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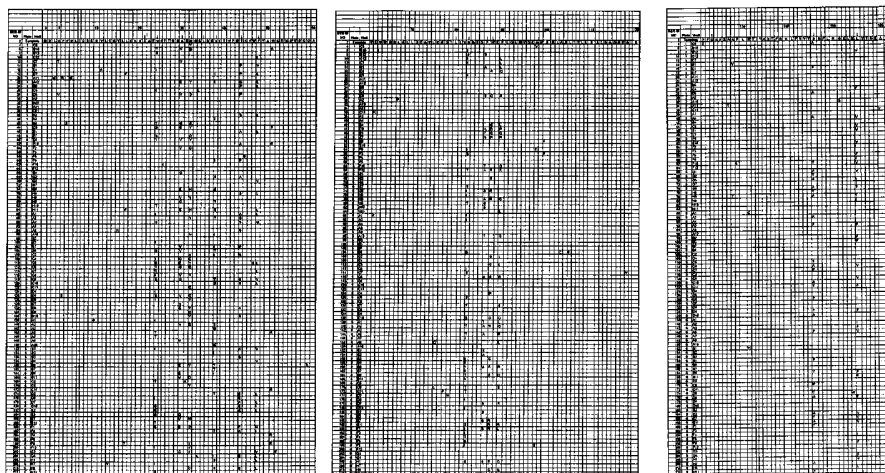
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(54) **Title:** ENHANCED VARIANTS OF ERYTHROPOIETIN AND METHODS OF USE



(57) **Abstract:** The invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin activity, or a functional fragment thereof. Also provided is a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and a moderated erythropoietin activity, or a functional fragment thereof. The invention further provides a composition containing a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, and a pharmaceutically acceptable medium.



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ENHANCED VARIANTS OF ERYTHROPOIETIN AND METHODS OF USE

BACKGROUND OF THE INVENTION

This invention relates to molecular medicine and, more specifically to erythropoietin (EPO) variant polypeptides having beneficial therapeutic properties.

Erythropoietin is a glycoprotein hormone involved in the proliferation and differentiation of bone marrow erythroid progenitor cells. In this way erythropoietin controls the number of red blood cells in the circulation and hence the oxygen-carrying capacity of the blood. The peripheral red cell count is kept constant by a controlled feedback mechanism involving oxygen supply, erythropoietin secretion and erythropoiesis. However, the system can become unbalanced in conditions such as chronic renal disease, chronic inflammation and prematurity.

Naturally occurring erythropoietin is produced by the liver during fetal life and by the kidney of adults. Chronic renal disease can result in a decrease in the amount of erythropoietin which leads to anemia. Anemia can result in many debilitating symptoms such as tiredness, lethargy, muscle fatigue, and poor exercise capability. Recombinant erythropoietin, produced by genetic engineering methods involving the expression of erythropoietin from a transformed host cell, has been used in the treatment of anemia resulting from chronic renal failure or from complications associated with chemotherapy. In addition, recombinant human erythropoietin is used as hormonal replacement therapy to correct various types of anemia and replenish the red cell count following hemorrhage or blood donation for autologous transfusion.

However, undesirable side effects of erythropoietin therapy have also been encountered. For example, increases in blood pressure and blood viscosities have been noted in some patients. Also, in some patients drastic increases in hematocrit, hemoglobin and the number of erythroid precursor cells have been observed while in other patients the increase in hematocrit is too low. For patients who respond poorly to erythropoietin, a non-physiological dose increase of erythropoietin is contraindicated because of possible immune

reactions. In addition, increasing the amount of erythropoietin can increase non-specific effects of the polypeptide. One non-specific effect of erythropoietin is the stimulation of megakaryocytes to form thrombocytes which can increase the risk of thrombosis.

5 An alternative to increasing the dosage of recombinant erythropoietin is to generate new versions of the erythropoietin polypeptide that have altered activities compared to human erythropoietin. Such altered activities can include, for example, greater or lesser potency, or a faster or slower time of onset of an erythropoietin activity.

10 Thus, there exists a need for a human erythropoietin variant polypeptide with an altered erythropoietin activity which can be used, for example, as a therapeutic agent. The present invention satisfies this need and provides related advantages as well.

SUMMARY OF THE INVENTION

15 The invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin activity, or a functional fragment thereof. Also provided is a human erythropoietin polypeptide variant containing a human erythropoietin
20 amino acid sequence having an amino acid difference in two or more different Epo-modification regions and a moderated erythropoietin activity, or a functional fragment thereof. The invention further provides a composition containing a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50,
25 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, and a pharmaceutically acceptable medium.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a chart containing erythropoietin polypeptide variants with SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 218, 220, 222, 224 referred to herein for convenience as SEQ ID NOS: 2-212 and 218-224 EVEN. The top line shows the amino acid sequence of human erythropoietin polypeptide variant SEQ ID NO:2. For the remaining erythropoietin polypeptide variants, an open box indicates the same amino acid as in SEQ ID NO:2 while a filled box indicates the single letter code of an amino acid difference from SEQ ID NO:2.

Figure 2 shows a chart containing erythropoietin polypeptide variants with SEQ ID NOS:214, 218, 220, 222 and 224, following the drawing indications shown set forth above for Figure 1.

DETAILED DESCRIPTION OF THE INVENTION

This invention is directed to a human erythropoietin polypeptide variant or variants having an altered erythropoietin activity. These human erythropoietin polypeptide variants are advantageous in that can have desirable features when compared to the human erythropoietin polypeptide. For example, the human erythropoietin polypeptide variants of the invention can have increased or decreased erythroid precursor proliferation activity compared to the human erythropoietin polypeptide shown as SEQ ID NO:214. In addition, for example, the human erythropoietin polypeptide variants of the invention can be faster-acting or slower-acting when compared to the human erythropoietin polypeptide. Erythropoietin polypeptide variants of differing levels of activity or times to reach a maximal level of activity can be useful in the clinic in order to customize the level of erythropoietin activity to the needs of a particular individual. For example, an individual who does not respond to recombinant human

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erythropoietin therapy, or who responds sub-optimally, can respond to therapy with a more active human erythropoietin polypeptide variant. The invention therefore provides human erythropoietin polypeptide variants having altered erythropoietin activities which can be used therapeutically.

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Even when therapy with recombinant human erythropoietin (rHuEPO) or a variant of rHuEPO called novel erythropoiesis-stimulating protein (NESP) (also known as darbepoetin or AranespTM), has been effective for some individuals in the clinic, adverse side-effects of these therapies have been reported. For example, stimulating megakaryocytes to form thrombocytes is a side effect of erythropoietin therapy which occurs in some individuals. In this case a risk of thrombosis can arise during the treatment with erythropoietin, and the treatment must be stopped immediately. Here a higher specificity erythropoietin polypeptide variant would be desirable.

In addition, in a published study adverse events occurring in greater than 10% of individuals in either the NESP or rHuEO groups were hypertension, peripheral oedema, fatigue, diarrhea, headache, nausea and pruritus (Locatelli et al., Kidney International 60:741-747 (2001)). Some of these events can be attributed to concurrent medical conditions, however adverse events considered to be treatment-related were reported. Hypertension was the most common of these events. Another side-effect that has been reported in connection with certain forms of recombinant erythropoietin therapy is red-cell aplasia. Red-cell aplasia can result in the generation of antibodies in a subject that neutralize not only the drug, but also the individual's own natural erythropoietin. Therefore, there is a need for human erythropoietin polypeptide variants having altered erythropoietin activities which would reduce the number of side-effects of erythropoietin therapy.

In one embodiment, the invention is directed to a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin activity, or a functional fragment thereof. In another embodiment, the invention is directed to a human

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erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and a moderated erythropoietin activity, or a functional fragment thereof. In a further embodiment, the invention is directed to a human
5 erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220,
10 222, 224, or a functional fragment thereof.

As used herein, a "variant" when used in reference to a human erythropoietin polypeptide is intended to mean an erythropoietin polypeptide having a non-naturally occurring amino acid sequence that differs at one or more amino acid positions from the sequence of human erythropoietin. Human
15 erythropoietin, as used herein, is the polypeptide shown in SEQ ID NO:214. The amino acid sequence shown in SEQ ID NO:214 is derived from the sequence for human erythropoietin referenced in GenBank by accession number NP_000790. The only difference is the absence of a 27 amino acid leader sequence in SEQ ID NO:214 compared to accession number NP_000790.

20 Variants differ from a human erythropoietin polypeptide by some detectable structural property such as a difference in at least one amino acid residue or a difference introduced by the modification of an amino acid such as the addition of a chemical functional group. A difference in an amino acid at a particular position also includes, for example, the insertion or deletion of an amino
25 acid at that position. A human polypeptide variant can contain, for example, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 amino acid differences compared to human erythropoietin. In addition, for example, a human polypeptide variant can contain at least 1%, at least 2%, at least 3%, at least 4%, at least 5% or at least 6% amino acid differences compared to human erythropoietin.

30 As understood by one skilled in the art, a human erythropoietin polypeptide variant can contain additional sequences such as non-homologous

sequences. For example, a human erythropoietin polypeptide variant can contain an epitope tag at the amino or carboxy termini of the polypeptide. Also, for example, a human erythropoietin polypeptide variant can be fused to other polypeptides such as glutathione S-transferase (GST).

5 As used herein the term "Epo-modification region" is intended to mean a region of the human erythropoietin polypeptide SEQ ID NO:214 that is associated with or has an activity directed to the carbohydrate content of the polypeptide, aggregation properties of the polypeptide, or erythropoietin receptor (EPOR) binding by the polypeptide as described herein. For example, an Epo-
10 modification region can contain amino acids associated with or having an activity directed to the carbohydrate content of erythropoietin described herein as, A30, H32, P87, W88, P90; amino acids associated with or having an activity directed to aggregation of erythropoietin described herein as N24, N38, N83; and amino acids associated with or having an activity directed to binding to EPOR described herein
15 as T44, F48, N147, and L155.

The term "Epo-modification region" can be sub-divided into three different groups; the carbohydrate content region, the aggregation region, and the EPOR binding region. Therefore, the term "two or more different Epo-modification regions" refers to two or more of these three different Epo-
20 modification regions. As described above, the carbohydrate content region includes amino acids associated with or having an activity directed to the carbohydrate content of erythropoietin such as, A30, H32, P87, W88, P90. The aggregation region includes amino acids associated with or having an activity directed to aggregation of erythropoietin such as N24, N38, N83. The EPOR
25 binding region includes amino acids associated with or having an activity directed to binding to EPOR such as T44, F48, N147, and L155.

As used herein the term "amino acid difference" in reference to an Epo-modification region is intended to mean a difference between the amino acid sequence of a human erythropoietin polypeptide variant in the identified Epo-
30 modification regions when compared to the amino acid sequence of human erythropoietin SEQ ID NO:214. A difference in amino acid sequence includes,

for example, the substitution of one amino acid for another amino acid or the insertion or deletion of an amino acid. For example, a human erythropoietin polypeptide variant referenced herein as SEQ ID NO:90 has an amino acid difference in an Epo-modification region associated with aggregation (amino acid N24 is changed to S24) and an amino acid difference in an Epo-modification region associated with EPOR binding (amino acid T44 is changed to S44). SEQ ID NO:90 also contains a third mutation in an Epo-modification region associated with EPOR binding where amino acid F48 is changed to M48. These amino acid differences in Epo-modification regions also are present in versions of SEQ ID NO:90 that include a leader sequence directing secretion in mammalian cells. These versions are described further below and referenced herein as SEQ ID NOS:222 and 224. A difference in amino acid sequence can also include, for example, the inclusion of a modified amino acid instead of the naturally occurring amino acid at a particular location.

