resolvin, a protectin, a thromboxane, a lipoxin, a maresin, a sphingolipid, tryptophan, N-acetyl tryptophan or a salt, methyl ester or derivative thereof.

By “short-chain fatty acid” is meant a fatty acid that comprises an aliphatic chain of between two and 30 carbon atoms.

By “albumin” is meant a protein that is highly soluble in water, by way of non-limiting example, human serum albumin.

By “associated molecule” is meant a molecule that is non-covalently bound to another molecule.

By “associated-molecule-component of albumin” is meant one or more molecules that are bound to an albumin polypeptide, by way of non-limiting example, lipids, hormones, cholesterol, calcium ions, etc. that are bound to an albumin polypeptide.

By “treated albumin” is meant albumin that is treated to reduce, remove, replace or otherwise inactivate the associated-molecule-component of the albumin, by way of non-limiting example, human serum albumin that is incubated at an elevated temperature, human serum albumin that is contacted with sodium octanoate or human serum albumin that is contacted with a porous material.

By “ion-exchange resin” is meant a material that, when contacted with a solution containing ions, can replace one or more of the ions with one or more different ions, by way of non-limiting example, a material that can replace one or more calcium ions with one or more sodium ions.

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 “glucose-responsive insulin-producing cell” is meant a cell that, when exposed to a certain concentration of glucose, can produce and/or secrete an amount of insulin that is different from (either less than or more than) the amount of insulin that the cell produces and/or secretes when the cell is exposed to a different concentration of glucose, by way of non-limiting example, a β-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 “Wnt signaling agonist” is meant a molecule that can perform one or more of the biological functions of one or more members of the Wnt family of proteins, by way of non-limiting example, Wnt1, Wnt2, Wnt3, Wnt3a or 2-amino-4-[3,4-(methylenedioxy)benzylamino]-6-(3-methoxyphenyl)pyrimidine.

By “IL-6 signaling agonist” is meant a molecule that can perform one or more of the biological functions of IL-6 protein, by way of non-limiting example, IL-6 protein or IL-6 receptor (also known as soluble IL-6 receptor, IL-6R, IL-6R alpha, etc.).

By “TGF-β signaling agonist” is meant a molecule that can perform one or more of the biological functions of one or more members of the TGF-β superfamily of proteins, by way of non-limiting example, TGF-β1, TGF-β3, Activin A, BMP-4 or Nodal.

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.

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 or a natural or engineered variant, family-member, orthologue, 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 U.S. Application No. 13/465,490, U.S. Provisional Application No. 61/664,494, U.S. Provisional Application No. 61/721,302, International Application No. PCT/US12/67966, U.S. Provisional Application No. 61/785,404, U.S. Provisional Application No. 61/842,874, International Application No. PCT/US13/68118, U.S. Provisional Application No. 61/934,397, U.S. Application No. 14/296,220, U.S. Provisional Application No. 62/038,608, and U.S. Provisional Application No. 62/069,667, the contents of which are hereby incorporated by reference in their entireties.

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.

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.

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. 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.

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, 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 dsRNA molecule, a ssRNA molecule, a plasmid, an oligonucleotide, a synthetic RNA molecule, a miRNA molecule, an mRNA molecule, and an siRNA molecule.

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. It has been further discovered that synthetic RNA comprising at least one member of the group: 5-hydroxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-hydroxyuridine, 5-hydroxymethyluridine, 5-carboxyuridine, and 5-formyluridine can evade detection by the innate immune system, and can be translated at high efficiency into protein. 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 member of the group: 5-hydroxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-hydroxyuridine, 5-hydroxymethyluridine, 5-carboxyuridine, and 5-formyluridine. 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.

It has now been further discovered that 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. In one embodiment, the steroid is hydrocortisone. In another embodiment, the steroid is dexamethasone. Still other embodiments are directed to administering to a patient a member of the group: an antibiotic, an antimycotic, and an RNAse inhibitor.

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.

Certain embodiments are directed to a synthetic RNA molecule. In one embodiment, the synthetic RNA molecule encodes a protein of interest. In another embodiment, the synthetic RNA molecule comprises a member of the group: 5-hydroxycytidine, 5-hydroxymethylcytidine, 5-carboxycytidine, 5-formylcytidine, 5-hydroxyuridine, 5-hydroxymethyluridine, 5-carboxyuridine, and 5-formyluridine. Other embodiments are directed 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, and hyaluronan synthase.

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 synthetic RNA. 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.

Other embodiments are directed to a therapeutic 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. 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 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 1, and are given by way of example, and not by way of limitation. In one embodiment, the indication is selected from Table 1. In another embodiment the protein or peptide is selected from Table 1. In yet another embodiment, the indication and the protein or peptide are selected from the same row of Table 1. 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 1. 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.

*Table 1. Illustrative Indications*

| **Illustrative Indication** | **Illustrative Protein / Peptide** |
|---|---|
| Acne | Retinol Dehydrogenase 10 |
| Aging | Elastin |
| Aging | Collagen Type I |
| Aging | Collagen Type III |
| Aging | Collagen Type VII |
| Aging | Hyaluronan Synthase |
| Aging | Telomerase Reverse Transcriptase |
| Albinism | Tyrosinase |
| Alport Syndrome | Collagen Type IV |
| Anemia | Erythropoietin |
| Atopic Dermatitis | Filaggrin |
| Cutis Laxa | Elastin |
| Dystrophic Epidermolysis Bullosa | Collagen Type VII |
| Ehlers-Danlos Syndrome | Collagen Type V |
| Ehlers-Danlos Syndrome | Collagen Type I |
| Epidermolysis bullosa, lethal acantholytic | ADAM17 |
| Epidermolysis bullosa, type IV | Collagen Type III |
| Erythropoietic Protoporphyria | Ferrochelatase |
| Excess Fat | Thermogenin |
| Excess Fat | Lipase |
| Hypotrichosis | ADAM17 |

| | |
|---|---|
| Ichthyosis Vulgaris | Filaggrin |
| Infections | Genetic Antibiotics (e.g. Anti-Sigma Factors) |
| Inflammatory and Bullous Skin Bowel Syndrome | Desmoglein 2 |
| Keratosis Pilaris | Retinol Dehydrogenase 10 |
| Oily Skin | Retinol Dehydrogenase 10 |
| Osteoarthritis | Hyaluronan Synthase |
| Pemphigus Vulgaris | Plakophilin-1 |
| Pseudoxanthoma elasticum | Elastin |
| Psoriasis | Retinol Dehydrogenase 10 |
| Scar Treatment | Tyrosinase |
| Scarring | Elastin |
| Scarring | Collagen Type I |
| Scarring | Collagen Type III |
| Skin Cancer | Interferon |
| Striate Palmoplantar Keratoderma | ADAM17 |
| Tanning | Tyrosinase |
| Vitiligo | Melanocyte-Stimulating Hormone |
| Vitiligo | Tyrosinase |
| Warts | Interferon |
| Wound Healing | Elastin |
| Wound Healing | Collagen Type I |
| Wound Healing | Collagen Type III |
| Xeroderma Pigmentosum | DNA Polymerase Eta |

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.

Further, 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 to treat 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 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 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 (PSORSl - PSORS9).

Various embodiments relate to the treatment 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 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 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 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 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 treating 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 targetted transmembrane channel-like 6 (EVER1) or transmembrane channellike 8 (EVER2) genes.

In some embodiments, skin sagging, thinning or wrinkling may be treated 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 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, a variety of cancers are treated 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, basal cell cancer (BCC), squamous cell cancer (SCC), and melanoma. 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).

In various embodiments, one or more rare diseases are treated 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 certain situations, 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, 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.

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 (e.g. a residue other than adenine, guanine, thymine, uracil, and cytosine or the standard nucleoside, nucleotide, deoxynucleoside or deoxynucleotide derivatives thereof). Of particular note, 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 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 *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: zinc finger nucleases and TALENs. 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: 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 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 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.

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 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, 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.

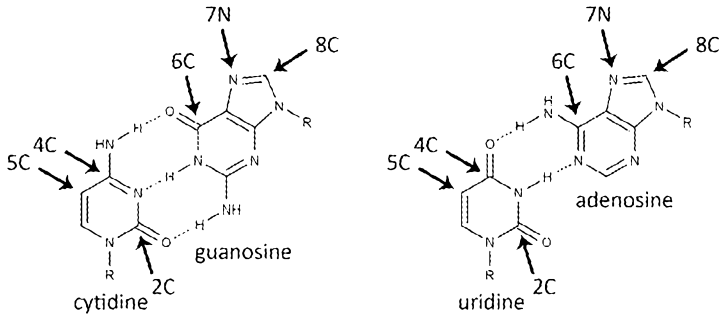
Certain embodiments are directed to a therapeutic comprising a nucleic acid. In one embodiment, the nucleic acid encodes one or more gene-editing proteins. Other embodiments are directed to a therapeutic comprising one or more cells that are transfected, reprogrammed, and/or gene-edited *in vivo* according 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.

Certain non-canonical nucleotides, when incorporated into synthetic RNA molecules, can reduce the toxicity of the synthetic RNA molecules, in part 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 synthetic 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 synthetic 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 synthetic RNA molecules can be translated into protein, limiting the utility of synthetic RNA molecules containing these nucleotides in applications that require protein expression. In addition, while pseudouridine can be completely substituted for uridine in synthetic 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 synthetic 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-aminouridine, 5-hydroxyuridine, 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-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, and 6-thio-7-deaza-8-azaguanosine. 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 a synthetic RNA molecule, wherein the synthetic 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 synthetic RNA molecules, and wherein the one or more synthetic RNA molecules 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, and 6-thio-7-deazaguanosine. 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 synthetic RNA molecule is present *in vivo*.

Certain non-canonical nucleotides can be incorporated more efficiently than other non-canonical nucleotides into synthetic 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 synthetic 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, 0.1 – 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, 0.1 – 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, 0.1 – 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 synthetic RNA 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 synthetic 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 synthetic RNA composition or synthetic polynucleotide composition may further contain (e.g., consist of) one or more (e.g., two, three or four) of 5-hydroxymethylcytidine, 5-hydroxycytidine, 5-carboxycytidine, and 5-formylcytidine 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 synthetic RNA composition or synthetic polynucleotide composition may further contain (e.g., consist of) one or more (e.g., two, three, or four) of 5-hydroxymethyluridine, 5-hydroxyuridine, 5-carboxyurdine, and 5-formyluridine at 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 synthetic 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 synthetic 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 synthetic 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 synthetic RNA molecule is produced by *in vitro* transcription. In one embodiment, the synthetic 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 synthetic RNA molecule that encodes Sox2 protein. In yet another embodiment, the cell is also contacted with a synthetic RNA molecule that encodes Klf4 protein. In yet another embodiment, the cell is also contacted with a synthetic RNA molecule that encodes c-Myc protein. In yet another embodiment, the cell is also contacted with a synthetic 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.

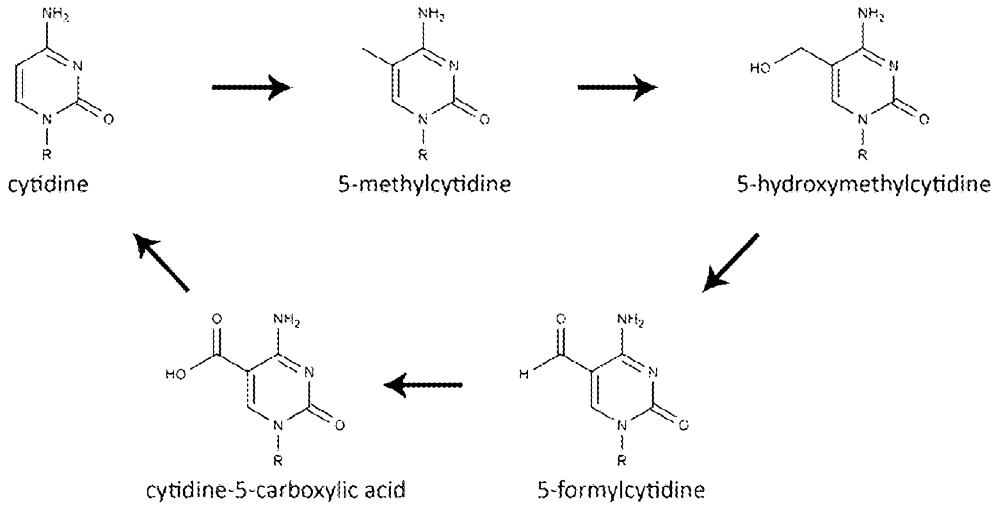
Certain embodiments are directed to a kit containing one or more materials needed to practice the present invention. In one embodiment, the kit contains one or more synthetic RNA molecules. In one embodiment, the kit contains one or more synthetic RNA molecules that encode one or more reprogramming factors 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, 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, 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.

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. 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. 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.

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 2. 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 viv*o. 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 2, 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 at least one 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.

*Table 2. 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 | dioctadecyl amidoglyceryl spermine (DOGS) |
| 25 | dioleoyl phosphatidyl ethanolamine (DOPE) |

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.

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 20nt and about 250nt or between about 120nt and about 150nt long. In a further embodiment, the 3'-poly(A) tail is about 20nt, or about 30nt, or about 40nt, or about 50nt, or about 60nt, or about 70nt, or about 80nt, or about 90nt, or about 100nt, or about 110nt, or about 120nt, or about 130nt, or about 140nt, or about 150nt, or about 160nt, or about 170nt, or about 180nt, or about 190nt, or about 200nt, or about 210nt, or about 220nt, or about 230nt, or about 240nt, or about 250nt long.

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.

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.

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.

For instance, botulinum toxin type A has been approved by the U.S. 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.

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 U.S. 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 |

Pharmaceutical preparations may additionally comprise delivery reagents (a.k.a. “transfection reagents”) 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.

In various embodiments, the compositions described herein can administered in an effective dose of, for example, from about 1 mg/kg to about 100 mg/kg, about 2.5 mg/kg to about 50 mg/kg, or about 5 mg/kg to about 25 mg/kg. The precise determination of what would be considered an effective dose may be based on factors individual to each patient, including their size, age, and type of disease. Dosages can be readily ascertained by those of ordinary skill in the art from this disclosure and the knowledge 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.

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 or intravenous injection, or by direct injection into 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.

Upon formulation, solutions may be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective. 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.

Exemplary 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.

Administration of the compositions described herein may be, for example, by injection, topical administration, ophthalmic administration and intranasal administration. The injection may include injections such as, but not limited to, intradermal, subcutaneous and intramuscular. 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.

**Sequences**

| SEQ ID NO | Description |
|---|---|
| 1 | StsI |
| 2 | StsI-HA |
| 3 | StsI-HA2 |
| 4 | StsI-UHA |
| 5 | StsI-UHA2 |
| 6 | StsI-HF |
| 7 | StsI-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 |
| 58 | GHGG-FokI |
| 59 | EO-GHGG-StsI |
| 60 | GHGG-StsI |
| 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 |

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

## EXAMPLES

*Example 1 RNA Synthesis*

RNA encoding green fluorescent protein or the human proteins Elastin, Tyrosinase, Melanocortin 1 receptor, Hyaluronan synthase 1, Hyaluronan synthase 2, Hyaluronan synthase 3, Collagen type III a1, Collagen type VII a1, Interleukin 10, P-selectin glycoprotein ligand-1, Alpha-(1,3)-fucosyltransferase Oct4, Sox2, Klf4, c-Myc-2 (T58A), and Lin28 or TALENs targeting the human genes XPA, CCR5, TERT, MYC, and BIRC5, 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 (U.S. Application No. 13/465,490 (now U.S. Patent No. 8,497,124), International Application No. PCT/US12/67966, U.S. Application No. 13/931,251, and International Application No. PCT/US13/68118, 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 1000ng/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 4C. For reprogramming experiments, RNA encoding Oct4, Sox2, Klf4, c-Myc-2 (T58A), and Lin28 was mixed at a molar ratio of 3:1:1:1:1.

*Table 4. RNA Synthesis*

| Template | Nucleotides | Reaction Volume/µL | ivT Yield/µg |
|---|---|---|---|
| hELN | A, 0.5 7dG, 0.4 5mU, 5mC | 20 | 34.1 |
| Oct4 (SEQ ID NO: 8) | A, 0.5 7dG, 0.4 5mU, 5mC | 300 | 2752.0 |
| Sox2 (SEQ ID NO: 9) | A, 0.5 7dG, 0.4 5mU, 5mC | 100 | 965.0 |
| Klf4 (SEQ ID NO: 10) | A, 0.5 7dG, 0.4 5mU, 5mC | 100 | 1093.8 |
| c-Myc-2 (T58A) | A, 0.5 7dG, 0.4 5mU, 5mC | 100 | 1265.6 |
| Lin28 | A, 0.5 7dG, 0.4 5mU, 5mC | 100 | 1197.8 |

| | | | |
|---|---|---|---|
| ELN | A, G, U, 5hmC | 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, 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, 0.4 5mU, 5hmC | 20 | 178.4 |
| HAS2 | A, G, 0.4 5mU, 5hmC | 20 | 59.3 |
| HAS3 | A, G, 0.4 5mU, 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 |
| IL10 | A, G, psU, C | 75 | 569.5 |
| SELPLG | A, G, psU, C | 75 | 542.6 |
| FUT7 | A, G, psU, C | 75 | 564.5 |
| Oct4 (SEQ ID NO: 8) | A, G, U, C | 10 | 100.7 |
| Oct4 (SEQ ID NO: 8) | A, G, U, 5mC | 10 | 120.6 |
| Oct4 (SEQ ID NO: 8) | A, G, U, 5mC | 10 | 115.3 |
| Oct4 (SEQ ID NO: 8) | A, G, U, 5hmC | 10 | 101.4 |
| Oct4 (SEQ ID NO: 8) | A, G, U, 5cC | 10 | 50.8 |

| | | | |
|---|---|---|---|
| Oct4 (SEQ ID NO: 8) | A, G, U, 5fC | 10 | 84.0 |
| Oct4 (SEQ ID NO: 8) | A, G, U, 5hmC | 10 | 99.5 |
| Sox2 (SEQ ID NO: 9) | A, G, U, 5hmC | 10 | 84.0 |
| Klf4 (SEQ ID NO: 10) | A, G, U, 5hmC | 10 | 72.6 |
| c-Myc-2 (T58A) | A, G, U, 5hmC | 10 | 82.4 |
| Lin28 | A, G, U, 5hmC | 10 | 83.1 |
| Oct4 (SEQ ID NO: 8) | A, G, 0.4 5mU, 5hmC | 10 | 78.9 |
| Sox2 (SEQ ID NO: 9) | A, G, 0.4 5mU, 5hmC | 10 | 91.9 |
| Klf4 (SEQ ID NO: 10) | A, G, 0.4 5mU, 5hmC | 10 | 91.2 |
| c-Myc-2 (T58A) | A, G, 0.4 5mU, 5hmC | 10 | 104.6 |
| Lin28 | A, G, 0.4 5mU, 5hmC | 10 | 103.2 |
| Oct4 (SEQ ID NO: 8) | A, G, 5hU, 5hmC | 300 | 1925.5 |
| Sox2 (SEQ ID NO: 9) | A, G, 5hU, 5hmC | 100 | 641.8 |
| Klf4 (SEQ ID NO: 10) | A, G, 5hU, 5hmC | 100 | 739.0 |
| c-Myc-2 (T58A) | A, G, 5hU, 5hmC | 100 | 574.0 |
| Lin28 | A, G, 5hU, 5hmC | 100 | 556.0 |

"A" refers to adenosine-5'-triphosphate, "G" refers to guanosine-5'-triphosphate, "U" refers to uridine-5'-triphosphate, "C" refers to cytidine-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, "psU" refers to 5-pseudouridine-5'-triphosphate, "5mU" refers to 5-methyluridine-5'-triphosphate, "5hU" refers to the 5'-triphosphate of uridine with a methyl group bound to an oxygen atom bound to the 5C position of the uridine, and "7dG" refers to 7-deazaguanosine-5'-triphosphate.

*Example 2 Transfection of Cells with Synthetic RNA*

For transfection in 6-well plates, 2µg RNA and 6µL transfection reagent (Lipofectamine RNAiMAX, 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 60µL each. Diluted RNA and transfection reagent were then mixed and incubated for 15min at room temperature, according to the transfection reagent-manufacturer's instructions. Complexes were then added to cells in culture. Between 12µL and 240µL 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). Volumes were scaled for transfection in 24-well and 96-well plates. Alternatively, between 0.5µg and 5µg of RNA and between 2-3µL of transfection reagent (Lipofectamine 2000, Life Technologies Corporation) per µg of RNA 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. Complexes were then added to cells in culture. Between 10µL and 200µL of complexes were added to each well of a 6-well plate, which already contained 2mL of transfection medium per well. In certain experiments, DMEM + 10% FBS or DMEM + 50% FBS was used in place of transfection medium. Plates were shaken gently to distribute the complexes throughout the well. Cells were incubated with complexes for 4 hours to overnight. In certain experiments, the medium was replaced with fresh transfection medium (2mL/well) 4h or 24h after transfection.

*Example 3 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 4 Transfection Medium Formulation*

A cell-culture medium was developed to support efficient transfection of cells with nucleic acids and efficient reprogramming ("transfection medium"):

DMEM/F12 + 15mM HEPES + 2mM L-alanyl-L-glutamine + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 2µg/mL ethanolamine + 50µg/mL L-ascorbic acid 2-phosphate sesquimagnesium salt hydrate + 4µg/mL cholesterol + 1µM hydrocortisone + 25µg/mL polyoxyethylenesorbitan monooleate + 2µg/mL D-alpha-tocopherol acetate + 20ng/mL bFGF + 5mg/mL treated human serum albumin.

A variant of this medium was developed to support robust, long-term culture of a variety of cell types, including pluripotent stem cells ("maintenance medium"):

DMEM/F12 + 2mM L-alanyl-L-glutamine + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 2µg/mL ethanolamine + 50µg/mL L-ascorbic acid 2-phosphate sesquimagnesium salt hydrate + 20ng/mL bFGF + 2ng/mL TGF-β1.

Transfection medium, in which the treated human serum albumin was treated by addition of 32mM sodium octanoate, followed by heating at 60C for 4h, followed by treatment with ion-exchange resin (AG501-X8(D), Bio-Rad Laboratories, Inc.) for 6h at room temperature, followed by treatment with dextran-coated activated charcoal (C6241, Sigma-Aldrich Co. LLC.) overnight at room temperature, followed by centrifugation, filtering, adjustment to a 10% solution with nuclease-free water, followed by addition to the other components of the medium, was used as the transfection medium in all Examples described herein, unless otherwise noted. For reprogramming experiments, cells were plated either on uncoated plates in DMEM + 10%-20% serum or on fibronectin and vitronectin-coated plates in transfection medium, unless otherwise noted. The transfection medium was not conditioned, unless otherwise noted. It is recognized that the formulation of the transfection

medium can be adjusted to meet the needs of the specific cell types being cultured. It is further recognized that treated human serum albumin can be replaced with other treated albumin, for example, treated bovine serum albumin, without negatively affecting the performance of the medium. It is further recognized that other glutamine sources can be used instead of or in addition to L-alanyl-L-glutamine, for example, L-glutamine, that other buffering systems can be used instead of or in addition to HEPES, for example, phosphate, bicarbonate, etc., that selenium can be provided in other forms instead of or in addition to sodium selenite, for example, selenous acid, that other antioxidants can be used instead of or in addition to L-ascorbic acid 2-phosphate sesquimagnesium salt hydrate and/or D-alpha-tocopherol acetate, for example, L-ascorbic acid, that other surfactants can be used instead of or in addition to polyoxyethylenesorbitan monooleate, for example, Pluronic F-68 and/or Pluronic F-127, that other basal media can be used instead of or in addition to DMEM/F12, for example, MEM, DMEM, etc., and that the components of the culture medium can be varied with time, for example, by using a medium without TGF-β from day 0 to day 5, and then using a medium containing 2ng/mL TGF-β after day 5, without negatively affecting the performance of the medium. It is further recognized that other ingredients can be added, for example, fatty acids, lysophosphatidic acid, lysosphingomyelin, sphingosine-1-phosphate, other sphingolipids, ROCK inhibitors, including Y-27632 and thiazovivin, members of the TGF-β/NODAL family of proteins, IL-6, members of the Wnt family of proteins, etc., at appropriate concentrations, without negatively affecting the performance of the medium, and that ingredients that are known to promote or inhibit the growth of specific cell types and/or agonists and/or antagonists of proteins or other molecules that are known to promote or inhibit the growth of specific cell types can be added to the medium at appropriate concentrations when it is used with those cell types without negatively affecting the performance of the medium, for example, sphingosine-1-phosphate and pluripotent stem cells. The present invention relates equally to ingredients that are added as purified compounds, to ingredients that are added as parts of well-defined mixtures, to ingredients that are added as parts of complex or undefined mixtures, for example, animal or plant oils, and to ingredients that are added by biological processes, for example, conditioning. The concentrations of the components can be varied from the listed values within ranges that will be obvious to persons skilled in the art without negatively affecting the performance of the medium. An animal component-free version of the medium was produced by using recombinant versions of all protein ingredients, and non-animal-derived versions of all other components, including semi-synthetic plant-derived cholesterol (Avanti Polar Lipids, Inc.).

*Example 5 Transfection Medium Formulation*

A medium was developed to support efficient transfection, reprogramming, and gene-editing of cells:

DMEM/F12 + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 20ng/mL bFGF + 5mg/mL treated human serum albumin.