As shown in Figure 1, the sequence used as a template for the generation of erythropoietin polypeptide variants herein, disclosed as SEQ ID NO:2, contains no amino acid differences in Epo-modification regions compared to the amino acid sequence of human erythropoietin SEQ ID NO:214. The polypeptide referenced as SEQ ID NO:2 does have amino acid differences compared to SEQ ID NO:214 outside of the Epo-modification regions, for example the substitution of an alanine at amino acid position 79 in SEQ ID NO:2 compared to threonine in SEQ ID NO:214.

As used herein, the term "functional fragment" is intended to mean a portion of a full-length human erythropoietin polypeptide variant or nucleic acid molecule where the portion retains an erythropoietin activity. For example, a functional fragment of a human erythropoietin polypeptide variant can be a fragment with the ability to increase erythroid precursor proliferation. Fragments can include, for example, amino terminal, carboxyl terminal, or internal deletions of a human erythropoietin polypeptide variant. For example, a fragment can contain at least about 25, 50, 75, 100, 125, or 150 contiguous or non-contiguous

amino acid residues of a human erythropoietin polypeptide variant where the fragment retains an erythropoietin activity.

As used herein, the term "functional fragment" when used in reference to an antibody is intended to refer to a portion of an antibody which still
5 retains some or all of the erythropoietin or erythropoietin variant binding activity. Such functional fragments can include, for example, antibody functional fragments such as Fv, single chain Fv (scFv), Fab, F(ab'), F(ab)2, F(ab')2, and minibody. Other functional fragments can include, for example, heavy or light chain polypeptides, variable region polypeptides, CDR polypeptides, single
10 domain antibodies, or portions thereof so long as such functional fragments retain binding activity.

As used herein, an "erythropoietin activity" is intended to mean an activity associated with a human erythropoietin polypeptide. In addition, the term an "erythropoietin activity" includes temporal qualities of the activity such as the
15 time it takes to reach a maximal level of an erythropoietin activity or the time of onset of an erythropoietin activity. An erythropoietin activity can be a directly associated with a human erythropoietin polypeptide or indirectly associated with a human erythropoietin polypeptide. An activity directly associated with a human erythropoietin polypeptide can include, for example, the induction of erythroid
20 precursor proliferation or the induction of erythroid precursor cell differentiation. An activity indirectly associated with a human erythropoietin polypeptide can include a result of an activity directly associated with an erythropoietin polypeptide such as, for example, an increased number of erythrocytes in an individual, an increased hematocrit in an individual, or reduction in anemia in an
25 individual.

An erythropoietin activity can be an activity that is measured, for example, *in vitro* or *in vivo*. For example, an erythropoietin activity such as the induction of erythroid precursor cell differentiation can be measured *in vitro* using a bioassay in a cell line or *in vivo* by measuring hematocrit in a test animal.
30 Different properties of an erythropoietin polypeptide can affect activity *in vivo*

compared to *in vitro*. For example, the plasma half-life of a polypeptide can affect activity *in vivo*, but this property can have less effect on activity *in vitro*.

As used herein the term “enhanced erythropoietin activity” is intended to mean an increase in an erythropoietin activity or a faster time of an erythropoietin activity compared to the same activity or time of activity from human erythropoietin SEQ ID NO:214. For example, an enhanced erythropoietin activity can be an increase in erythroid precursor proliferation or a faster time to reach a maximal level of erythroid precursor proliferation. An enhanced erythropoietin activity can be measured, for example, *in vitro* or *in vivo*.

As understood by one skilled in the art, different preparations or sources of human erythropoietin SEQ ID NO:214 are available. For example, a source of human erythropoietin can be a commercially available form such as is available from Amgen. In addition, for example, a source of human erythropoietin can be the World Health Organization Second International Reference Preparation.

Furthermore, a polypeptide variant with essentially identical activity as human erythropoietin referenced as SEQ ID NO:214 can be used as a surrogate for human erythropoietin in subsequent assays. For example, as disclosed herein, the erythroid precursor proliferation activity of the polypeptide variant referenced as SEQ ID NO:2 is essentially identical to that of human erythropoietin obtained commercially from Amgen. Therefore, comparison of human erythropoietin polypeptide variants to the SEQ ID NO:2 polypeptide variant can be used to determine whether a human erythropoietin polypeptide variant has altered erythrocyte precursor proliferation activity compared to human erythropoietin.

As disclosed herein, specific examples of a human erythropoietin polypeptide variant with an enhanced activity are the polypeptides referenced as SEQ ID NOS:90, 222, 224 (Figures 1 and 2). For example, the polypeptides referenced as SEQ ID NOS:90, 222, 224 show increased activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID

NO:2 (Table 1). Another example of a human erythropoietin polypeptide variant disclosed herein with an enhanced activity is the polypeptide referenced as SEQ ID NO:96 (Figure 1). For example, the polypeptide referenced as SEQ ID NO:96 shows a faster time to reach a maximal level of activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID NO:2 (Table 1).

As used herein the term "moderated erythropoietin activity" is intended to mean a decrease in an erythropoietin activity or a slower time of an erythropoietin activity compared to the same activity or time of activity from human erythropoietin SEQ ID NO:214. For example, a moderated erythropoietin activity can be a decrease in erythroid precursor proliferation or a slower time to reach a maximal level of erythroid precursor proliferation. A moderated erythropoietin activity can be measured, for example, *in vitro* or *in vivo*.

As disclosed herein, a specific example of a human erythropoietin polypeptide variant with a moderated activity is the polypeptide referenced as SEQ ID NO:198 (Figure 1). For example, the polypeptide referenced as SEQ ID NO:198 shows decreased activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID NO:2 (Table 1). Another example of a human erythropoietin polypeptide variant disclosed herein with a moderated activity is the polypeptide referenced as SEQ ID NO:8 (Figure 1). For example, the polypeptide referenced as SEQ ID NO:8 shows a slower time to reach a maximal level of activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID NO:2 (Table 1).

In addition, a human erythropoietin polypeptide variant can have an enhanced activity in regard to one type of activity and a moderated activity in regard to another type of activity. For example, the polypeptide referenced as SEQ ID NO:212 shows increased activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID NO:2, but a slower time to reach a maximal level of activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID NO:2 (Table 1). Another example of a human erythropoietin polypeptide variant disclosed herein with both

an enhanced and moderated activity is the polypeptide referenced as SEQ ID NO:70 (Figure 1). For example, the polypeptide referenced as SEQ ID NO:70 shows a decreased activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID NO:2, but a faster time to reach a maximal level of activity in an erythrocyte precursor proliferation assay compared to the polypeptide referenced as SEQ ID NO:2 (Table 1).

As used herein, "effective amount" is intended to mean an amount sufficient to produce a desired effect. For example, when used in reference to a composition containing a human erythropoietin polypeptide variant it is intended to mean an amount of the composition sufficient to induce a therapeutic effect. For example, an effective amount of a composition, such as a pharmaceutical composition, containing a human erythropoietin polypeptide variant can be a range of protein concentrations correlated to the weight of an individual. For example, an effective amount can be at least 0.01 mg/kg, at least 0.05 mg/kg, at least 0.10 mg/kg, at least 0.25 mg/kg, at least 0.50 mg/kg, at least 0.75 mg/kg, at least 1.0 mg/kg, at least 1.5 mg/kg, at least 2.0 mg/kg, or more of a composition.

As used herein, the term "neurological condition" is intended to mean a pathological condition affecting neuronal or glial cells in the nervous system. Pathological conditions affecting neuronal or glial cells include ischemia, apoptosis, necrosis, oxidative or free radical damage, and excitotoxicity. For example, neurological conditions include cerebral and spinal ischemia, acute brain injury, spinal cord injury, retinal disease, and neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and ALS.

Human erythropoietin is an acidic glycoprotein hormone with a molecular mass of 34 kD. As a regulator of red cell production, it functions to promote erythroid proliferation and differentiation and to initiate hemoglobin synthesis. Information regarding erythropoietin can be found, for example, at the National Center for Biotechnology Information website at OMIM entry number 133170 (URL: www.ncbi.nlm.nih.gov/htbin-post/Omim/dispMim?133170).

The human erythropoietin cDNA was first cloned in *E. coli* by Lee-Huang (Lee-Huang, S. Proc. Nat. Acad. Sci. 81:2708-2712 (1984); see also U.S. Pat. No. 4,703,008). McDonald et al., and Shoemaker and Mitsock cloned the mouse gene and the latter investigators showed that the nucleotide and amino acid
5 sequence of erythropoietin are about 80% conserved between human and mouse (McDonald, et al. Mol. Cell. Biol. 6:842-848 (1986); Shoemaker and Mitsock, Mol. Cell. Biol. 6: 849-858 (1986)). This is a higher order of conservation than found in related polypeptides such as various interferons, interleukin-2, and GM-CSF. In addition, Sherwood and Shouval described a human renal carcinoma cell
10 line that continuously produces erythropoietin (Sherwood and Shouval, Proc. Nat. Acad. Sci. 83:165-169 (1986)).

The erythropoietin gene has 5 exons that code for a 193-amino acid pro-polypeptide. A 27-amino acid leader sequence is cleaved off the amino terminus of the pro-polypeptide, yielding the functional 166-amino acid
15 polypeptide. However, recombinant human erythropoietin expressed in Chinese hamster ovary cells contains only 165 amino acids, having lost arg166. The mechanism for this is undefined, and whether erythropoietin circulating in the plasma also lacks arg166 is not known. Both the nucleotide and amino acid sequences of erythropoietin are highly conserved among mammals.

20 Law et al. assigned erythropoietin to chromosome 7 by Southern blot analysis of DNA from human/Chinese hamster cell hybrids with a cDNA clone for the entire coding region of the gene (Law et al., Proc. Nat. Acad. Sci. 83:6920-6924 (1986)). Further localization to 7q11-q22 was achieved by *in situ* hybridization. They found a restriction fragment length polymorphism (RFLP)
25 with a frequency of about 20% in a Chinese population. Using somatic cell hybrid analysis, Watkins et al., placed erythropoietin on the proximal half of 7q, closely linked to COL1A2 (see OMIM Entry 120160) and to DNA markers linked to CF (see OMIM entry 219700). Because of the close linkage of erythropoietin to COL1A2 and markers linked to CF, it can be justified to narrow the
30 assignment of erythropoietin to 7q21-q22 (Watkins, et al., Cytogenet. Cell Genet. 42:214-218 (1986)). By *in situ* hybridization and genetic analysis using RFLPs in

interspecific mouse backcross DNAs, Lacombe et al. demonstrated that erythropoietin is located on chromosome 5 in the mouse (Lacombe et al., (Letter) Blood 72:1440-1442 (1988)).