Variants of this medium were also developed to provide improved performance when used with specific transfection reagents, specific nucleic acids, and specific cell types: DMEM/F12 + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 4.5µg/mL cholesterol + 20ng/mL bFGF + 5mg/mL treated human serum albumin, DMEM/F12 + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 1µM hydrocortisone + 20ng/mL bFGF + 5mg/mL treated human serum albumin, and DMEM/F12 + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 4.5µg/mL cholesterol + 1µM hydrocortisone + 20ng/mL bFGF + 5mg/mL treated human serum albumin.

Examples of additional components that were added to the cell-culture medium in certain experiments (listed with example concentrations) include: 15mM HEPES, 2mM L-alanyl-L-glutamine, 2µg/mL ethanolamine, 10µg/mL fatty acids, 10µg/mL cod liver oil fatty acids (methyl esters), 25µg/mL polyoxyethylenesorbitan monooleate, 2µg/mL D-alpha-tocopherol acetate, 1-50µg/mL L-ascorbic acid 2-phosphate sesquimagnesium salt hydrate, 200ng/mL B18R, and 0.1% Pluronic F-68.

For certain experiments in which the medium was conditioned, the following variant was used:

DMEM/F12 + 15mM HEPES + 2mM L-alanyl-L-glutamine + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 2µg/mL ethanolamine + 4.5µg/mL cholesterol + 10µg/mL cod liver oil fatty acids (methyl esters) + 25µg/mL polyoxyethylenesorbitan monooleate + 2µg/mL D-alpha-tocopherol acetate + 1µg/mL L-ascorbic acid 2-phosphate sesquimagnesium salt hydrate + 0.1% Pluronic F-68 + 20ng/mL bFGF + 5mg/mL treated human serum albumin.

For certain experiments in which the medium was not conditioned, the following variant was used.

DMEM/F12 + 15mM HEPES + 2mM L-alanyl-L-glutamine + 10µg/mL insulin + 5.5µg/mL transferrin + 6.7ng/mL sodium selenite + 2µg/mL ethanolamine + 4.5µg/mL cholesterol + 1µM hydrocortisone + 0-25µg/mL polyoxyethylenesorbitan monooleate + 2µg/mL D-alpha-tocopherol acetate + 50µg/mL L-ascorbic acid 2-phosphate sesquimagnesium salt hydrate + 20ng/mL bFGF + 5mg/mL treated human serum albumin.

For the preparation of the these variants, the treated human serum albumin was treated by addition of 32mM sodium octanoate, followed by heating at 60C for 4h, followed by treatment with ion-exchange resin (AG501-X8(D)) for 6h at room temperature, followed by treatment with dextran-coated activated charcoal (C6241, Sigma-Aldrich Co. LLC.) overnight at room temperature, followed by centrifugation, filtering, adjustment to a 10% solution with nuclease-free water, followed by addition to the other components of the medium. For certain experiments in which the medium was conditioned, the medium was conditioned for 24h on irradiated human neonatal fibroblast feeders. The cells were plated on fibronectin-coated plates or fibronectin and vitronectin-coated plates, unless otherwise noted.

The formulation of the medium can be adjusted to meet the needs of the specific cell types being cultured. Furthermore, in certain situations, treated human serum albumin can be replaced with other treated albumin,

for example, treated bovine serum albumin, other glutamine sources can be used instead of or in addition to L-alanyl-L-glutamine, for example, L-glutamine, other buffering systems can be used instead of or in addition to HEPES, for example, phosphate, bicarbonate, etc., selenium can be provided in other forms instead of or in addition to sodium selenite, for example, selenous acid, other antioxidants can be used instead of or in addition to L-ascorbic acid 2-phosphate sesquimagnesium salt hydrate and/or D-alpha-tocopherol acetate, for example, L-ascorbic acid, other surfactants can be used instead of or in addition to polyoxyethylenesorbitan monooleate and/or Pluronic F-68, for example, Pluronic F-127, other basal media can be used instead of or in addition to DMEM/F12, for example, MEM, DMEM, etc., and the components of the culture medium can be varied with time, for example, by using a medium without TGF-β from day 0 to day 5, and then using a medium containing 2ng/mL TGF-β after day 5. In certain situations, other ingredients can be added, for example, fatty acids, lysophosphatidic acid, lysosphingomyelin, sphingosine-1-phosphate, other sphingolipids, members of the TGF-β/NODAL family of proteins, IL-6, members of the Wnt family of proteins, etc., at appropriate concentrations, and ingredients that are known to promote or inhibit the growth of specific cell types and/or agonists and/or antagonists of proteins or other molecules that are known to promote or inhibit the growth of specific cell types can be added to the medium at appropriate concentrations when it is used with those cell types, for example, sphingosine-1-phosphate and pluripotent stem cells. Ingredients can take the form of purified compounds, parts of well-defined mixtures, parts of complex or undefined mixtures, for example, animal or plant oils, and may be added by biological processes, for example, conditioning. The concentrations of the components can be varied from the listed values within ranges that will be obvious to persons skilled in the art.

*Example 6 Transfection of Cells with Synthetic RNA*

For transfection in 6-well plates, 2µg RNA 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 60µL each. Diluted RNA and transfection reagent were then mixed and incubated for 15min at room temperature, according to the transfection reagent-manufacturer's instructions. Complexes were then added to cells in culture. Between 30µL and 240µL of complexes were added to each well of a 6-well plate, which already contained 2mL of transfection medium per well. Plates were then shaken gently to distribute the complexes throughout the well. Cells were incubated with complexes for 2 hours to overnight, before replacing the medium with fresh transfection medium (2mL/well). Volumes were scaled for transfection in 24-well and 96-well plates. Cells were fixed and stained 20-24h after transfection using an antibody against Oct4. Nuclei were stained and counted to determine the relative toxicity of the RNA.

*Example 7 Analysis of the Ability of Untreated Human Serum Albumin Preparations to Support Nucleic Acid Transfection and RNA Reprogramming*

Primary human neonatal fibroblasts were cultured in medium with or without 5mg/mL HSA. Cohn Fraction V (A6784, Sigma-Aldrich Co. LLC.), and four different recombinant HSA preparations (A6608, A7736, A9731, and A9986, all from Sigma-Aldrich Co. LLC.) were screened. Cells were transfected according to Example 2, with RNA synthesized according to Example 1. While untransfected cells grew well in media containing any of the HSA preparations, in transfected wells, each of the HSA preparations yielded dramatically different cell morphologies and cell densities, and none resulted in morphological changes indicative of reprogramming.

*Example 8 Production of Octanoate-Treated Human Serum Albumin*

A 10% solution of HSA was pre-incubated with 22mM sodium chloride and 16mM sodium octanoate (Sigma-Aldrich Co. LLC), and was incubated at 37C for 3 hours before assembly of the complete medium.

*Example 9 Treatment of Human Serum Albumin Using Ion-Exchange Chromatography*

A 20% solution of recombinant HSA produced in *Pichia pastoris* (A7736, Sigma-Aldrich Co. LLC.) was prepared by dissolving 2g of HSA in 10mL of nuclease-free water with gentle agitation at room temperature. The HSA solution was then deionized by first adding 1g of mixed-bed deionizing resin (AG 501-X8(D), Bio-Rad Laboratories, Inc.), and rocking for 1h at room temperature. The HSA solution was then decanted into a tube containing 5g of fresh resin, and was rocked for 4h at room temperature. Finally, the deionized HSA solution was decanted, adjusted to a 10% total protein content with nuclease-free water, filter-sterilized using a 0.2μm PES-membrane filter, and stored at 4C.

*Example 10 Analysis of Transfection Efficiency and Viability of Cells Cultured in Media Containing Octanoate-Treated Human Serum Albumin*

Primary human neonatal fibroblasts were cultured in media containing recombinant HSA treated according to Example 8 and/or Example 9 or containing treated blood-derived HSA (Bio-Pure HSA, Biological Industries). Cells were transfected daily, according to Example 2, with RNA synthesized according to Example 1, beginning on day 0. Pictures were taken on day 3. Several small areas of cells undergoing morphological changes resembling mesenchymal to epithelial transition were observed in the wells containing octanoate, indicating an increased transfection efficiency. Many large areas of morphological changes resembling mesenchymal to epithelial transition were observed in the samples containing the treated blood-derived HSA. In both cases, the morphological changes were characteristic of reprogramming.

*Example 11 Reprogramming Human Fibroblasts Using Media Containing Octanoate-Treated Human Serum Albumin*

Primary human neonatal fibroblasts were plated in 6-well plates at a density of 5000 cells/well in fibroblast medium (DMEM + 10% fetal bovine serum). After 6 hours, the medium was replaced with transfection medium containing octanoate-treated HSA. The cells were transfected daily, according to Example 2, with RNA synthesized according to Example 1, beginning on day 0. By day 5, the well contained several areas of cells exhibiting morphology consistent with reprogramming. This experiment did not include the use of feeders or immunosuppressants.

*Example 12 Analysis of Transfection Efficiency and Viability of Cells Cultured in Media Containing Ion-Exchange-Resin-Treated Human Serum Albumin*

Primary human neonatal fibroblasts were transfected according to Example 2, with RNA synthesized according to Example 1, beginning on day 0. Pictures were taken on day 2. Cells in the well containing untreated HSA exhibited low viability compared to either the well containing treated blood-derived HSA or ion-exchange-resin-treated recombinant HSA.

*Example 13 Reprogramming Human Fibroblasts Using Ion-Exchange-Resin-Treated Human Serum Albumin*

Primary human neonatal fibroblasts were plated in 6-well plates on feeders at a density of 10,000 cells/well in fibroblast medium (DMEM + 10% fetal bovine serum). The cells were transfected daily according to Example 2, with RNA synthesized according to Example 1, beginning on day 0. A passage with a split ratio of 1:20 was performed on day 4. Pictures were taken on day 10. The well contained many large colonies of cells exhibiting morphology consistent with reprogramming. No colonies were observed in wells exposed to cell-culture media containing untreated HSA.

*Example 14 Reprogramming Human Fibroblasts without Using Feeders or Immunosuppressants*

Primary human fibroblasts were plated in 6-well plates at a density of 20,000 cells/well in fibroblast medium (DMEM + 10% fetal bovine serum). After 6 hours, the medium was replaced with transfection medium containing treated HSA and not containing immunosuppressants, and the cells were transfected daily according to Example 2, with RNA synthesized according to Example 1, except that the dose of RNA was reduced to 1µg/well and a total of 5 transfections were performed. Pictures were taken on day 7. Small colonies of cells exhibiting morphology consistent with reprogramming became visible as early as day 5. On day 7, the medium was replaced with DMEM/F12 + 20% Knockout™ Serum Replacement (Life Technologies Corporation) + 1X non-essential amino acids + 2mM L-glutamine, conditioned on irradiated mouse embryonic fibroblasts for 24 hours, and then supplemented with 20ng/mL bFGF and 10µM Y-27632. Large colonies with a reprogrammed morphology became visible as early as day 8. Colonies were picked on day 10, and plated in wells coated with basement membrane extract (Cultrex® Human BME Pathclear®, Trevigen Inc.). Cells

grew rapidly, and were passaged to establish lines. Established lines stained positive for the pluripotent stem-cell markers Oct4 and SSEA4. The entire protocol was repeated, and similar results were obtained.

*Example 15 Efficient, Rapid Derivation and Reprogramming of Cells from Human Skin Biopsy Tissue*

A full-thickness dermal punch biopsy was performed on a healthy, 31 year-old volunteer, according to an approved protocol. Briefly, an area of skin on the left, upper arm was anesthetized by topical application of 2.5% lidocaine. The field was disinfected with 70% isopropanol, and a full-thickness dermal biopsy was performed using a 1.5 mm-diameter punch. The tissue was rinsed in phosphate-buffered saline (PBS), and was placed in a 1.5mL tube containing 250µL of TrypLE™ Select CTS™ (Life Technologies Corporation), and incubated at 37C for 30min. The tissue was then transferred to a 1.5mL tube containing 250µL of DMEM/F12-CTS™ (Life Technologies Corporation) + 5mg/mL collagenase, and incubated at 37C for 2h. The epidermis was removed using forceps, and the tissue was mechanically dissociated. Cells were rinsed twice in DMEM/F12-CTS™ and were plated in fibronectin-coated wells of 24-well and 96-well plates. Phlebotomy was also performed on the same volunteer, and venous blood was collected in Vacutainer® SST™ tubes (Becton, Dickinson and Company). Serum was isolated according to the manufacturer's protocol. Isogenic plating medium was prepared by mixing DMEM/F12-CTS™ + 2mM L-alanyl-L-glutamine (Sigma-Aldrich Co. LLC.) + 20% human serum. Cells from the dermal tissue sample were plated either in transfection medium or in isogenic plating medium. After 2 days, the wells were rinsed, and the medium was replaced with transfection medium. Many cells with a fibroblast morphology attached and began to spread by day 2. Cells were transfected according to Example 2, with RNA synthesized according to Example 1, beginning on day 2, with all volumes scaled to accommodate the smaller wells. By day 5, areas of cells with morphologies consistent with reprogramming were observed.

*Example 16 Reprogramming Human Fibroblasts Using Synthetic RNA Containing Non-Canonical Nucleotides*

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, incubated at room temperature for 1h) at a density of 20,000 cells/well in transfection medium. The following day, the cells were transfected as in Example 2, with RNA synthesized according to Example 1, except that the dose of RNA was 0.5µg/well on day 1, 0.5µg/well on day 2, and 2µg/well on day 3. Pictures were taken on day 4. Small colonies of cells exhibiting morphology consistent with reprogramming were visible on day 4.

*Example 17 Reprogramming Human Fibroblasts with a Non-Conditioned Transfection Medium*

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, incubated at room temperature for 1h) at a density of 20,000 cells/well in transfection medium. The following

day, the cells were transfected as in Example 2, with RNA synthesized according to Example 1, except that the dose of RNA was 0.5µg/well on day 1, 0.5µg/well on day 2, 2µg/well on day 3, 2µg/well on day 4, and 4µg/well on day 5. Small colonies of cells exhibiting morphology consistent with reprogramming became visible as early as day 5. On day 7, the medium was replaced with DMEM/F12 + 20% Knockout™ Serum Replacement (Life Technologies Corporation) + 1X non-essential amino acids + 2mM L-glutamine, conditioned on irradiated mouse embryonic fibroblasts for 24 hours, and then supplemented with 20ng/mL bFGF and 10µM Y-27632. Large colonies with a reprogrammed morphology became visible as early as day 8. Colonies were picked on day 10, and plated in wells coated with basement membrane extract (Cultrex® Human BME Pathclear®, Trevigen Inc.). Cells grew rapidly, and were passaged to establish lines.

*Example 18 Reprogramming Human Fibroblasts Using Synthetic RNA Containing Non-Canonical Nucleotides*

Primary human neonatal 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, using RNA containing A, 0.5 7dG, 0.5 5mU, and 5mC, and an RNA dose of 0.5µg/well on day 1, 0.5µg/well on day 2, 2µg/well on day 3, 2µg/well on day 4, and 4µg/well on day 5. Small colonies of cells exhibiting morphology consistent with reprogramming became visible as early as day 5. The medium was replaced with maintenance medium on day 6. Cells were stained using an antibody against Oct4. Oct4-positive colonies of cells exhibiting a morphology consistent with reprogramming were visible throughout the well.

*Example 19 Feeder-Free, Passage-Free, Immunosuppressant-Free, Conditioning-Free Reprograming of Primary Adult Human Fibroblasts Using Synthetic RNA*

Wells of a 6-well plate were coated with a mixture of recombinant human fibronectin and recombinant human vitronectin (1µg/mL in DMEM/F12, 1mL/well) for 1h at room temperature. Primary adult human fibroblasts were plated in the coated wells in transfection medium at a density of 10,000 cells/well. Cells were maintained at 37C, 5% $CO_2$, and 5% $O_2$. Beginning the following day, cells were transfected according to Example 2 daily for 5 days with RNA synthesized according to Example 1. The total amount of RNA transfected on each of the 5 days was 0.5µg, 0.5µg, 2µg, 2µg, and 4µg, respectively. Beginning with the fourth transfection, the medium was replaced twice a day. On the day following the final transfection, the medium was replaced with transfection medium, supplemented with 10µM Y-27632. Alternatively, the total amount of RNA transfected on each day was 0.25µg, 0, 0.5µg, 0.5µg, and 0.5µg, respectively or 0.25µg, 0, 0.25µg, 0.25µg, 0.25µg, and 0.25µg, respectively. In certain experiments, transfection medium was changed only once per day, at the time of transfection. Compact colonies of cells with a reprogrammed morphology were visible in each transfected well by day 4.

*Example 20 Efficient, Rapid Derivation and Reprogramming of Cells from Adult Human Skin Biopsy Tissue*

A full-thickness dermal punch biopsy was performed on a healthy, 31 year-old volunteer, according to an approved protocol. Briefly, an area of skin on the left, upper arm was anesthetized by topical application of 2.5% lidocaine. The field was disinfected with 70% isopropanol, and a full-thickness dermal biopsy was performed using a 1.5 mm-diameter punch. The tissue was rinsed in phosphate-buffered saline (PBS), was placed in a 1.5mL tube containing 250µL of TrypLE Select CTS (Life Technologies Corporation), and was incubated at 37C for 30min. The tissue was then transferred to a 1.5mL tube containing 250µL of DMEM/F12-CTS (Life Technologies Corporation) + 5mg/mL collagenase, and was incubated at 37C for 2h. The epidermis was removed using forceps, and the tissue was mechanically dissociated. Cells were rinsed twice in DMEM/F12-CTS. Phlebotomy was also performed on the same volunteer, and venous blood was collected in Vacutainer SST tubes (Becton, Dickinson and Company). Serum was isolated according to the manufacturer's instructions. Isogenic plating medium was prepared by mixing DMEM/F12-CTS + 2mM L-alanyl-L-glutamine (Sigma-Aldrich Co. LLC.) + 20% human serum. Cells from the dermal tissue sample were plated in a fibronectin-coated well of a 6-well plate in isogenic plating medium. Many cells with a fibroblast morphology attached and began to spread by day 2. Cells were expanded and frozen in Synth-a-Freeze (Life Technologies Corporation).

Cells were passaged into 6-well plates at a density of 5,000 cells/well. The following day, the medium was replaced with transfection medium, and the cells were transfected as in Example 2, using RNA containing A, 0.5 7dG, 0.4 5mU, and 5mC, and an RNA dose of 0.5µg/well on day 1, 0.5µg/well on day 2, 2µg/well on day 3, 2µg/well on day 4, and 2µg/well on day 5. Certain wells received additional 2µg/well transfections on day 6 and day 7. In addition, certain wells received 2ng/mL TGF-β1 from day 4 onward. The medium was replaced with maintenance medium on day 6. Colonies of cells exhibiting morphology consistent with reprogramming became visible between day 5 and day 10. Colonies grew rapidly, and many exhibited a morphology similar to that of embryonic stem-cell colonies. Colonies were picked and plated in wells coated with recombinant human fibronectin and recombinant human vitronectin (each diluted in DMEM/F12 to a concentration of 1µg/mL, 1mL/well, incubated at room temperature for 1h). Cells grew rapidly, and were passaged to establish lines.

*Example 21 High-Efficiency Gene Editing by Repeated Transfection with RiboSlice*

Primary human fibroblasts were plated as in Example 19. 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 22 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 23 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 100-150$mm^3$, 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 24 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 25 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 26 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 35-50$mm^3$, 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 27 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 28 Folate-Targeted Liposome Formulation*

Liposomes are prepared according to Example 62, except that 0.27mg/mL 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[folate(polyethylene glycol)-5000] (FA-MPEG5000-DSPE) is added to the lipid mixture.

*Example 29 Therapy Comprising Liposomal Protein-Encoding RNA*

Liposomes encapsulating synthetic RNA encoding a therapeutic protein, synthesized according to Example 1, are prepared according to Example 27 or Example 28. The liposomes are administered by injection or intravenous infusion.

*Example 30 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. 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, and R: AAAAAAACCGGTTCATTTTCTCTTCCGGCCAC. 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 31 Synthesis of Elastin RNA*

RNA encoding human elastin was synthesized using the DNA template of Example 30 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 (**FIG. 1**).

The RNA was then diluted to 200ng/µL and an RNase inhibitor (Superase·In™, Life Technologies Corporation) was added at a concentration of 1µL/200µg of RNA. The RNA solution was stored at 4C.

*Example 32 Production of Octanoate-Treated Human Serum Albumin*

A 10% solution of HSA was pre-incubated with 16mM sodium octanoate (Sigma-Aldrich Co. LLC), and was incubated at 37C for 3 hours before assembly of the complete medium.

*Example 33 Formulation for in vivo delivery of nucleic acids*

The formulation for *in vivo* delivery of nucleic acids is prepared by combining RNA synthesized according to Example 31 and human serum albumin treated according to Examples 8, 9 and/or 32 in a suitable buffer (*e.g.,* water, DMEM/F12, complexation medium, Opti-MEM, etc.).

*Example 34 Increasing elastin production in skin by transdermal injection via syringe of treated albumin and RNA encoding elastin*

The formulation of example 33 is loaded into an insulin syringe with a 28-gauge 0.5-inch needle and delivered to the dermis of a patient through the epidermis. Additional doses are administered as necessary.

*Example 35 Increasing elastin production in skin by intradermal injection via motorized microneedle array of treated albumin and RNA encoding elastin*

The formulation of example 33 is loaded into the chamber of a motorized microneedle array set to a penetration depth of approximately 0.1 mm. The microneedle array delivers the formulation to the dermis of a patient through the epidermis.

*Example 36 Increasing collagen production in skin by transdermal injection of treated albumin and RNA encoding collagen*

The formulation of example 33 is prepared using RNA encoding human collagen type I and/or type III. The formulation is delivered as in Example 34 or 35.

*Example 37 Increasing production of actin in skeletal muscle by intramuscular injection of treated albumin and RNA encoding actin*

The formulation of example 33 is prepared using RNA encoding skeletal alpha actin. The formulation is delivered to the patient via intramuscular injection.

*Example 38 Wound healing treatment*

The formulation of example 33 is prepared using RNA encoding basic fibroblast growth factor. The formulation is delivered as in Example 34 or 35.

*Example 39 Anti-scarring treatment*

The formulation of example 33 is prepared using RNA encoding collagenase. The formulation is delivered as in Example 34 or 35.

*Example 40 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 41 Synthesis of Tyrosinase RNA*

RNA encoding human tyrosinase was synthesized according to Example 1, using the DNA template of Example 40 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 42 Production of Octanoate-Treated Human Serum Albumin*

A 10% solution of HSA was pre-incubated with 16mM sodium octanoate (Sigma-Aldrich Co. LLC), and was incubated at 37C for 3 hours before assembly of the complete medium.

*Example 43 Increasing Melanin Production in Skin by Transdermal Injection via Syringe of RNA Encoding Tyrosinase*

The RNA of Example 41 was loaded into a syringe and delivered to the dermis of the ventral forearm of a healthy 33 year-old male patient over the course of approximately 30 seconds.

*Example 44 Increasing Melanin Production in Skin by Combined Delivery of RNA Encoding Tyrosinase and Electroporation*

The area of skin treated in Example 43 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 (see **FIG. 16**). The experiment was repeated several times, with similar results.

*Example 45 Increasing Melanin Production in Skin by Topical or Intradermal Application of RNA Encoding Tyrosinase*

The RNA of Example 41 or the liposomes of Example 29 are applied directly to the skin, with or without disruption of the stratum corneum or injected intradermally using a dose of one microgram or less per square centimeter. Optionally, an electric field is applied as in Example 44 or using a surface-contact patch to enhance delivery of the RNA.

*Example 46 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 43, 44 or 45.

*Example 47 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 43, 44 or 45.

*Example 48 Anemia Therapy Comprising Delivery of RNA Encoding Erythropoietin or Darbepoetin*

RNA encoding darbepoetin alfa was prepared according to Example 1. The RNA is delivered as in Example 43, 44 or 45.

*Example 49 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 43, 44 or 45.

*Example 50 Wound Healing Treatment*

RNA encoding basic fibroblast growth factor is prepared according to Example 1. The RNA is delivered as in Example 43, 44 or 45.

*Example 51 Anti-Scarring Treatment*

RNA encoding collagenase is prepared according to Example 1. The RNA is delivered as in Example 43, 44 or 45.

*Example 52 Production of Botulinum Toxin*

RNA encoding botulinum toxin is prepared according to Example 1. The RNA is delivered as in Example 43, 44 or 45.

*Example 53 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 (**FIG. 17**).

*Example 54 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 (**FIG. 18**).

*Example 55 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 43, 44 or 45.

*Example 56 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 55 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.

## EQUIVALENTS

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.

**THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:**

1. An *in vivo* method for treating a dystrophic epidermolysis bullosa patient comprising
delivering a synthetic RNA encoding collagen type VII to the patient's keratinocytes by injection to the epidermis, thereby resulting in the amelioration of one or more of the dystrophic epidermolysis bullosa patient's symptoms.

2. The method of claim 1, wherein the synthetic RNA comprises a non-canonical nucleotide selected from the group consisting of 5-methyluridine, 5-hydroxyuridine, pseudouridine, 5-methylpseudouridine, 5-hydroxypseudouridine, 5-methylcytidine, and 5-hydroxycytidine.

3. The method of claim 1 or claim 2, wherein the synthetic RNA comprises 5-hydroxymethylcytidine.

4. The method of any one of claims 1 to 3, wherein the synthetic RNA comprises 5-methyluridine at about 40% of the uridine residues.