Synthesis of erythropoietin in the kidney and liver in response to hypoxia depends on both protein synthesis and heme synthesis. Goldberg et al. proposed a model in which a ligand-dependent conformational change in a heme protein accounts for the mechanism by which hypoxia as well as cobalt and nickel stimulates the production of erythropoietin (Goldberg et al., Science 242:1412-1415 (1988)). Semenza et al. generated transgenic mice containing the human erythropoietin gene and found increased erythropoietin mRNA expression not only in liver and kidney, but in all other transgenic tissues analyzed (Semenza et al., (Abstract) Am. J. Hum. Genet. 45 (suppl.):A116 only (1989); Semenza et al., Proc. Nat. Acad. Sci. 86:2301-2305 (1989)). The mice were polycythemic, with increased erythroid precursors in hematopoietic tissues and increased erythrocytic indices in peripheral blood. From further studies in these transgenic mice, Semenza et al. concluded that different DNA sequences flanking the erythropoietin gene control liver versus kidney expression of the gene and that some of these sequences are located 3-prime to the gene.

Erythropoiesis occurs in 2 distinct waves during embryogenesis: the primitive wave in the extraembryonic yolk sac followed by the definitive wave in the fetal liver and spleen. Even though progenitors for both cells types are present in the yolk sac blood islands, only primitive cells are formed in the yolk sac during early embryogenesis. Lee et al. presented results that led them to propose that erythropoietin expression and the resultant erythropoietin receptor activation regulate the timing of the definitive wave (Lee et al., Blood 98:1408-1415 (2001)). They demonstrated that erythropoietin and EPOR gene expression are temporally and spatially segregated: though EPOR is expressed early (embryonic days 8.0-9.5) in the yolk sac blood islands, no erythropoietin expression could be detected in this extraembryonic tissue. Only at a later stage can Erythropoietin expression be detected intraembryonically, and the onset of erythropoietin expression correlates with the initiation of definitive erythropoiesis.

By 'knocking in' a constitutively active form of EPOR, R129C, they demonstrated further that the activation of the EPOR signaling pathway can lead to earlier onset of definitive erythropoiesis in the yolk sac. The observations provided insight into the *in vivo* mechanism by which two erythroid progenitor populations can coexist in the yolk sac yet always differentiate successively during embryogenesis.

Eschbach et al. demonstrated the effectiveness of recombinant human erythropoietin in treating the anemia of end-stage renal disease (Eschbach et al., New Eng. J. Med. 316:73-78 (1987)). Recombinant human erythropoietin has also been approved for the treatment of anemia associated with cancer, HIV infection, and use in the surgical setting to decrease the need for allogeneic blood transfusions. In addition to its role as a kidney cytokine regulating hematopoiesis, erythropoietin is also produced in the brain after oxidative or nitrosative stress. The role of erythropoietin in neurological conditions will be discussed further below.

Site-directed mutagenesis studies of human erythropoietin have identified several regions that are required for activity. For example, Elliot et al., have identified four regions to be important for bioactivity: amino acids 11 to 15, 44 to 51, 100 to 108, and 147 to 151 (Elliott et al., Blood 89:493-502 (1997)). Several mutants have been generated that have reduced or no activity when compared to human erythropoietin, however fewer mutants have been generated that have increased activity.

One mutant form of erythropoietin with enhanced activity *in vivo* is novel erythropoiesis-stimulating protein (NESP). The amino acid sequence of NESP differs from that of human erythropoietin at 5 positions (Ala30Asn, His32Thr, Pro87Val, Trp88Asn, and Pro90Thr) allowing for additional oligosaccharide attachment at asparagine residues at positions 30 and 88 (Elliott et al., Blood 96:82a (2000)). NESP is distinct from erythropoietin in that it has additional sialic acid which has been shown to confer an increased terminal half-life in animal models, patients with chronic renal failure, and cancer patients receiving multiple cycles of chemotherapy (Macdougall, et al., J. Am. Soc.

Nephrol. 10:2392-2395 (1999)). In studies of 89 patients with non-myeloid malignancies, Smith et al. found that NESP was tolerated, with response rates ranging from 61 to 83%, depending on dosage (Smith et al., Brit. J. Cancer 84:24-30 (2001)).

5 One way to increase the activity of erythropoietin *in vivo*, is to increase the plasma half-life of the polypeptide *in vivo*. This can be accomplished, for example, by increasing the size of the polypeptide. For example, erythropoietin monomers can be chemically modified to form dimers and trimers. Indeed, dimerized and trimerized forms of human erythropoietin
10 have been found to have increased plasma half-life and increased *in vivo* activity (Sytkowski et al., Proc. Natl. Acad. Sci. USA 95:1184-1188 (1998)).

 As disclosed herein, several human erythropoietin polypeptide variants were generated and tested for erythropoietin activities. Mutations were targeted to Epo-modification regions which include amino acids associated with
15 carbohydrate content, aggregation, and EPOR binding properties of erythropoietin (see Example I). In addition, mutations outside of Epo-modification regions were generated. Several of the human erythropoietin polypeptide variants of the invention demonstrated increase or decreased activity in an erythroid precursor proliferation assay (see Example II). In addition, several of the erythropoietin
20 polypeptide variants of the invention demonstrated a faster or slower time to reach a maximal level of erythroid precursor proliferation activity.

 In one embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification
25 regions and an enhanced erythropoietin activity, or a functional fragment thereof.

 The invention additionally includes the use of synthetic polypeptides and peptidomimetics of the disclosed human erythropoietin polypeptide variants. Peptidomimetics include chemically modified peptides, peptide-like molecules containing non-naturally occurring amino acids, and
30 peptoids, which are peptide-like molecules resulting from oligomeric assembly of

N-substituted glycines. Peptidomimetics useful in the invention include, for example, peptide-like molecules which contain a constrained amino acid, a non-peptide component that mimics peptide secondary structure, or an amide bond isostere. See, for example, Goodman and Ro, Peptidomimetics for Drug Design, 5 in "Burger's Medicinal Chemistry and Drug Discovery" Vol. 1 (ed. M.E. Wolff; John Wiley & Sons 1995), pages 803-861.

The human erythropoietin polypeptide variants, or functional fragments thereof, of the invention can be generated using any of several methods known in the art. Methods for efficient synthesis and expression of populations 10 of mutated polypeptides synthesized using oligonucleotide-directed mutagenesis can be performed, for example, as described in Wu et al., J. Mol. Biol., 294:151-162 (1999) and Kunkel, Proc. Natl. Acad. Sci. USA, 82:488-492 (1985) which are incorporated herein by reference. Also, for example, single or multiple amino acids mutations can be generated using oligonucleotides that code for the 15 mutated amino acid(s) such as utilized in PCR based site-directed mutagenesis (for example, QuikChange TM, Stratagene). Oligonucleotide-directed mutagenesis is a well known and efficient procedure for systematically introducing mutations, independent of their phenotype and is, therefore, suited for directed evolution approaches to protein engineering. The methodology is 20 flexible, permitting precise mutations to be introduced without the use of restriction enzymes, and is relatively inexpensive.

Populations of changed polypeptides can also be generated using gene shuffling. Gene shuffling or DNA shuffling is a method that generates diversity by recombination as described, for example, in Stemmer, Proc. Natl. Acad. Sci. USA 91:10747-10751 (1994); Stemmer, Nature 370:389-391 (1994); 25 Cramer et al., Nature 391:288-291 (1998); Stemmer et al., U.S. Patent No. 5,830,721, which are incorporated herein by reference. Gene shuffling or DNA shuffling is a method using *in vitro* homologous recombination of pools of selected mutant genes. For example, a pool of point mutants of a particular gene 30 can be used. The genes are randomly fragmented, for example, using DNase, and reassembled by PCR. If desired, DNA shuffling can be carried out using

homologous genes from different organisms to generate diversity (Cramer et al., *supra*, 1998). The fragmentation and reassembly can be carried out, for example, in multiple rounds, if desired. The resulting reassembled genes are a population of variants that can be used in the invention.

5 Simultaneous incorporation of all of the encoding nucleic acids and all of the selected amino acid position changes can be accomplished by a variety of methods known to those skilled in the art, including for example, recombinant and chemical synthesis. Simultaneous incorporation can be accomplished by, for example, chemically synthesizing the nucleotide sequence for the region and
10 incorporating at the positions selected for harboring variable amino acid residues a plurality of corresponding amino acid codons.

One method well known in the art for rapidly and efficiently producing a large number of alterations in a known amino acid sequence or for generating a diverse population of variable or random sequences is known as
15 codon-based synthesis or mutagenesis. This method is the subject matter of U.S. Patent Nos. 5,264,563 and 5,523,388 and is also described in Glaser et al. *J. Immunology* 149:3903 (1992), all of which are incorporated herein by reference. Variations to this synthesis method also exist and include, for example, the synthesis of predetermined codons at desired positions and the biased synthesis of
20 a predetermined sequence at one or more codon positions. Other methods well known in the art for producing a large number of alterations in a known amino acid sequence or for generating a diverse population of variable or random sequences include, for example, degenerate or partially degenerate oligonucleotide synthesis. Codons specifying equal mixtures of all four nucleotide monomers,
25 represented as NNN, results in degenerate synthesis. Whereas partially degenerate synthesis can be accomplished using, for example, the NNG/T codon.

The human erythropoietin polypeptide variants of the invention can be generated from corresponding nucleic acid molecules that encode the erythropoietin polypeptide variants. For example, the nucleic acid molecules
30 disclosed herein as SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71,

73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 5 209, 211, 217, 219, 221, 223, can be used to generate human erythropoietin polypeptide variants of the invention. This group of nucleic acid molecules will be referred to herein for convenience as SEQ ID NOS: 1-211 and 217-223 ODD. The nucleic acid molecules of the invention can be produced by any method of nucleic acid synthesis known to those skilled in the art. Such methods include, for 10 example, chemical synthesis, recombinant synthesis, enzymatic polymerization and combinations thereof. These and other synthesis methods are well known to those skilled in the art.

For example, methods for synthesizing oligonucleotides can be found described in, for example, Oligonucleotide Synthesis: A Practical 15 Approach, Gate, ed., IRL Press, Oxford (1984); Weiler et al., Anal. Biochem. 243:218 (1996); Maskos et al., Nucleic Acids Res. 20(7):1679 (1992); Atkinson et al., Solid-Phase Synthesis of Oligodeoxyribonucleotides by the Phosphitetriester Method, in Oligonucleotide Synthesis 35 (M.J. Gait ed., 1984); Blackburn and Gait (eds.), Nucleic Acids in Chemistry and Biology, Second Edition, New York: 20 Oxford University Press (1996), and in Ansubel et al., Current Protocols in Molecular Biology, John Wiley and Sons, Baltimore, MD (1999).