5. The method of any one of claims 1 to 4, wherein the collagen type VII is collagen type VII (A1).

6. The method of any one of claims 1 to 5, wherein the synthetic RNA encodes the amino acid sequence of SEQ ID NO: 78.

7. The method of any one of claims 1 to 6, further resulting in increased expression of collagen type VII within between about 24 and about 72 hours of delivery.

8. The method of any one of claims 1 to 7, wherein the synthetic RNA encodes the coding sequence of a human COL7 gene.

9. An *in vivo* method for treating epidermolysis bullosa, comprising
delivering a synthetic RNA encoding a gene-editing protein that targets a COL7 gene to a patient in need thereof and
inducing a single-strand or double-strand break in the COL7 gene of the patient's keratinocytes,
thereby eliminating a mutation that is at least partially responsible for a disease phenotype, wherein:
the synthetic RNA is delivered to the patient's keratinocytes by injection to the epidermis and
the gene-editing protein comprises a DNA-binding domain and a nuclease domain.

10. The method of claim 9, wherein the synthetic RNA comprises a non-canonical nucleotide selected from the group consisting of 5-methyluridine, 5-hydroxyuridine, pseudouridine, 5-methylpseudouridine, 5-hydroxypseudouridine, 5-methylcytidine, and 5-hydroxycytidine.

11. The method of claim 9 or claim 10, further comprising delivering a repair template to the patient.

12. The method of claim 11, wherein the repair template is a single-stranded DNA molecule or a double-stranded DNA molecule.

13. The method of claim 11, wherein the repair template does not contain a binding site of the gene-editing protein.

14. The method of claim 13, wherein 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.

15. The method of any one of claims 9 to 14, wherein the gene-editing protein targets a nucleic acid sequence that encodes the amino acid sequence of SEQ ID NO: 78.

16. The method of any one of claims 9 to 15, wherein the gene-editing protein is selected from the group consisting of a nuclease, a transcription activator-like effector nuclease (TALEN), a zinc-finger nuclease, a meganuclease, a nickase, and a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein.

17. The method of any one of claims 9 to 16, further resulting in editing of the COL7 gene.

18. An *in vivo* method for treating dystrophic epidermolysis bullosa, comprising

delivering a synthetic RNA encoding a gene-editing protein that targets a COL7 gene to a patient in need thereof and

delivering a COL7 repair template to the patient, thereby editing the COL7 gene, wherein:

the synthetic RNA and repair template are delivered to the patient's keratinocytes by injection to the epidermis and

the gene-editing protein comprises a DNA-binding domain and a nuclease domain and causes a double-strand break in the COL7 gene of the patient's keratinocytes.

19. The method of claim 18, wherein 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 partially responsible for a disease phenotype.

20. The method of claim 18 or 19, wherein the COL7 repair template is a single-stranded DNA molecule or a double-stranded DNA molecule.

21. The method of any one of claims 18 to 20, wherein the COL7 repair template does not contain a binding site of the gene-editing protein.

22. The method of any one of claims 18 to 21, wherein the gene-editing protein targets a nucleic acid sequence that encodes the amino acid sequence of SEQ ID NO: 78.

23. The method of any one of claims 18 to 22, wherein the gene-editing protein is selected from the group consisting of a nuclease, a transcription activator-like effector nuclease (TALEN), a zinc-finger nuclease, a meganuclease, a nickase, and a clustered regularly interspaced short palindromic repeat (CRISPR)-associated protein.

24. The method of any one of claims 18 to 23, wherein the synthetic RNA molecule further comprises one or more of a 5'-cap, a 5'-cap 1 structure, and a 3'-poly(A) tail.

FIG. 1

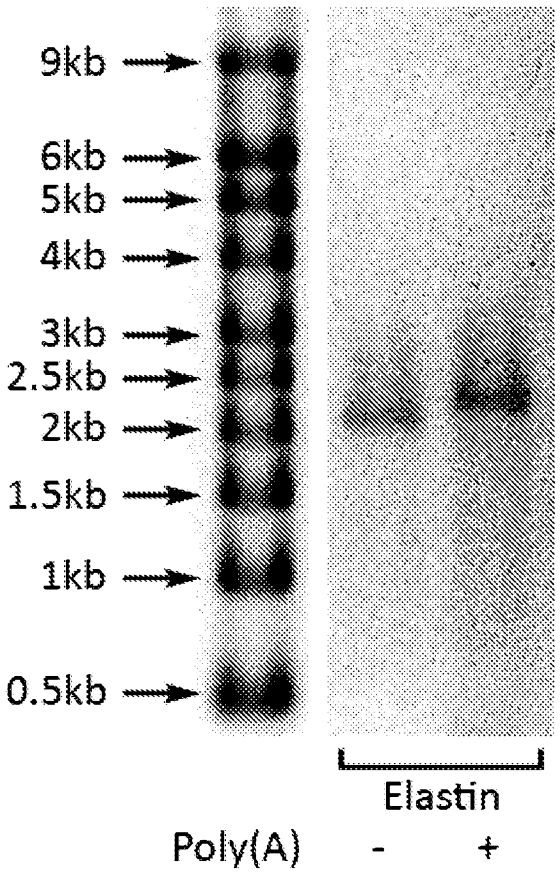



FIG. 2

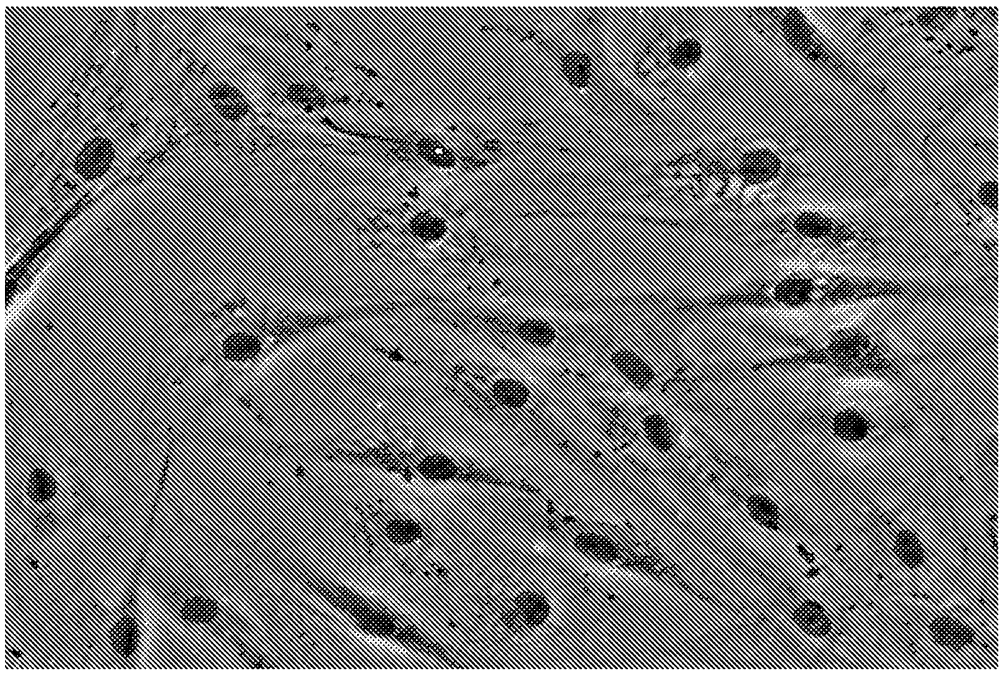


FIG. 3

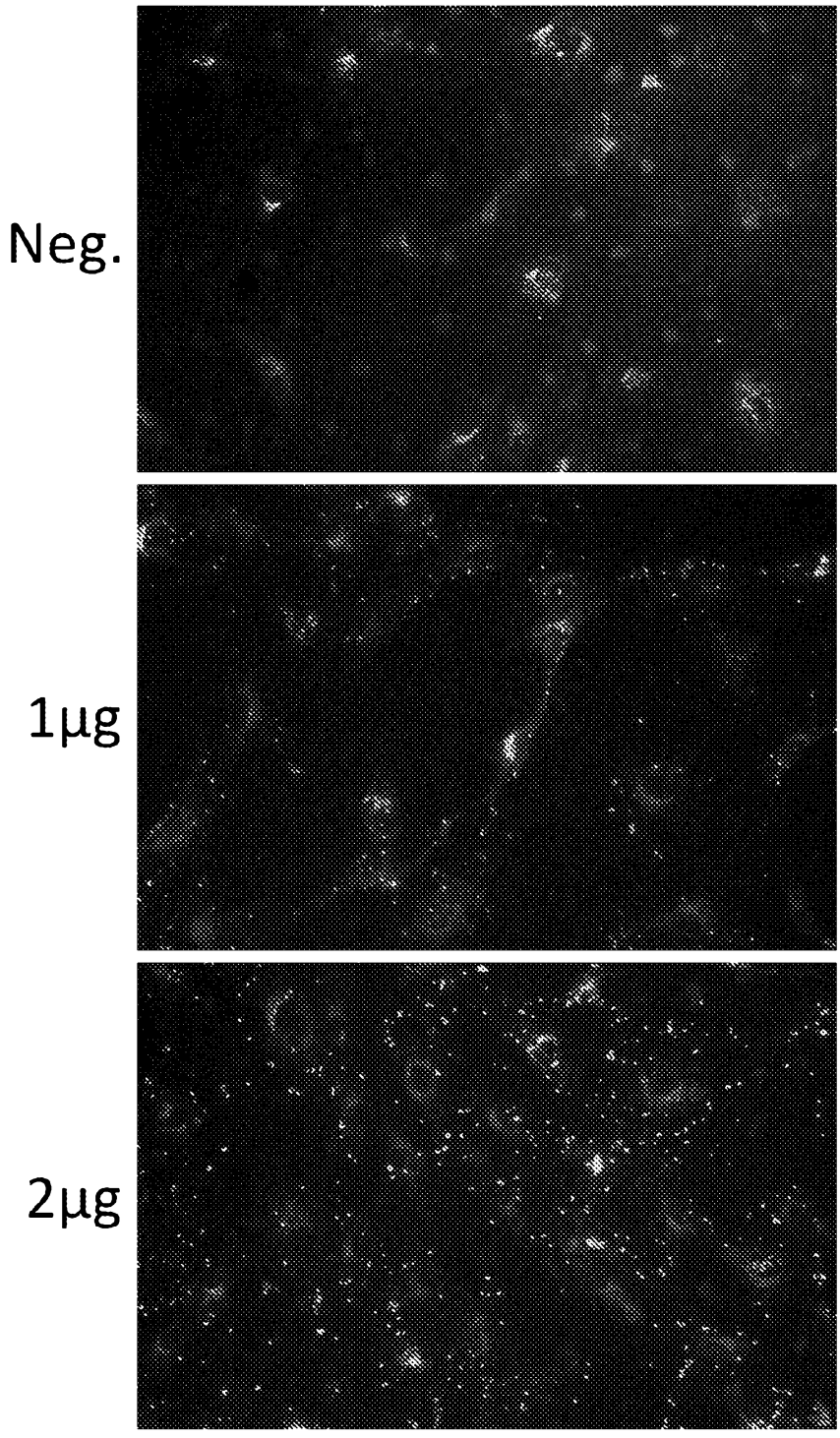


FIG. 4

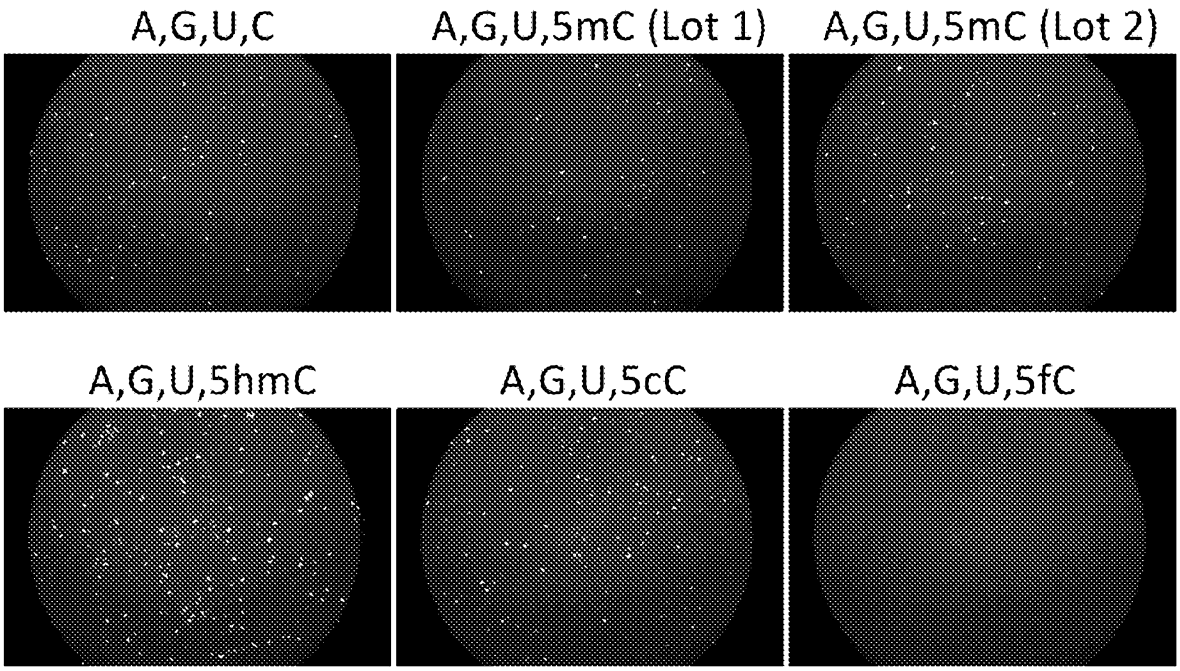



FIG. 5

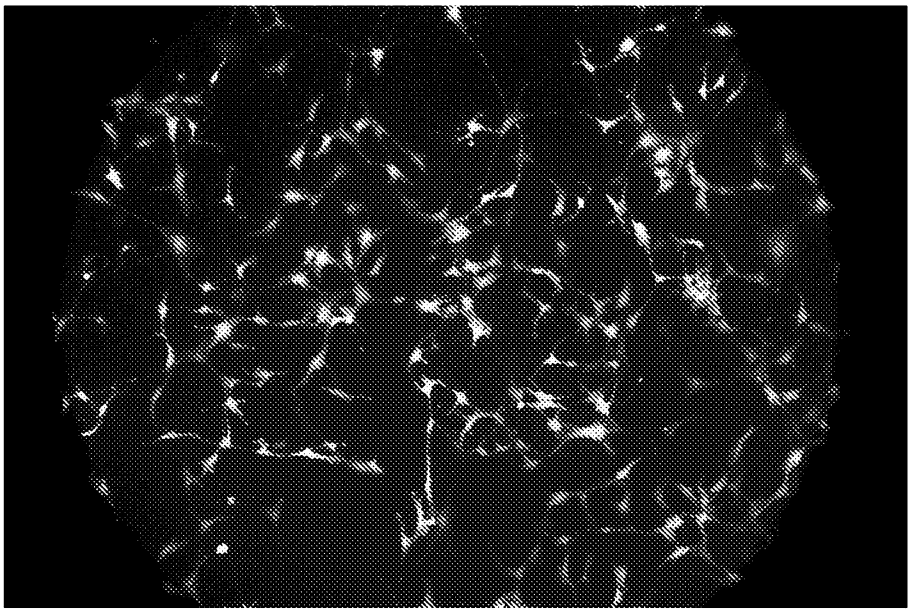


FIG. 6

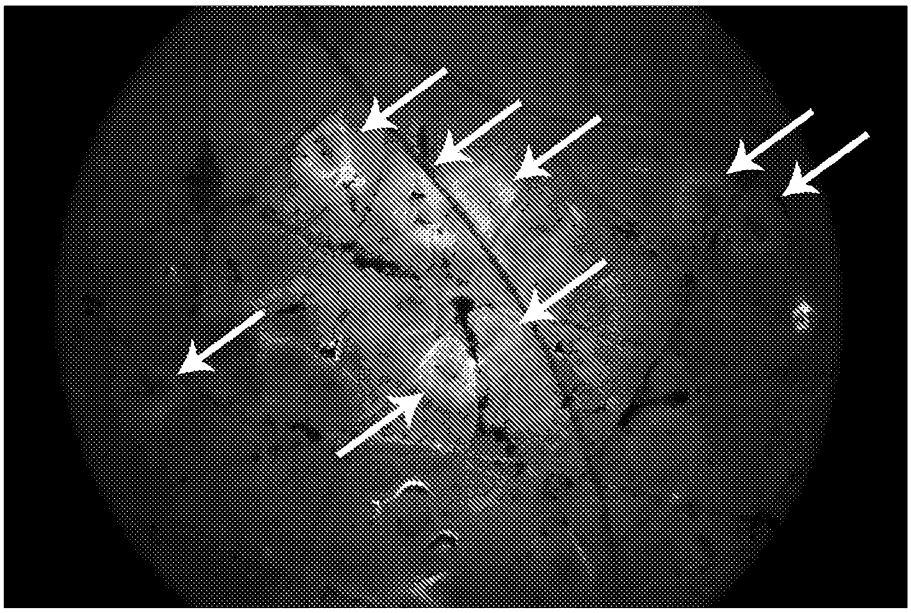


FIG. 7

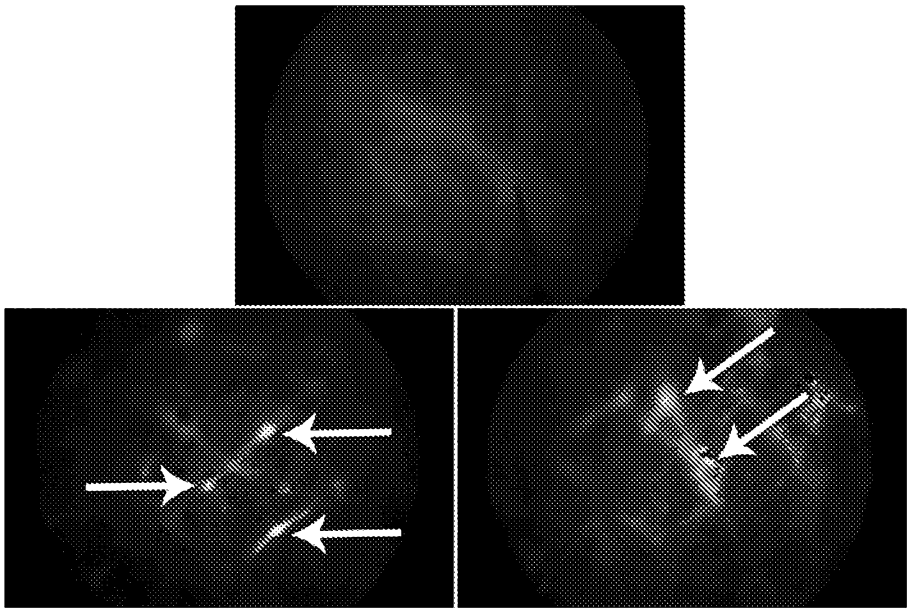


FIG. 8

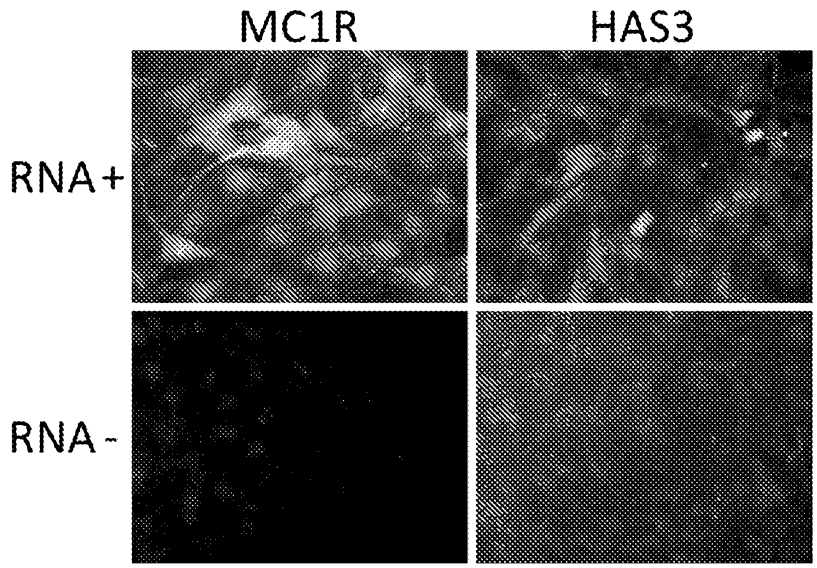



FIG. 9

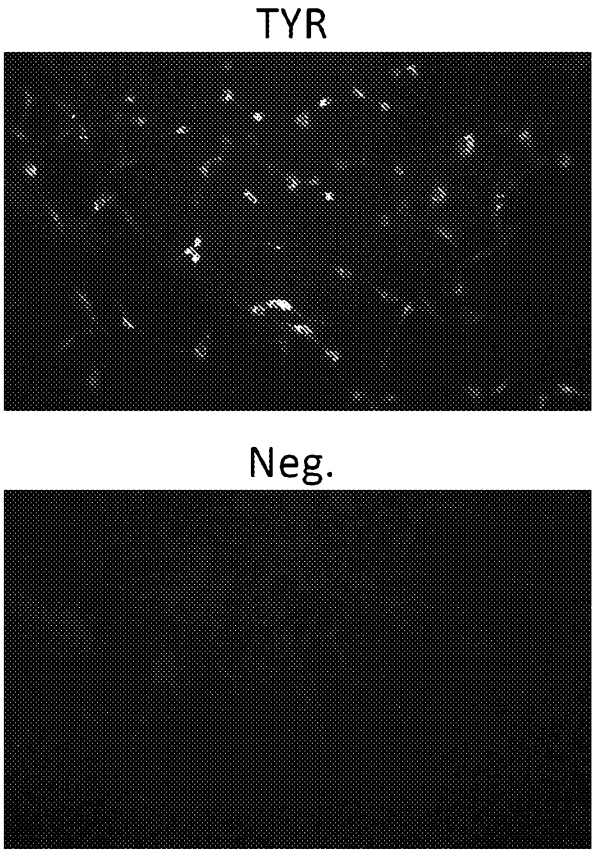


FIG. 10

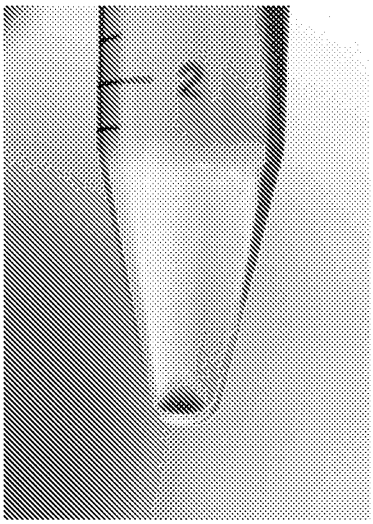


FIG. 11

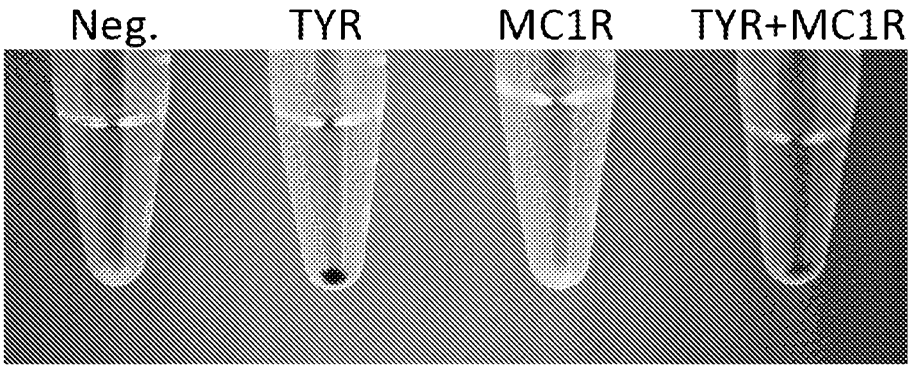



FIG. 12

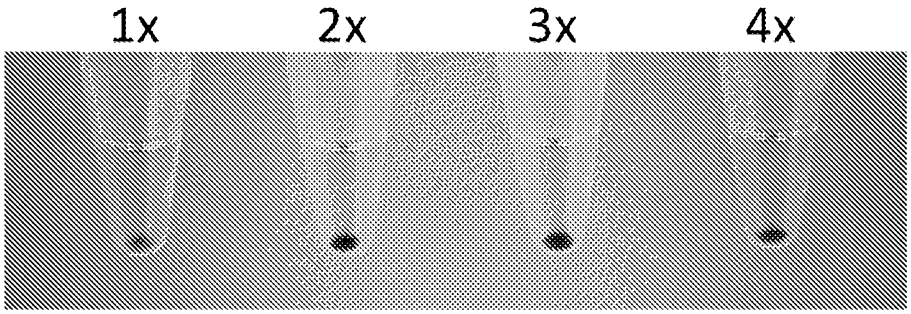
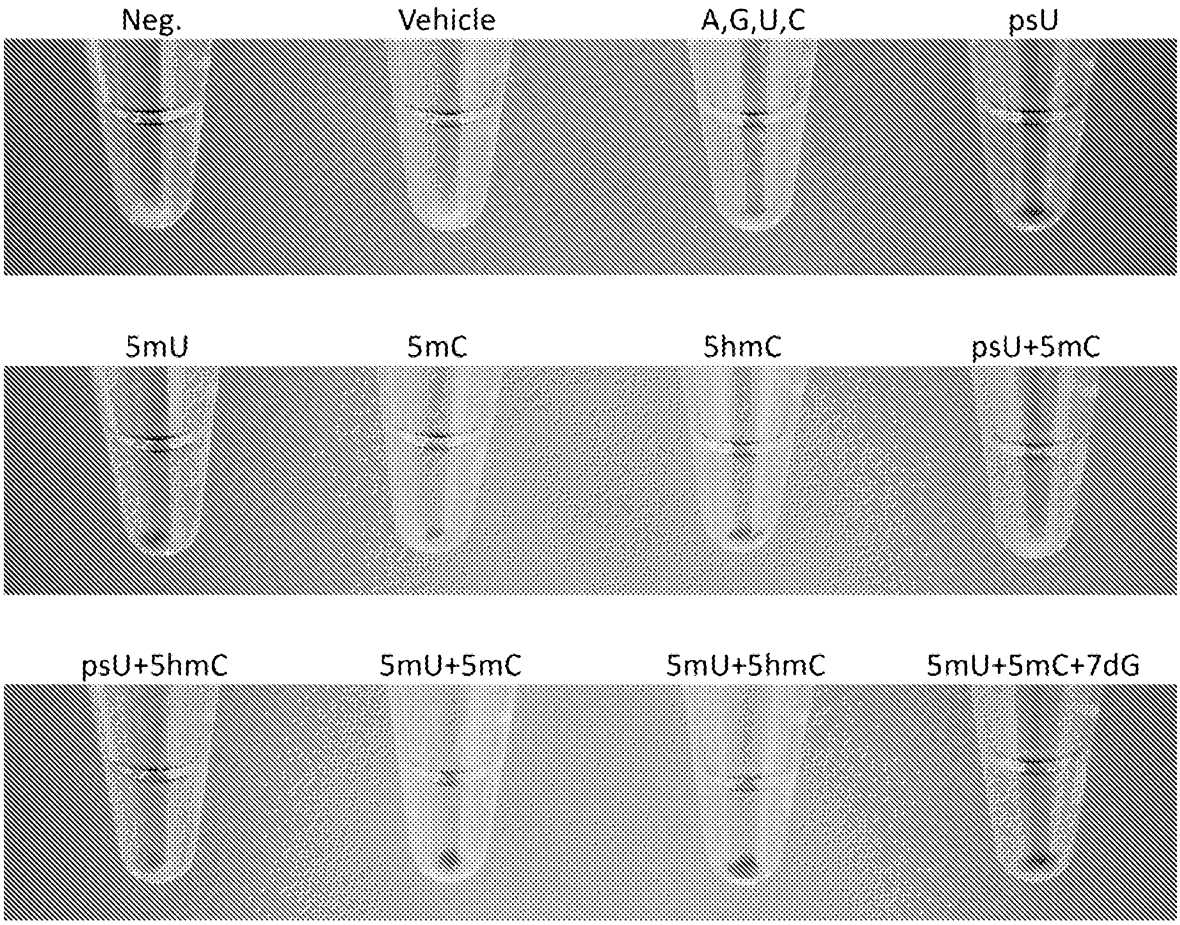


FIG. 13


Neg.
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A,G,U,C