Recombinant and enzymatic synthesis, including polymerase chain reaction and other amplification methodologies can be found described in, for example, Sambrook et al., Molecular Cloning: A Laboratory Manual, Third Ed., 25 Cold Spring Harbor Laboratory, New York (2001) and in Ansubel et al., (1999), supra. Solid-phase synthesis methods for generating arrays of oligonucleotides and other polymer sequences can be found described in, for example, Pirrung et al., U.S. Pat. No. 5,143,854 (see also PCT Application No. WO 90/15070), Fodor et al., PCT Application No. WO 92/10092; Fodor et al., Science (1991) 30 251:767-777, and Winkler et al., U.S. Pat No. 6,136,269; Southern et al. PCT Application No. WO 89/10977, and Blanchard PCT Application No. WO

98/41531. Such methods include synthesis and printing of arrays using micropins, photolithography and ink jet synthesis of oligonucleotide arrays.

Methods for synthesizing large nucleic acid polymers by sequential annealing of oligonucleotides can be found described in, for example, in PCT application No. WO 99/14318 and in U.S. Patent No. 6,521,427, both to Evans and also described briefly below. Methods for automated synthesis and assembly similarly can be found described, for example, in the above patent publications as well as in WO 02/081490A2. These methods provide the ability to rapidly produce large polypeptide libraries with directed changes.

10 The design and computer synthesis of the human erythropoietin polypeptide variants can be performed by sequentially combining fragments of the complete gene, for example, in a 5' to 3' direction with overlapping oligonucleotides so that the complete gene is assembled. Assembly of the complete gene is accomplished by first electronically parsing the gene sequence
15 into smaller oligonucleotide sequences (fragments) that can be more efficiently synthesized. The electronic parsing is performed for both the sense and complementary antisense strands of the full gene sequence. Parsing also is performed by maintaining partial complementarity between the 5' terminus of either the sense or antisense strand and the 3' terminus of its corresponding
20 complementary sequence so that adjacent oligonucleotides can be annealed with a complementary oligonucleotide to form an overlapping oligonucleotide assembly for both strands that span the gene. The size of each parsed oligonucleotide can vary, but generally, will be between about 50-100 nucleotides (nt) in length with an about 50% overlap between complementary sense and antisense strands. For
25 example, the oligonucleotides can be parsed using ParseOligoTM, a proprietary computer program that optimizes nucleic acid sequence assembly. Optional steps in sequence assembly can include identifying and eliminating sequences that can give rise to hairpins, repeats or other difficult sequences. Additionally, the algorithm can first direct the synthesis of coding regions for each gene to
30 correspond to a desired codon preference.

Following parsing into two sets of overlapping, partially complementary oligonucleotides, which represent the complete gene, the oligonucleotides are then synthesized. In this regard, the computer output of the parsed set of oligonucleotides for both the sense and antisense strand of the gene
5 can be transferred to oligonucleotide synthesizer driver software. The synthesis of sequences of about 25 to 150 nt in length can be manufactured and assembled using the array synthesizer system and can be used without further purification. For example, two 96-well plates containing 100 nt oligonucleotides can yield a 9600 bp fragment of a gene cassette. Once synthesized, the individual
10 oligonucleotides can be maintained in the original plates or transferred to new multi-well format plates for oligonucleotide assembly.

Assembly can be accomplished using, for example, robotics or microfluidics well known in the art for manipulating large numbers of oligonucleotide samples. Robotics and microfluidics allow synthesis and
15 assembly to be performed rapidly and in a highly controlled manner. Such methods are described, for example, in WO 99/14318 and in U.S. Application Serial Nos. 60/262,693 and 09/922,221.

For example, oligonucleotide parsing from the genome sequence designed in the computer can be programmed for synthesis where sense and
20 antistrands are placed in alternating wells of an array. Following synthesis in this format, the 12 row sequences of the gene are directed into a pooling manifold that systematically pools, for example, three wells into reaction vessels forming the triplex structure. Following temperature cycling for annealing and ligation, four sets of annealed triplex oligonucleotides are pooled into 2 sets of 6
25 oligonucleotide products, then 1 set of 12 oligonucleotide products. Each row of the synthetic array is associated with a similar manifold resulting in the first stage of assembly of 8 sets of assembled oligonucleotides representing 12 oligonucleotides each. The second manifold pooling stage is controlled by a single manifold that pools the 8 row assemblies into a single complete assembly.
30 Passage of the oligonucleotide components through the two manifold assemblies (the first 8 and the second single) results in the complete assembly of all 96

oligonucleotides from the array. The assembly module of Genewriter™ can include a complete set of 7 pooling manifolds produced using microfabrication in a single plastic block that sits below the synthesis vessels. Various configurations of the pooling manifold will allow assembly of 96,384 or 1536 well arrays of 5 parsed component oligonucleotides. A similar strategy can be performed where pairs of oligonucleotides are pooled instead of triplets. The final complete gene can be generated using PCR with outside primers and the resulting product analyzed on an agarose gel.

Human erythropoietin polypeptide variants of the invention contain 10 an amino acid difference in two or more different Epo-modification regions. The Epo-modification regions include internal amino acids associated with carbohydrate content, aggregation, and EPOR binding properties of erythropoietin. The inventors have found that the addition of a small number amino acids at the N-terminus of erythropoietin and the deletion of a small 15 number of amino acids at the C-terminus of erythropoietin does not significantly change the erythroid precursor proliferation activity of the variant polypeptide. Other investigators have identified regions of erythropoietin that are associated with carbohydrate content, aggregation, and EPOR binding properties of erythropoietin.

20 A human erythropoietin polypeptide variant can have one amino acid difference in an Epo-modification region such as the aggregation region and one amino acid difference in a different Epo-modification region such as the EPOR binding region. In addition, a human erythropoietin polypeptide variant can have several amino acid difference in an Epo-modification region such as the 25 aggregation region and one amino acid difference in a different Epo-modification region such as the EPOR binding region. Furthermore, a human erythropoietin polypeptide variant can have several amino acid difference in an Epo-modification region such as the aggregation region and several amino acid difference in a different Epo-modification region such as the EPOR binding region. Accordingly, 30 a human erythropoietin polypeptide variant can contain, for example, from single to multiple amino acid differences in two or more Epo-modification regions.

Specific examples of human erythropoietin polypeptide variants containing one or more amino acid differences in two or more Epo-modification regions include SEQ ID NOS:6, 218, 220, 90, 222 and 224. These human erythropoietin polypeptide variants have been described above and also further 5 below. For example, SEQ ID NO:90 contains one amino acid difference in an Epo-modification region corresponding to an aggregation region. This difference corresponds to the substitution of N to S at residue 24 (N24S) as set forth in Figure 1. SEQ ID NO:90 also contains one or more amino acid differences in an Epo-modification region corresponding to an EPOR binding region. One 10 difference corresponds to a change at residue 44 from T to S (T44S). Another difference corresponds to a change at residue 48 from F to M (F48M). Both T44S and F48M are located within an EPOR binding region. The human erythropoietin polypeptide variant set forth as SEQ ID NO:90 is encoded by the nucleic acid sequence shown in SEQ ID NO:89.

15 SEQ ID NOS:222 and 224 are related to SEQ ID NO:90 in that the three amino terminal residues set forth in Figure 1 as residues -3 to -1 have been substituted with a mammalian leader sequence for directing extracellular secretion of the expressed human erythropoietin polypeptide variant. The leader sequence is encoded by the nucleotide sequence set forth in SEQ ID NO:225 and has the 20 amino acid sequence set forth in SEQ ID NO:226, which is MGVHECPAWLWLLLSLLSLPLGLPVLG. Other mammalian or eukaryotic expression sequences well known in the art can substitute for this leader sequence. The polypeptide sequences of the unprocessed forms are shown in Figure 2 for SEQ ID NOS:222 and 224. Other than the leader sequence replacement for 25 mammalian extracellular expression, SEQ ID NO:222 is substantially identical to SEQ ID NO:90, in that it contains the amino acid differences in two or more different Epo-modification regions corresponding to N24S, T44S and F48M.

Compared to SEQ ID NO:222, SEQ ID NO:224 additionally contains amino acid differences compared to human erythropoietin at positions in 30 an Epo-modification region directed to carbohydrate content. These amino acid differences in SEQ ID NO:224 correspond to P87V, W88N and P90T.

Accordingly, SEQ ID NOS:90 and 222 contain, for example, three amino acid differences in two Epo-modification regions and SEQ ID NO:224 contains, for example, six amino acid differences in three Epo-modification regions. Following expression and processing in mammalian cells, the mature polypeptides of SEQ ID NOS:222 and 224 begin at residue 28, which corresponds to residue 1 (Ala) in Figure 2. The human erythropoietin polypeptide variants set forth as SEQ ID NOS:222 and 224 are encoded by the nucleic acid sequences shown in SEQ ID NOS:221 and 223, respectively.

Human erythropoietin polypeptide variants containing one or more amino acid differences in two or more Epo-modification regions set forth as SEQ ID NOS:6, 218 and 220 are similarly related, for example, as variants with or without a mammalian leader sequence for extracellular expression. For example, SEQ ID NO:6 contains two amino acid differences in an Epo-modification region corresponding to an aggregation region. These differences correspond to substitutions at N24T and N83I as set forth in Figure 1. SEQ ID NO:6 also contains two amino acid differences in an Epo-modification region directed to carbohydrate content. One difference corresponds to a change at A30V. Another difference corresponds to a change at H32D. SEQ ID NO:6 additionally contains amino acid differences outside of an Epo-modification region. These differences correspond to changes at W51R and V63I. The human erythropoietin polypeptide variant set forth as SEQ ID NO:6 is encoded by the nucleic acid sequence shown in SEQ ID NO:5.

SEQ ID NOS:218 and 220 are related to SEQ ID NO:6 by, for example, the replacement of the three amino terminal residues set forth in Figure 1 as residues -3 to -1 with the leader sequence set forth as SEQ ID NO:226. The polypeptide sequences of the unprocessed forms of SEQ ID NOS:218 and 220 are shown in Figure 2. Other than the leader sequence replacement, SEQ ID NO:218 is substantially identical to SEQ ID NO:6, in that it contains the above-described six amino acid differences in two or more different Epo-modification regions. Compared to SEQ ID NO:218, SEQ ID NO:220 contains the additional amino acid differences P87V, W88N and P90T for a total of nine amino acid changes

compared to human erythropoietin. Following expression and processing in mammalian cells, the mature polypeptides of SEQ ID NOS:218 and 220 begin at residue 28, which corresponds to residue 1 (Ala) in Figure 2. The human erythropoietin polypeptide variants set forth as SEQ ID NOS:218 and 220 are encoded by the nucleic acid sequences shown in SEQ ID NOS:217 and 219, respectively.

The carbohydrate portions of different glycoprotein molecules have been shown to have many diverse functions, including effects on the biosynthesis and secretion, immune protection, conformation, stability, solubility and biological activity of molecules (Skehel et al, Proc. Natl. Acad. Sci. USA 81:1779-1783 (1984); Cumming, D., Glycobiology 1:115-130 (1991)). For rHuEPO, in particular, it has been shown that the addition of carbohydrate is important for secretion from the cell, and for increasing the solubility of the molecule (Dube et al, J. Biol. Chem. 263:17516-17521 (1988); Narhi et al, J. Biol. Chem. 266:23022-23026 (1991); Delorme et al, Biochemistry 31:9871-9876 (1992)). Early research on erythropoietin from natural sources indicated that the sialic acid residues were important for biological activity *in vivo* (Lowry et al, Nature 185:102-103 (1960); Lukowsky and Painter, Can. J. Biochem. 50:909-917 (1972); Goldwasser et al, J. Biol. Chem. 249:4202-4206 (1974)). Removal of the sialic acid from either native erythropoietin or rHuEPO resulted in molecules having an increased activity *in vitro*, but low activity *in vivo*, presumably due to removal from circulation by the asialoglycoprotein receptor in the liver (Fukuda et al, Blood 73:84-89 (1989); Spivak and Hogans, Blood 73:90-99 (1989)). Similarly, it was shown that erythropoietin molecules, which have been deglycosylated to remove carbohydrate (or produced in *E. coli* to allow expression of only the non-glycosylated erythropoietin polypeptide), are active *in vitro*, but have low *in vivo* activity (Dordal et al, Endocrinology 116:2293-2299 (1985); Higuchi et al, J. Biol. Chem. 267:7703-7709 (1992)).

Carbohydrate addition (glycosylation) is a post-translational event that results in the addition of sugar chains to specific asparagine (N-linked) or serine/threonine (O-linked) amino acids in the polypeptide. The carbohydrate

portion of natural and recombinant human erythropoietin consists of 3 N-linked sugar chains at Asn 24, 38 and 83, and one O-linked (mucin-type) sugar chain at Ser 126 (Browne et al, Cold Spring Harb. Symp. Quant. Biol. 51:693-702 (1986); Egrie et al, Immunobiology 172:213-224 (1986)).

- 5 In contrast to the invariant amino acid sequence of the protein portion of glycoproteins, the carbohydrate structures are variable, a feature referred to as microheterogeneity. For example, N-glycosylation sites on the same protein may contain different carbohydrate structures. Furthermore, even at the same glycosylation site on a given glycoprotein, different structures can be found.
- 10 This heterogeneity is a consequence of the non-template directed synthesis of carbohydrates.

- The carbohydrate structures of erythropoietin have been determined and the extent of the microheterogeneity defined for both rHuEPO and the natural hormone (Sasaki et al, J. Biol. Chem. 262:12059-12076 (1987); Sasaki
- 15 et al., Biochemistry 27:8618-8626 (1988); Takeuchi et al, J. Biol. Chem. 263:3657-3663 (1988); Tsuda et al, Biochemistry 27:5646-5654 (1988)). An example of microheterogeneity for erythropoietin is seen on the N-linked carbohydrate chains, where the oligosaccharides can contain 2, 3 or 4 branches (or antennae), each of which is typically terminated with the negatively charged sugar
- 20 molecule, sialic acid. With the exception of sialic acid, all of the other sugar molecules on erythropoietin are neutral. Similarly, the single O-linked carbohydrate can contain 0 to 2 sialic acid molecules. Since each of the 3 N-linked oligosaccharides can contain up to 4 sialic acid residues, and the single O-linked chain can contain 2, the erythropoietin molecule can have a maximum of
- 25 14 sialic acid residues. Therefore, because of the variability in sugar structure, the number of sialic acid molecules on erythropoietin varies, and as a consequence, so does the molecule's net negative charge. An isoform of erythropoietin is defined as a subset of the erythropoietin molecules that has a defined charge due to its sialic acid content. For reference, epoetin alfa (EPOGEN®, Amgen Inc,
- 30 Thousand Oaks, CA), the source of the purified rHuEPO has been purified so as to contain isoforms 9-14.

It has been shown that a difference in biological activity can be attributed to the individual isoforms, with those isoforms having a higher sialic acid content exhibiting a progressively higher *in vivo* efficacy (Egrie and Brown, Brit. J. Cancer 84: (suppl.1) 3-10 (2001)). In addition, it was shown that the

5 isoforms that have a higher sialic acid content have a higher *in vivo* biological activity, longer serum half-life and slower serum clearance. When a radioreceptor assay was used to determine binding of the various isoforms to the EPOR, it was found that the isoforms having a higher sialic acid content had a lower relative affinity for the EPO receptor. Taken together, these experiments indicate that the

10 carbohydrate moieties of erythropoietin have an effect on the biological activity of the hormone, modulating both receptor affinity and serum clearance. There is a direct relationship between sialic acid content, *in vivo* biological activity, and serum half-life, but an inverse relationship with receptor affinity. Thus, modification of sialic acid content can alter erythropoietin properties.

15 Additional N-linked carbohydrate chains can be added to the rHuEPO molecule. N-linked carbohydrate is attached to the polypeptide backbone at a consensus sequence for carbohydrate addition (Asn-XXX-Ser/Thr). To introduce new carbohydrate attachment sites into the polypeptide backbone, the DNA sequence of the cloned human erythropoietin gene can be modified to

20 code for one or more new consensus sequences. The consensus sequences are added at positions that are compatible with carbohydrate addition, for example, positions that do not interfere with receptor binding, or compromise the folding, conformation, or stability of the molecule. The erythropoietin analog, NESP, was generated by combining the carbohydrate addition sites of 2 successfully

25 glycosylated 4-chain analogues into one molecule. The amino acid sequence of NESP differs from that of human erythropoietin at 5 positions (Ala30Asn, His32Thr, Pro87Val, Trp88Asn, and Pro90Thr) allowing for additional oligosaccharide attachment at asparagine residues at positions 30 and 88 (Elliott et al, Blood 96:82a (2000)).

30 Epo-modification regions also include regions that are known to be involved in erythropoietin polypeptide aggregation. Deglycosylated or

Escherichia coli-derived non-glycosylated erythropoietin is prone to aggregation, making it difficult to carry out high-resolution structure analysis (Narhi *et al.*, J. Biol. Chem. 266:23022-23026 (1991); Endo *et al.*, J. Biochem. 112:700-706 (1992)). The isoelectric point of the non-glycosylated erythropoietin, determined by isoelectric focusing in the presence of urea, is about 9.2 (Davis *et al.*, Biochemistry 26:2633-2638 (1987)). Mutation of the three Asn residues at positions 24, 38, and 83 at the N-linked glycosylation sites to Lys makes the isoelectric point more basic, resulting in an increase in the net positive charge at or below neutral pH and resulting in a decrease in the aggregation of the protein (Nahri *et al.*, *supra*). Aggregation can be measured, for example, by monitoring the absorbance of a polypeptide solution at 287 nm. The refolded mutant erythropoietin was comparable to the human polypeptide in a receptor binding assay, yet showed a greater stability against heating and storage, with less aggregation. Thus, modification of amino acid residues at positions 24, 38, and 83 can alter erythropoietin properties.

Epo-modification regions also include regions that are known to be involved in erythropoietin binding to the erythropoietin receptor (EPOR). The EPOR is expressed on erythroid cells and also on embryonic stem cells, endothelial cells and neuronal cells. The structure of human erythropoietin complexed with EPOR shows that one molecule of erythropoietin binds two receptors (Syed *et al.*, *supra*). Dimerization of the EPOR leads to activation of intercellular signaling pathways. Several allelic variations in the EPOR gene have been identified in different families. Some of these allelic variations result in disease while others appear to have no effect.

Mutagenesis analysis has identified four amino acids in erythropoietin, T44, F48, N147, and L155 as being involved in binding to EPOR (Castelli *et al.*, Pharm. Res. 41:313-318 (2000); Gareau *et al.*, Nature 380:113 (1996); Lanse *et al.*, Nature 405:635 (2000); Rich, I Molecular and Cellular Aspects of Erythropoietin and Erythropoiesis, Springer-Verlag, Berlin (1998); Syed *et al.*, Nature 395:511-516 (1998); Middleton *et al.*, J. Biol. Chem., 271:14045-14054 (1996); Middleton *et al.*, J. Biol. Chem., 274:14163-14169

(1999). Binding of erythropoietin to its receptor can be determined using any of the receptor binding assay methods known in the art. For example, a radioreceptor assay (Broudy et al. Proc. Natl. Acad. Sci. USA 85:6513-6517 (1988)) can be used to measure the quantity of erythropoietin or erythropoietin polypeptide variant needed to displace ¹²⁵I-rHuEPO bound to the EPOR on the surface of cells such as OCIM1 cells. The IC₅₀, or amount of test compound required to compete 50% of the receptor-bound ¹²⁵I-rHuEPO can be determined.

In addition to amino acid differences in two or more different Epo-modification domains, a human erythropoietin polypeptide variant of the invention can contain one or more amino acid differences outside of an Epo-modification domain. For example, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions, an amino acid difference located outside an Epo-modification region, and an enhanced erythropoietin activity, or a functional fragment thereof. Amino acid differences located outside an Epo-modification region can be located anywhere outside of the defined Epo-modification regions, for example, amino acid position 79 and amino acid position 146. A specific example of a human erythropoietin polypeptide variant of the invention with amino acid difference in two or more different Epo-modification regions and an amino acid difference in outside an Epo-modification region, with an enhanced erythropoietin activity is the polypeptide shown in SEQ ID NO:82 which contains amino acid differences at position 24 (aggregation region), position 97 (carbohydrate region) and position 79 (outside of Epo-modification region). Another example is SEQ ID NO:76 which contains amino acid differences at position 44 and 48 (EPOR region), position 83 (aggregation region), and position 79 and 146 (outside of Epo-modification region).

In a further embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in three Epo-modification regions, and an enhanced erythropoietin activity, or a functional fragment thereof. A specific

example of a human erythropoietin polypeptide variant of the invention with amino acid difference in three Epo-modification regions and an enhanced erythropoietin activity is the polypeptide shown in SEQ ID NO:74 which contains amino acid differences at amino acid positions 30, 32, 87, and 88 (carbohydrate 5 region), amino acid positions 38 and 83 (aggregation region), and amino acid position 155 (EPOR region).

The invention further provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in three Epo-modification regions, an amino acid difference 10 located outside an Epo-modification region, and an enhanced erythropoietin activity, or a functional fragment thereof. In a related embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in three Epo-modification regions, an amino acid difference located outside an Epo- 15 modification region, and an enhanced erythropoietin activity, or a functional fragment thereof, where an amino acid difference is located at position 146. As described above, the polypeptide shown in SEQ ID NO:74 is a specific example since it contains amino acid differences in all three Epo-modification regions and additionally contains amino acid differences at amino acid position 79 and 146.

20 The invention provides a human erythropoietin polypeptide variant, or functional fragment thereof, having an altered erythropoietin activity. For example, the human erythropoietin polypeptide variant can have enhanced or moderated activity compared to human erythropoietin.

As described further above, comparisons between human 25 erythropoietin polypeptide variants and human erythropoietin can be determined using various types of human erythropoietin for comparison. For example, a source of human erythropoietin can be the World Health Organization Second International Reference Preparation. In addition, a source of human erythropoietin can be a commercially available form of human erythropoietin such 30 as is available from Amgen. In addition, for example, a polypeptide variant with essentially identical activity as human erythropoietin can be used as a surrogate

for human erythropoietin in subsequent assays. For example, as disclosed herein, the erythroid precursor proliferation activity of the polypeptide SEQ ID NO:2 is essentially identical to that of human erythropoietin obtained commercially from Amgen. Therefore, comparison of human erythropoietin polypeptide variants to
5 the SEQ ID NO:2 polypeptide can be used to determine whether human erythropoietin polypeptide variant has altered activity compared to human erythropoietin.