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5mC
5hmC
psU+5mC
psU+5hmC
5mU+5mC
5mU+5hmC
5mU+5mC+7dG

FIG. 14

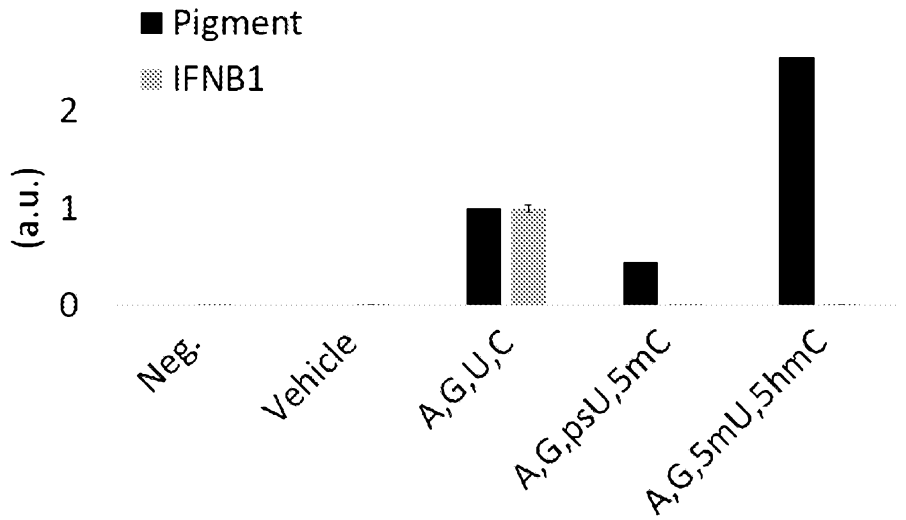

Pigment
IFNB1
(a.u.)
2
1
0
Neg.
Vehicle
A,G,U,C
A,G,psU,5mC
A,G,5mU,5hmC

FIG. 15

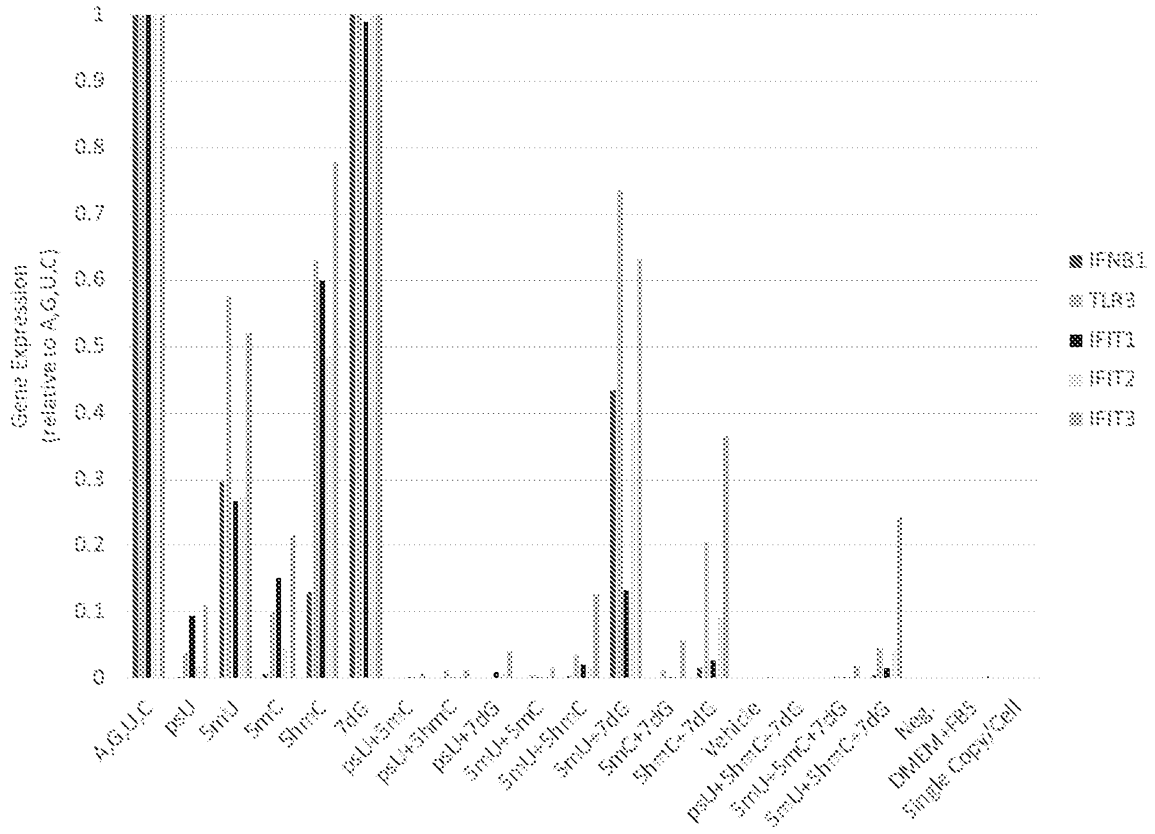

Gene Expression
(relative to A,G,U,C)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
IFNB1
TLR3
IFIT1
IFIT2
IFIT3
A,G,U,C
psU
5mU
5mC
5hmC
7dG
psU+5mC
psU+5hmC
psU+7dG
5mU+5mC
5mU+5hmC
5mU+7dG
5mC+7dG
5hmC+7dG
Vehicle
psU+5hmC+7dG
5mU+5mC+7dG
5mU+5hmC+7dG
Neg.
DMEM+FBS
Single Copy/Cell

FIG. 16

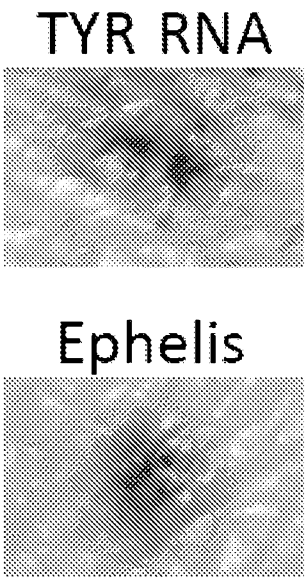

TYR RNA
Ephelis

FIG. 17

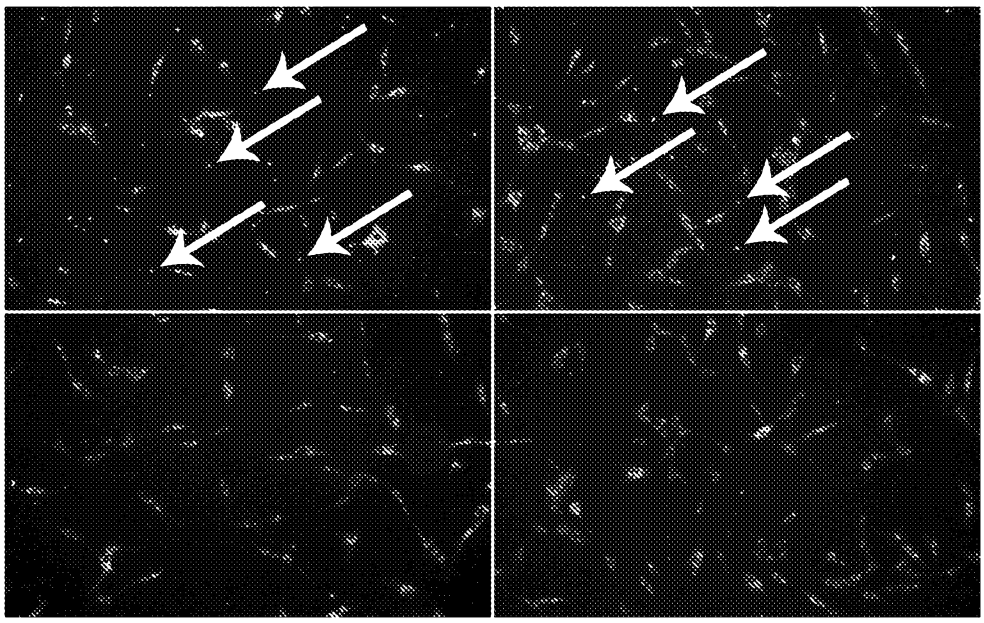
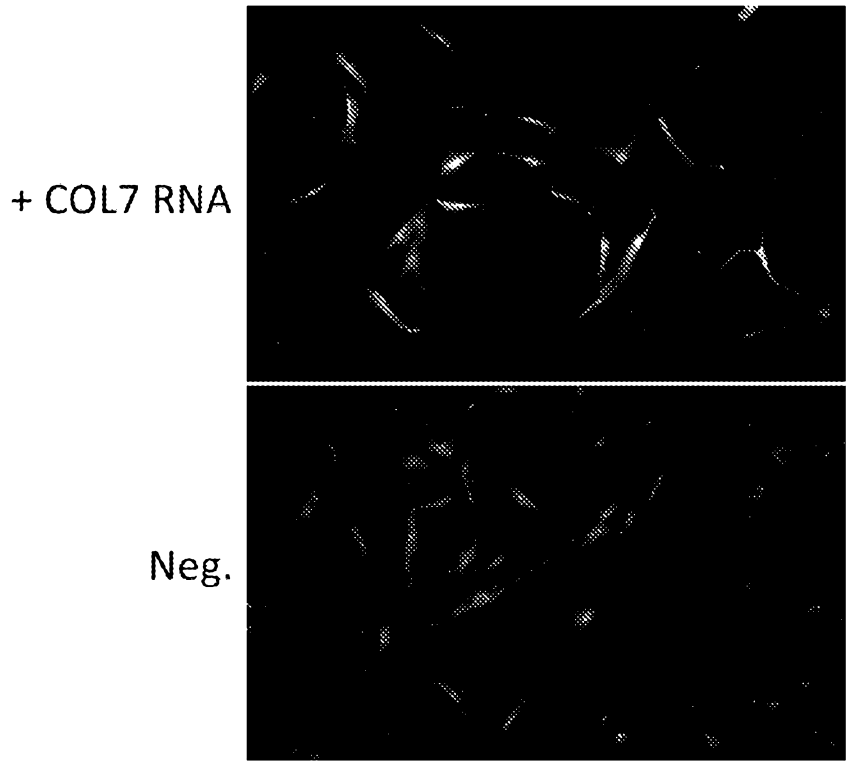