The human erythropoietin polypeptide variants of the invention with altered erythropoietin activities can have different activities depending on the
10 cell type that is being tested. For example, a human erythropoietin polypeptide variant of the invention can have a faster time to reach a maximal level of an erythropoietin activity in a T lymphocyte cell type and an slower time to reach a maximal level of same erythropoietin activity in an erythroid precursor cell type.

In addition, some human erythropoietin polypeptide variants of the
15 invention may not show activity in one cell type, but can have activity in a different cell type. Furthermore, some erythropoietin polypeptide variants that do not show an activity in one cell type can show an activity in the same cell type if the time of the assay is extended. For example, a slow-acting erythropoietin polypeptide variant of the invention may not show any activity if an assay, such as
20 an erythroid precursor proliferation assay, is monitored at 24 hours post-treatment, however an activity can be detected at 78 hours post-treatment. Therefore, erythropoietin polypeptide variants of the invention that do not appear to have activity can still have activity if tested in different cell types or under different conditions such as assay time length.

25 In one embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin activity, or a functional fragment thereof, where the enhanced erythropoietin activity includes increased erythroid precursor
30 proliferation. For example, the invention provides a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS:

6, 14, 18, 26, 28, 40, 48, 60, 62, 74, 76, 82, 90, 92, 94, 96, 100, 102, 104, 112, 132, 134, 138, 152, 160, 166, 184, 188, 192, 206, 212, 218, 220, 222, 224 or a functional fragment thereof.

A human erythropoietin polypeptide variant having increased
5 erythroid precursor proliferation activity can be useful in the treatment of individuals who have a disease such as anemia, chronic renal failure, cancer or a neurological condition. In one embodiment, a composition containing a human erythropoietin polypeptide variant of the invention having increased erythroid precursor proliferation activity is used to treat an individual who does not respond,
10 or who responds sub-optimally to therapy with available erythropoietin polypeptides such as rHuEPO or NESP.

Erythroid precursor proliferation and erythroid cell viability can be determined using several assays that are known in the art. For example, methods of measuring cell proliferation include the detection of proliferation associated
15 antigens by immunohistochemistry, quantitation of DNA synthesis by measuring tritiated thymidine or bromodeoxyuridine uptake, and quantitation of reduction of the intracellular environment by tetrazolium salt reduction. For example, an *in vitro* bioassay that measures tritiated thymidine uptake in an erythropoietin dependent cell line such as 32D + EPOR can be used in the invention (Pacifci and
20 Thomason, J. Biol. Chem. 269:1571 (1994)).

The invention provides a method useful for rapidly screening several erythropoietin polypeptide variants in real-time. For example, the invention provides a method of measuring erythroid precursor proliferation activity of an erythropoietin polypeptide over time, by: (a) contacting an erythroid
25 precursor cell line with a erythropoietin polypeptide and a non-toxic proliferation-sensitive dye under conditions sufficient for cell viability, and (b) measuring a signal of the dye at various times after the contacting, where changes in the signal of the dye correlate with erythroid precursor proliferation activity. The invention further provides a method of measuring erythroid precursor proliferation activity
30 of a human erythropoietin polypeptide variant over time, by: (a) contacting an erythroid precursor cell line with a human erythropoietin polypeptide variant and

a non-toxic proliferation-sensitive dye under conditions sufficient for cell viability, and (b) measuring a signal of the dye at various times after the contacting, where changes in the signal of the dye correlate with erythroid precursor proliferation activity.

5 As described herein the UT-7 cell line is an example of an erythroid precursor cell line that can be used in the methods of the invention (Example II). An example of a non-toxic proliferation-sensitive dye is the alamarBlueTM (BioSource) dye reagent which can be used to measure the intracellular environment. The internal environment of proliferating cells is
10 known to be more reduced than that of non-proliferating cells and this reduced state can be measured using alamarBlueTM. Specifically the ratios of NADPH/NADP, FADH/FAD, FMNH/FMN and NADH/NAD increase during proliferation. AlamarBlueTM is a soluble, non-toxic stable dye that changes color in response to oxidation and reduction. Because alamarBlueTM is non-toxic, an
15 advantage to this method is that continuous monitoring of cells in culture is permitted. Non-toxicity is advantageous when assaying variant polypeptides because variants with activity that may not be detected in a single time point assay can be detected when measurements can be made in real-time. Another advantage is that a single well containing the variant polypeptide can be assayed several
20 times which reduces the amount of reagents that are required compared to setting up several wells with different time points. In addition, a single well assay as described herein has reduced variability compared to multiple well assays.

A signal from the dye can be measured at various time points, for example, by measuring the absorbance of the dye at various time points (Example
25 II). For example, proliferation measurements with alamarBlueTM can be made either spectrophotometrically by monitoring the absorption of alamarBlueTM supplemented cell culture media at two wavelengths, or alternatively, proliferation measurement with alamarBlueTM can be made fluorometrically.

The assays described above for determining erythroid precursor
30 proliferation can be used as a an initial screen to test for activity or can be used to more precisely determine activity. For example, a pre-determined volume of a

supernatant containing a human erythropoietin polypeptide variant can be tested in such an assay as an initial screen to find variants with enhanced activity. A further assay can then be performed using a pre-determined quantity of polypeptide variant to obtain more precise comparisons to human erythropoietin or to other variants. The quantity of erythropoietin polypeptide present in a sample such as a supernatant can be determined using several assays well known in the art. For example, an immunoassay, such as an ELISA, utilizing an antibody or antibodies that react with human erythropoietin can be used to quantitate the level of human erythropoietin polypeptide or polypeptide variant in a sample.

Several antibodies are known in the art that can be used in immunoassays such as RIA-P, RIA-N, E1A/P11, E1A/F13 and RIA-9G8A (Elliott et al., Blood 87:2702-2713 (1996))). In order to detect the quantity of a variant polypeptide, more than one antibody can be used in case the variant has changes in an epitope recognized by one of the antibodies.

As disclosed herein, several of the human erythropoietin polypeptide variants disclosed herein show increased erythroid precursor proliferation activity in an alamarBlueTM based assay using the UT-7 cell line (Example II and Table I). For example, the polypeptides shown as SEQ ID NOS:90, 222, 224 have increased erythroid precursor proliferation activity.

In addition to the UT-7 cell line, erythropoietin activity can also be measured, for example, using the human erythroleukaemic cell line TF-1. Erythropoietin activity can also be measured using phenylhydrazin-treated mouse spleen cells as a source of erythroid precursor cells. Furthermore, bone marrow colony assays can be used to detect erythropoietin either by monitoring colonies or burst-forming units of erythrocytes in methylcellulose cultures.

In one embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin activity, or a functional fragment thereof, where the enhanced erythropoietin activity includes increased erythroid precursor differentiation. Methods for determining erythroid precursor differentiation are

known in the art and include, for example, microscopic techniques which identify morphological changes that accompany differentiation and antibody staining techniques such as FACS which identify cell surface markers associated with differentiated cells. In addition, erythroid precursor differentiation can be
5 assessed by hemoglobin formation assayed by dianisidine staining and subsequent cell counting.

In addition to *in vitro* assays used to determine erythroid precursor proliferation and differentiation, measurements of these processes can be determined indirectly *in vivo*, for example, by a hematocrit or hemoglobin
10 measurement from a blood sample as described herein.

A hematocrit is described as the percent of whole blood that is comprised of red blood cells (RBCs). Hematocrit is also known by the terms erythrocyte count or red blood cell count. The hematocrit is a compound measure of RBC number and size. The test is performed from blood drawn from a vein of
15 an individual. The blood is centrifuges and the cellular portion is compared to the total amount of blood and expressed as a percent. The cellular portion is almost entirely red blood cells, the percent that is white blood cells is small. Normal hematocrit values depend on the gender of the individual and health status of the individual. For example, hematocrit can be influenced by dehydration and
20 dialysis. A normal value can be, for example, males: 40% to 54% of total blood volume made up of RBCs, females: 37% to 47% of total blood volume made up of RBCs, and dialysis patients: 30% to 36% of total blood volume made up of red blood cells.

In another embodiment, the invention provides a human
25 erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin activity, or a functional fragment thereof, where the enhanced erythropoietin activity includes a faster time to reach a maximal level of an erythropoietin activity. For example, the invention
30 provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or

more different Epo-modification regions and an enhanced erythropoietin activity, or a functional fragment thereof, where the enhanced erythropoietin activity includes a faster time to reach a maximal level of erythroid precursor proliferation. For example, the invention provides a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 26, 70, 96, 112, 138, 152, or a functional fragment thereof.

The time to reach a maximal level of an erythroid activity, such as erythroid precursor proliferation, can be determined using several assays that are known in the art. For example, any of the assays described above for determining the level of activity of erythroid precursor proliferation can be used to determine the time to reach a maximal level of proliferation activity. For example, the time to reach a maximal level of erythroid proliferation activity was measured in Example II and Table 1 using the alamarblueTM assay described above. In this assay, the time to reach a maximal level of erythroid proliferation activity of erythropoietin variant polypeptides is compared to the time to reach a maximal level of activity by the polypeptide encoded by SEQ ID NO:2. Since the polypeptide encoded by SEQ ID NO:2 had essentially identical activity when compared to human erythropoietin SEQ ID NO:214, the polypeptide encoded by SEQ ID NO:2 was used as a surrogate for human erythropoietin.

Several temporal aspects of an erythropoietin activity can be utilized in the invention. For example, in addition to the time it takes to reach a maximal level of an erythropoietin activity, the initial time of onset of an erythropoietin activity can be measured. For example, a human erythropoietin polypeptide variant of the invention can have a faster or slower time of onset of an activity such as onset of erythroid precursor proliferation.

In one embodiment, a composition containing a human erythropoietin polypeptide variant of the invention having a faster time to reach a maximal level of erythroid precursor proliferation is used to treat an individual who does not respond, or who responds sub-optimally to therapy with available erythropoietin polypeptides such as rHuEPO or NESP. In addition, because the therapeutic effects of treatment with available erythropoietin polypeptides such as

rHuEPO or NESP can take several days, a faster-acting erythropoietin polypeptide variant can be used to get therapeutic results more rapidly. A more rapid result can be useful in an individual, for example, who has critically low hematocrit or hemoglobin levels.

5 As described above, a human erythropoietin polypeptide variant of the invention can have an altered erythropoietin activity compared to human erythropoietin shown as SEQ ID NO:214. Different properties of an erythropoietin polypeptide can affect activity *in vitro* or *in vivo*. Enhanced activity can be due to a change in any property of the polypeptide such as
10 increased binding to receptor, increased plasma stability, or changes in the pharmacological properties of an erythropoietin polypeptide such as absorption, distribution, metabolism and/or elimination (ADME) of the polypeptide. Altered properties in a human erythropoietin polypeptide variant can result in increased or decreased levels of activity, an different side-effect profile, a different time of
15 onset or time to reach a maximal activity, differences in the ability of a patient to tolerate the polypeptide, and increased circulating half-life of an erythropoietin polypeptide variant.

Properties associated with erythropoietin polypeptide variants such as *in vivo* half-life and ADME properties can be determined using methods well
20 known in the art. For example, *in vivo* half-life of an erythropoietin polypeptide can be determined using New Zealand white rabbits that are injected intravenously with specified amounts of an erythropoietin polypeptide of interest. Blood samples are then obtained at specified times and serum prepared. Serum erythropoietin levels are then determined using an *in vitro* bioassay, for example,
25 an alamarBlue™ assay as described herein and compared to human erythropoietin.

In addition to providing human erythropoietin polypeptide variants with enhanced activity, the invention likewise provides human erythropoietin polypeptide variants with moderated activity. In one embodiment, the invention
30 provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or

more different Epo-modification regions and a moderated erythropoietin activity, or a functional fragment thereof.

In addition to amino acid differences in two or more different Epo-modification domains, a human erythropoietin polypeptide variant of the
5 invention can contain one or more amino acid differences outside of an Epo-modification domain. For example, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions, an amino acid difference located outside an Epo-
10 modification region, and a moderated erythropoietin activity, or a functional fragment thereof. Amino acid differences located outside an Epo-modification region can be located anywhere outside of the defined Epo-modification regions, for example, amino acid position 79 and amino acid position 146. A specific example of a human erythropoietin polypeptide variant of the invention with
15 amino acid difference in two or more different Epo-modification regions and an amino acid difference in outside an Epo-modification region, with a moderated erythropoietin activity is the polypeptide shown in SEQ ID NO:174 which contains amino acid differences at position 38 (aggregation region), positions 44 and 48 (EPOR region), position 79, 146, and 154 (outside of Epo-modification
20 region).

In a further embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in three Epo-modification regions, and a moderated erythropoietin activity, or a functional fragment thereof. A specific
25 example of a human erythropoietin polypeptide variant of the invention with amino acid difference in three Epo-modification regions and a moderated erythropoietin activity is the polypeptide shown in SEQ ID NO:198 which contains amino acid differences at amino acid position 32 (carbohydrate region), amino acid position 38 (aggregation region), and amino acid position 155 (EPOR
30 region).

The invention further provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in three Epo-modification regions, an amino acid difference located outside an Epo-modification region, and a moderated erythropoietin activity, or a functional fragment thereof. As described above, the polypeptide shown in SEQ ID NO:198 is a specific example since it contains amino acid differences in all three Epo-modification regions and additionally contains amino acid differences at amino acid position 17, 51, 79, and 98. In a related embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in three Epo-modification regions, an amino acid difference located outside an Epo-modification region, and a moderated erythropoietin activity, or a functional fragment thereof, where an amino acid difference is located at position 146. For example, the polypeptide shown in SEQ ID NO:68 contains an amino acid difference at positions 24 and 38 (aggregation region), position 87 (carbohydrate region), position 44 (EPOR region) and amino acid positions 79 and 146 (outside of Epo-modification region).

In one embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and a moderated erythropoietin activity, or a functional fragment thereof, where the moderated erythropoietin activity includes decreased erythroid precursor proliferation. For example, the invention provides a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 4, 8, 68, 70, 150, 170, 174, 198, or a functional fragment thereof. In one embodiment, a composition containing a human erythropoietin polypeptide variant of the invention having decreased erythroid precursor proliferation activity is used to treat an individual who, for example, responds to therapy with available erythropoietin polypeptides such as rHuEPO or NESP with a drastic increase in hematocrit.

In another embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and a moderated erythropoietin activity, or a functional
5 fragment thereof, where the moderated erythropoietin activity includes decreased erythroid precursor differentiation.

In a further embodiment, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-
10 modification regions and a moderated erythropoietin activity, or a functional fragment thereof, where the moderated erythropoietin activity includes a slower time to reach a maximal level of an erythropoietin activity. For example, the invention provides a human erythropoietin polypeptide variant containing a human erythropoietin amino acid sequence having an amino acid difference in
15 two or more different Epo-modification regions and a moderated erythropoietin activity, or a functional fragment thereof, where the moderated erythropoietin activity includes a slower time to reach a maximal level of erythroid precursor proliferation. For example, the invention provides a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS:
20 8, 14, 28, 40, 48, 60, 62, 68, 74, 90, 94, 100, 104, 132, 150, 166, 174, 184, 206, 212, or a functional fragment thereof.

In one embodiment, a composition containing a human erythropoietin polypeptide variant of the invention having a slower time to reach a maximal level of activity or having a slower time of onset of an activity is used to
25 treat an individual who, for example, responds to therapy with available erythropoietin polypeptides such as rHuEPO or NESP with a drastic increase in hematocrit. In this case, a slower-acting erythropoietin polypeptide variant can result in a more gradual increase in hematocrit. In addition, a slower-acting erythropoietin polypeptide variant can give a more even or sustained result in the
30 same way that a time-release formulation of a drug can result in a more even or sustained result.

The invention also provides an erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 2-212 and 218-224 EVEN, or functional fragment thereof. The invention further provides an erythropoietin polypeptide variant having an amino acid sequence selected from
5 SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, or functional fragment thereof.

10 Other human erythropoietin polypeptide variants useful in the invention are human erythropoietin polypeptide variants, or functional fragment thereof, where the human erythropoietin polypeptide variant has substantially the same amino acid sequence as referenced in SEQ ID NOS: 2-212 and 218-224
15 EVEN. Substantially the same amino acid sequence is intended to mean an amino acid sequence contains a considerable degree of sequence identity or similarity, such as at least 70%, 80%, 90%, 95%, 98%, or 100% sequence identity or similarity, to a reference amino acid sequence. Substantially the same amino acid sequence includes conservative and non-conservative amino acid changes, gaps, and insertions to an amino acid sequence. Conservative and non-conservative
20 amino acid changes, gaps, and insertions to an amino acid sequence can be compared to a reference sequence using available algorithms and programs such as the Smith-Waterman algorithm and the BLAST homology search program (Altschul et al., J. Mol. Biol. 215:403-410 (1990)).

Various modifications of a human erythropoietin polypeptide
25 variant primary amino acid sequence can result in polypeptides having substantially equivalent functions as compared to the un-modified sequence. Those skilled in the art can determine which residues and which regions of a human erythropoietin polypeptide variant sequence are likely to be tolerant of modification and still retain an activity associated with the un-modified sequence.
30 For example, amino acid substitutions or chemical or enzymatic modifications at residues that are less well conserved between species are more likely to be

tolerated than substitutions at highly conserved residues. Accordingly, an alignment can be performed among erythropoietin sequences of various species to determine residues and regions in which modifications are likely to be tolerated. Additional guidance for determining residues and regions of erythropoietin likely to be tolerant of modification is provided by studies of erythropoietin fragments and variants.

The invention also provides an isolated nucleic acid molecule containing a nucleic acid sequence encoding a human erythropoietin polypeptide variant having an amino acid sequence selected from the group consisting of SEQ ID NOS: 2-212 and 218-224 EVEN, or a functional fragment thereof. The invention further provides an isolated nucleic acid molecule containing a nucleic acid sequence encoding a human erythropoietin polypeptide variant having an amino acid sequence selected from the group consisting of SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 224, or a functional fragment thereof. The invention also provides an isolated nucleic acid molecule containing a nucleic acid sequence having a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 1-211 and 217-223 ODD, or a functional fragment thereof.

Other compositions useful in the invention are isolated nucleic acid molecules containing a nucleic acid sequence having substantially the same nucleic acid sequence as a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 1-211 and 217-223 ODD, or a functional fragment thereof. Substantially the same nucleic acid sequence is intended to mean a nucleic acid sequence contains a considerable degree of sequence identity or similarity, such as at least 70%, 80%, 90%, 95%, 98%, or 100% sequence identity or similarity, to a reference nucleic acid sequence. Substantially the same nucleic acid sequence can include gaps, and insertions to a nucleic acid sequence. Modifications to a nucleic acid sequence can be compared to a reference sequence

using available algorithms and programs such as the Smith-Waterman algorithm and the BLAST homology search program (Altschul et al., J. Mol. Biol. 215:403-410 (1990)).

Various modifications of a human erythropoietin polypeptide
5 variant nucleic acid sequence can result in nucleic acid molecules having substantially equivalent functions as compared to the un-modified sequence. Those skilled in the art can determine which nucleotides and which regions of a human erythropoietin nucleic acid sequence are likely to be tolerant of modification and still retain an activity associated with the un-modified sequence.

10 In one embodiment the invention provides a vector that contains an isolated nucleic acid molecule containing a nucleic acid sequence encoding a human erythropoietin polypeptide variant having an amino acid sequence selected from the group consisting of SEQ ID NOS: 2-212 and 218-224 EVEN, or a functional fragment thereof. In another embodiment the invention provides a host
15 cells containing this vector.

The invention further provides a method of producing a human erythropoietin polypeptide variant by growing the host cell described above under conditions sufficient for expression of the erythropoietin polypeptide variant. The invention further provides a method of producing a human erythropoietin
20 polypeptide variant by growing the host cell described above under conditions sufficient for expression of the erythropoietin polypeptide variant, and isolating the erythropoietin polypeptide variant from the host cell or host cell medium.

Vectors useful in the invention include autonomously replicating recombinant expression constructs such as plasmid and viral DNA vectors. The
25 invention includes vectors where erythropoietin polypeptide variant-encoding nucleic acids are operatively linked to an endogenous or exogenous promoter, enhancer, or operator sequence and a transcription terminator sequence. Promoter and enhancer sequences are generally selected for the ability to increase gene expression, while operator sequences are generally selected for the ability to
30 regulate gene expression. It is understood in the art that the choice of host cell is

relevant to selection of an appropriate regulatory sequence. Vectors used in the invention can also include sequences encoding one or more selectable markers that permit identification of host cells bearing the construct. Vectors can also include sequences that facilitate homologous recombination in a host cell.

5 Suitable vectors for expression in prokaryotic or eukaryotic cells are well known to those skilled in the art (see, for example, Ausubel et al., supra, 1999). Vectors useful for expression in eukaryotic cells can include, for example, regulatory elements including the SV40 early promoter, the cytomegalovirus (CMV) promoter, the mouse mammary tumor virus (MMTV) steroid-inducible
10 promoter, Moloney murine leukemia virus (MMLV) promoter, and the like. A vector can include, for example, viral vectors such as a bacteriophage, a baculovirus or a retrovirus; cosmids or plasmids; and, particularly for cloning large nucleic acid molecules, bacterial artificial chromosome vectors (BACs) and yeast artificial chromosome vectors (YACs). Such vectors are commercially
15 available, and their uses are well known in the art. One skilled in the art will know or can readily determine an appropriate promoter for expression in a particular host cell.

 Vectors useful for expression of a human erythropoietin polypeptide variant can contain a regulatory element that provides tissue specific
20 or inducible expression of an operatively linked nucleic acid. Such inducible systems, include, for example, tetracycline inducible system (Gossen & Bizard, Proc. Natl. Acad. Sci. USA, 89:5547-5551 (1992); Gossen et al., Science, 268:1766-1769 (1995); Clontech, Palo Alto, CA)); metallothionein promoter induced by heavy metals; insect steroid hormone responsive to ecdysone or
25 related steroids such as muristerone (No et al., Proc. Natl. Acad. Sci. USA, 93:3346-3351 (1996); Yao et al., Nature, 366:476-479 (1993); Invitrogen, Carlsbad, CA); mouse mammary tumor virus (MMTV) induced by steroids such as glucocorticoid and estrogen (Lee et al., Nature, 294:228-232 (1981); and heat shock promoters inducible by temperature changes.