FIG. 18



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Rohde, Christopher

<120> METHODS AND PRODUCTS FOR NUCLEIC ACID PRODUCTION AND DELIVERY

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<151> 2014-01-31

<150> US 62/038,608
<151> 2014-08-18

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<151> 2014-10-28

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<170> PatentIn version 3.5

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<213> Homo sapiens

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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
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<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

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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 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


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<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
```

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<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 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
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<210> 51
<211> 140
<212> PRT
<213> Homo sapiens

<400> 51

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Met Asp Val Phe Met Lys Gly Leu Ser Lys Ala Lys Glu Gly Val Val
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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
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<210> 52
<211> 140
<212> PRT
<213> Homo sapiens

<400> 52

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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
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<210> 53
<211> 196
<212> PRT
<213> Homo sapiens

<400> 53

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> 54
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<213> Homo sapiens

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<223> Xaa can be any naturally occurring amino acid

<400> 54

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

His Gly Gly Gly
35

<210> 55
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<212> PRT
<213> Homo sapiens

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<400> 55

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
<211> 36
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<213> Homo sapiens

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<400> 56

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

His Gly Ser Gly
35

<210> 57
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<400> 57

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 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
```

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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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<213>  Homo sapiens


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            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
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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

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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 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
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            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
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100 105 110

Ile Val Gly Val Gly Lys Gln Trp Ser Gly Ala Arg Ala Leu Glu Ala
115 120 125

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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
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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
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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
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Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys
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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
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Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
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Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg

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Leu Leu Pro Val Leu Cys Gln Ala His Gly Leu Thr Pro Glu Gln Val
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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
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Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
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Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa
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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
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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
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Phe Ala Tyr Val Ser Gly Ser Phe Ser Gly Asn Tyr Lys Glu Gln
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Leu Gln Lys Phe Arg Gln Asp Thr Asn His Leu Gly Gly Ala Leu
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Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr Lys Thr Gln
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Ile Ser Tyr
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Tyr Lys Asp Asp Asp Asp Lys Met Ala Pro Lys Lys Lys Arg Lys Val
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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
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Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
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Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
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Ile Ala Ser Xaa Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg
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Leu Leu Pro Val Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu
420 425 430

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Leu Thr Pro Glu Gln Val Val Ala Ile Ala Ser Xaa Xaa Gly Gly Lys
755 760 765

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Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val Leu Cys Gln Ala
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785                 790                 795                 800

Xaa Gly Gly Lys Gln Ala Leu Glu Thr Val Gln Arg Leu Leu Pro Val
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Leu Cys Gln Ala Gly His Gly Gly Leu Thr Pro Glu Gln Val Val Ala
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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
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Leu Val Ala Leu Ala Cys Leu Gly Gly Arg Pro Ala Leu Asp Ala Val
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Lys Lys Gly Leu Pro His Ala Pro Ala Leu Ile Lys Arg Thr Asn Arg
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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
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Gly Ala Leu Glu Phe Val Lys Leu Leu Leu Leu Ala Asn Asn Tyr
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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
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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
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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 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
```

<210>  62
<211>  1366
<212>  PRT

<213> Homo sapiens

<400> 62

```
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

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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 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
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 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

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

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 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

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<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

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
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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
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<210>  97
<211>  2355
<212>  PRT
<213>  Homo sapiens

<400>  97

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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
    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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<210>  98
<211>  2330
<212>  PRT

<213> Homo sapiens

<400> 98

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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
    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
```

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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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<210> 99
<211> 2296
<212> PRT
<213> Homo sapiens

<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
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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 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

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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
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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
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```
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
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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
```

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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  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
<211>  657
<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 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
    2855                 2860                 2865

Leu Leu  His
    2870
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<211> 2912
<212> PRT
<213> Homo sapiens

<400> 135

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Met Gly Arg Arg Arg Arg Leu Cys Leu Gln Leu Tyr Phe Leu Trp Leu
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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 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
1130 1135 1140

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
1160 1165 1170

Cys Val Asn Thr Glu Gly Ser Phe Gln Cys Asp Cys Pro Leu Gly
1175 1180 1185

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
1205 1210 1215

Met Ile Gly Thr Tyr Gln Cys Ser Cys Asn Pro Gly Tyr Gln Ala
1220 1225 1230

Thr Pro Asp Arg Gln Gly Cys Thr Asp Ile Asp Glu Cys Met Ile
1235 1240 1245

Met Asn Gly Gly Cys Asp Thr Gln Cys Thr Asn Ser Glu Gly Ser
1250 1255 1260

Tyr Glu Cys Ser Cys Ser Glu Gly Tyr Ala Leu Met Pro Asp Gly
1265 1270 1275

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
1370 1375 1380

Cys Leu Asn Ile Pro Gly Ser Phe Lys Cys Ser Cys Arg Glu Gly
1385 1390 1395

Trp Ile Gly Asn Gly Ile Lys Cys Ile Asp Leu Asp Glu Cys Ser
1400 1405 1410

Asn Gly Thr His Gln Cys Ser Ile Asn Ala Gln Cys Val Asn Thr
1415 1420 1425

Pro Gly Ser Tyr Arg Cys Ala Cys Ser Glu Gly Phe Thr Gly Asp
1430 1435 1440

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
1460 1465 1470

Cys Glu Cys Glu Met Gly Phe Thr Pro Ala Ser Asp Ser Arg Ser
1475 1480 1485

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
1505 1510 1515

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
1550 1555 1560

Leu Asn Pro Thr Gly Val Gly Cys Val Asp Asn Arg Val Gly Asn

1565 1570 1575

Cys Tyr Leu Lys Phe Gly Pro Arg Gly Asp Gly Ser Leu Ser Cys
1580 1585 1590

Asn Thr Glu Ile Gly Val Gly Val Ser Arg Ser Ser Cys Cys Cys
1595 1600 1605

Ser Leu Gly Lys Ala Trp Gly Asn Pro Cys Glu Thr Cys Pro Pro
1610 1615 1620

Val Asn Ser Thr Glu Tyr Tyr Thr Leu Cys Pro Gly Gly Glu Gly
1625 1630 1635

Phe Arg Pro Asn Pro Ile Thr Ile Ile Leu Glu Asp Ile Asp Glu
1640 1645 1650

Cys Gln Glu Leu Pro Gly Leu Cys Gln Gly Gly Asn Cys Ile Asn
1655 1660 1665

Thr Phe Gly Ser Phe Gln Cys Glu Cys Pro Gln Gly Tyr Tyr Leu
1670 1675 1680

Ser Glu Asp Thr Arg Ile Cys Glu Asp Ile Asp Glu Cys Phe Ala
1685 1690 1695

His Pro Gly Val Cys Gly Pro Gly Thr Cys Tyr Asn Thr Leu Gly
1700 1705 1710

Asn Tyr Thr Cys Ile Cys Pro Pro Glu Tyr Met Gln Val Asn Gly
1715 1720 1725

Gly His Asn Cys Met Asp Met Arg Lys Ser Phe Cys Tyr Arg Ser
1730 1735 1740

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

Pro Gly Thr Cys Gln Asn Leu Glu Gly Ser Phe Arg Cys Ile Cys
2030 2035 2040

Pro Pro Gly Tyr Glu Val Lys Ser Glu Asn Cys Ile Asp Ile Asn
2045 2050 2055

Glu Cys Asp Glu Asp Pro Asn Ile Cys Leu Phe Gly Ser Cys Thr
2060 2065 2070

Asn Thr Pro Gly Gly Phe Gln Cys Leu Cys Pro Pro Gly Phe Val

2075 2080 2085

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
2105 2110 2115

Phe Asn Thr Thr Lys Ala Lys Cys Cys Cys Ser Lys Met Pro Gly
2120 2125 2130

Glu Gly Trp Gly Asp Pro Cys Glu Leu Cys Pro Lys Asp Asp Glu
2135 2140 2145

Val Ala Phe Gln Asp Leu Cys Pro Tyr Gly His Gly Thr Val Pro
2150 2155 2160

Ser Leu His Asp Thr Arg Glu Asp Val Asn Glu Cys Leu Glu Ser
2165 2170 2175

Pro Gly Ile Cys Ser Asn Gly Gln Cys Ile Asn Thr Asp Gly Ser
2180 2185 2190

Phe Arg Cys Glu Cys Pro Met Gly Tyr Asn Leu Asp Tyr Thr Gly
2195 2200 2205

Val Arg Cys Val Asp Thr Asp Glu Cys Ser Ile Gly Asn Pro Cys
2210 2215 2220

Gly Asn Gly Thr Cys Thr Asn Val Ile Gly Ser Phe Glu Cys Asn
2225 2230 2235

Cys Asn Glu Gly Phe Glu Pro Gly Pro Met Met Asn Cys Glu Asp
2240 2245 2250

Ile Asn Glu Cys Ala Gln Asn Pro Leu Leu Cys Ala Phe Arg Cys
2255 2260 2265

Met Asn Thr Phe Gly Ser Tyr Glu Cys Thr Cys Pro Ile Gly Tyr
2270 2275 2280

Ala Leu Arg Glu Asp Gln Lys Met Cys Lys Asp Leu Asp Glu Cys
2285 2290 2295

Ala Glu Gly Leu His Asp Cys Glu Ser Arg Gly Met Met Cys Lys
2300 2305 2310

Asn Leu Ile Gly Thr Phe Met Cys Ile Cys Pro Pro Gly Met Ala
2315 2320 2325

Arg Arg Pro Asp Gly Glu Gly Cys Val Asp Glu Asn Glu Cys Arg

2330 2335 2340

Thr Lys Pro Gly Ile Cys Glu Asn Gly Arg Cys Val Asn Ile Ile
2345 2350 2355

Gly Ser Tyr Arg Cys Glu Cys Asn Glu Gly Phe Gln Ser Ser Ser
2360 2365 2370

Ser Gly Thr Glu Cys Leu Asp Asn Arg Gln Gly Leu Cys Phe Ala
2375 2380 2385

Glu Val Leu Gln Thr Ile Cys Gln Met Ala Ser Ser Ser Arg Asn
2390 2395 2400

Leu Val Thr Lys Ser Glu Cys Cys Cys Asp Gly Gly Arg Gly Trp
2405 2410 2415

Gly His Gln Cys Glu Leu Cys Pro Leu Pro Gly Thr Ala Gln Tyr
2420 2425 2430

Lys Lys Ile Cys Pro His Gly Pro Gly Tyr Thr Thr Asp Gly Arg
2435 2440 2445

Asp Ile Asp Glu Cys Lys Val Met Pro Asn Leu Cys Thr Asn Gly
2450 2455 2460

Gln Cys Ile Asn Thr Met Gly Ser Phe Arg Cys Phe Cys Lys Val
2465 2470 2475

Gly Tyr Thr Thr Asp Ile Ser Gly Thr Ser Cys Ile Asp Leu Asp
2480 2485 2490

Glu Cys Ser Gln Ser Pro Lys Pro Cys Asn Tyr Ile Cys Lys Asn
2495 2500 2505

Thr Glu Gly Ser Tyr Gln Cys Ser Cys Pro Arg Gly Tyr Val Leu
2510 2515 2520

Gln Glu Asp Gly Lys Thr Cys Lys Asp Leu Asp Glu Cys Gln Thr
2525 2530 2535

Lys Gln His Asn Cys Gln Phe Leu Cys Val Asn Thr Leu Gly Gly
2540 2545 2550

Phe Thr Cys Lys Cys Pro Pro Gly Phe Thr Gln His His Thr Ala
2555 2560 2565

Cys Ile Asp Asn Asn Glu Cys Gly Ser Gln Pro Ser Leu Cys Gly
2570 2575 2580

Ala Lys Gly Ile Cys Gln Asn Thr Pro Gly Ser Phe Ser Cys Glu

2585 2590 2595

Cys Gln Arg Gly Phe Ser Leu Asp Ala Thr Gly Leu Asn Cys Glu
2600 2605 2610

Asp Val Asp Glu Cys Asp Gly Asn His Arg Cys Gln His Gly Cys
2615 2620 2625

Gln Asn Ile Leu Gly Gly Tyr Arg Cys Gly Cys Pro Gln Gly Tyr
2630 2635 2640

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
```