30 In addition, viral vectors such as retroviral, adenovirus, adeno-associated virus, lentivirus, and herpesvirus vectors can be used to express ATX

polypeptides into a cell. Viral based systems provide the advantage of being able to introduce relatively high levels of a heterologous nucleic acid into a variety of cells. Additionally, such viruses can introduce heterologous DNA into nondividing cells. Viral vectors include, for example, Herpes simplex virus
5 vectors (U.S. Patent No. 5,501,979), Vaccinia virus vectors (U.S. Patent No. 5,506,138), Cytomegalovirus vectors (U.S. Patent No. 5,561,063), Modified Moloney murine leukemia virus vectors (U.S. Patent No. 5,693,508), adenovirus vectors (U.S. Patent Nos. 5,700,470 and 5,731,172), adeno-associated virus vectors (U.S. Patent No. 5,604,090), constitutive and regulatable retrovirus
10 vectors (U.S. Patent Nos. 4,405,712; 4,650,764 and 5,739,018, respectively), papilloma virus vectors (U.S. Patent Nos. 5,674,703 and 5,719,054), and the like.

The invention further provides a host cell containing a human erythropoietin polypeptide variant-encoding vector as described above. For example, the invention provides a host cell that contains a vector which contains
15 an isolated nucleic acid molecule having the same or substantially the same nucleotide sequence as SEQ ID NO: 1-211 and 217-223 ODD. Host cells include prokaryotic and eukaryotic cells. Nucleic acids of the invention can be introduced into the host cell as part of a circular plasmid, or as linear DNA having an isolated protein coding region or a viral vector. Methods for introducing DNA into the
20 host cell are well known in the art and include transformation, transfection, electroporation, nuclear injection, or fusion with carriers such as liposomes, micelles, ghost cells, protoplasts, and other transformed cells. Detailed procedures for these methods can be found in Sambrook et al., Molecular Cloning: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1989) and the
25 references cited therein). Expression systems of the invention include bacterial, yeast, fungal, plant, insect, invertebrate, and mammalian cells systems.

Useful mammalian expression vectors and methods of introducing such vectors into mammalian cells either *ex vivo* or *in vivo*, for expression of the encoded polypeptide, are well known in the art. For example, a plasmid
30 expression vector can be introduced into a cell by calcium-phosphate mediated transfection, DEAE-Dextran-mediated transfection, lipofection, polybrene- or

polylysine-mediated transfection, electroporation, or by conjugation to an antibody, gramicidin S, artificial viral envelopes or other intracellular carriers. A viral expression vector can be introduced into a cell in an expressible form by infection or transduction, for example, or by encapsulation in a liposome.

5 In one embodiment, the invention provides a method of producing a human erythropoietin polypeptide variant by growing a host cell that contains a human erythropoietin polypeptide variant vector under conditions sufficient for expression of the erythropoietin polypeptide variant. In a further embodiment, the erythropoietin polypeptide variant can be isolated from the host cell or the host
10 cell medium using methods described below and known in the art.

Erythropoietin polypeptide variants can be isolated from the cells, or from the medium in which the cells are grown, by purification methods known in the art, for example, conventional chromatographic methods including immunoaffinity chromatography, receptor affinity chromatography, hydrophobic
15 interaction chromatography, lectin affinity chromatography, size exclusion filtration, cation or anion exchange chromatography, high pressure liquid chromatography (HPLC), reverse phase HPLC, and the like. Still other methods of purification include those wherein the desired protein is expressed and purified as a fusion protein having a specific tag, label, or chelating moiety that is
20 recognized by a specific binding partner or agent. The purified protein can be cleaved to yield the desired protein, or be left as an intact fusion protein. A description of the purification of recombinant erythropoietin from cell medium that supported the growth of mammalian cells containing recombinant erythropoietin plasmids for example, is included in U.S. Pat. No. 4,667,016 to Lai
25 et al., which is incorporated herein by reference.

The nucleic acid composition of the invention can be used in gene therapy methods to restore erythropoietin activity thus treating those disease states described herein. Delivery of a functional erythropoietin polypeptide variant gene to appropriate cells can be effected *ex vivo*, *in situ*, or *in vivo* by use of vectors, for
30 example, viral vectors such as adenovirus, adeno-associated virus, or a retrovirus, or *ex vivo* by use of physical DNA transfer methods such as liposomes or

chemical treatments (Anderson, Nature, supplement to vol. 392, no. 6679, pp.25-20 (1998)). Alternatively, in some human disease states, preventing the expression of, or inhibiting the activity of, erythropoietin can be useful in treating the disease states. In this case, anti-sense therapy or gene therapy, for example, where a dominant negative erythropoietin mutant is introduced into a target cell type, can be applied to negatively regulate the expression of erythropoietin. In addition, interfering RNAs derived from compositions of the invention can be used to inhibit the activity of erythropoietin (Brummelkamp et al., Science 296:550-553 (2002); Elbashir et al., Nature 411:494-498 (2002)). RNAi is a process of sequence-specific gene silencing by post-transcriptional RNA degradation, which is initiated by double-stranded RNA (dsRNA) homologous in sequence to the silenced gene.

The invention provides an antibody, or functional binding fragment thereof, containing a region that specifically binds to a human erythropoietin polypeptide variant containing an amino acid sequence as shown in SEQ ID NOS: 2-212 and 218-224 EVEN. The invention further provides an antibody, or functional binding fragment thereof, which specifically binds to a human erythropoietin polypeptide variant containing an amino acid sequence as referenced in SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224.

The term specifically binds is intended to mean the molecule will have an affinity for the target molecule that is measurably higher than its affinity for a non-specific interaction. For example, an antibody that specifically binds another polypeptide will have an affinity for the target polypeptide or antigen that is measurably higher than its affinity for a non-specific interaction. Binding affinity can be low or high affinity so long as the binding is sufficient to be detectable. For example, an antibody can bind a human erythropoietin polypeptide variant with a binding affinity (K_d) of about 10^{-5} M or less, 10^{-6} M or

less, about 10^{-7} M or less, including about 10^{-8} M or less, such as 10^{-9} M or less. Several methods for detecting antibody binding are well known in art.

Antibodies of the invention include, for example, monoclonal and polyclonal antibodies, single chain antibodies, chimeric antibodies, bifunctional or 5 bispecific antibodies, humanized antibodies, human antibodies, and complementary determining region (CDR)-grafted antibodies, including compounds which include CDR or antigen-binding sequences, which specifically bind to a polypeptide of the invention. Antibody fragments, including Fab, Fab', F(ab')₂, and Fv, are also provided by the invention. Screening assays to determine 10 binding specificity or exclusivity of an antibody of the invention are well known in the art (see Harlow et al. (Eds), *Antibodies A Laboratory Manual*; Cold Spring Harbor Laboratory; Cold Spring Harbor, N.Y. (1988)).

Antibodies of the invention can be produced using any method well known in the art, using any polypeptide, or immunogenic fragment thereof, of the 15 invention. Immunogenic polypeptides can be isolated from natural sources, from recombinant host cells, or can be chemically synthesized. Polypeptide of the invention can also be conjugated to a hapten such as keyhole limpet hemocyanin (KLH) in order to increase immunogenicity. Methods for synthesizing such peptides are known in the art, for example, as in R. P. Merrifield, J. Amer. Chem. 20 Soc. 85: 2149-2154 (1963); J. L. Krstenansky, et al., FEBS Lett. 211:10 (1987).

Antibodies to a polypeptide of the invention can also be prepared through immunization using a nucleic acid of the invention, as described in Fan et al., Nat. Biotech. 17:870-872 (1999). DNA encoding a polypeptide can be used to generate antibodies against the encoded polypeptide following topical 25 administration of naked plasmid DNA or following injection, for example, intramuscular injection, of the DNA.

Non-human antibodies can be humanized by any methods known in the art. In one method, the non-human CDRs are inserted into a human antibody or consensus antibody framework sequence. Further changes can then 30 be introduced into the antibody framework to modulate affinity or immunogenicity. Antibodies of the invention further include plastic antibodies or

molecularly imprinted polymers (MIPs) (Haupt and Mosbauch, TIBTech 16:468-475 (1998)). Antibodies of this type can be useful in immunoaffinity separation, chromatography, solid phase extraction, immunoassays, for use as immunosensors, and for screening chemical or biological libraries. Advantages of antibodies of this type are that no animal immunization is required, the antibodies are relatively inexpensive to produce, they are resistant to organic solvents, and they are reusable over long period of time.

Antibodies that bind to erythropoietin polypeptide variants of the invention can be used in diagnostic and therapeutic methods. For example, an antibody of the invention can be labeled with a detection moiety and used to detect the presence, absence or amount of an erythropoietin polypeptide of the invention *in vivo*, *in vitro*, or *in situ*. In addition, an antibody of the invention can be labeled with a therapeutic moiety such as chemotherapeutic agent and used, for example, to reduce the number of cells that can internalize these polypeptides. Further, an antibody of the invention can act in a competitive or dominant negative fashion to interfere with or reduce an erythropoietin activity.

A moiety, such as a fluorescent molecule, can be linked to a polypeptide, including an antibody, of the invention at any location within the polypeptide. Chemistries used for the linkage of various moieties to polypeptides are well known in the art. A moiety such as detection moiety can be linked to a polypeptide, including an antibody, of the invention using, for example, carbodiimide conjugation (Bauminger and Wilchek, Meth. Enzymol. 70:151-159 (1980)). Carbodiimides comprise a group of compounds that have the general formula $R-N=C=N-R'$, where R and R' can be aliphatic or aromatic, and are used for synthesis of polypeptide bonds. The preparative procedure is simple, relatively fast, and is carried out under mild conditions. Carbodiimide compounds attack carboxylic groups to change them into reactive sites for free amino groups. Carbodiimide conjugation has been used to conjugate a variety of compounds to carriers for the production of antibodies. The water soluble carbodiimide, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) is useful for conjugating a moiety to a polypeptide, including an antibody of the invention.

The invention provides a composition containing a human erythropoietin polypeptide variant containing an amino acid sequence selected from SEQ ID NOS: 2-212 and 218-224 EVEN and a pharmaceutically acceptable medium. The invention further provides a composition containing a human
5 erythropoietin polypeptide variant containing an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212,
10 218, 220, 222, 224, and a pharmaceutically acceptable medium. For example, the composition can be a pharmaceutical composition comprising an effective amount of a human erythropoietin polypeptide variant and a pharmaceutically acceptable diluent, adjuvant or carrier. Pharmaceutically acceptable carriers are well known in the art and include, for example, aqueous solutions such as water or
15 physiologically buffered saline or other solvents or vehicles such as glycols, glycerol, oils such as olive oil or injectable organic esters.

A pharmaceutically acceptable carrier can contain a physiologically acceptable compound that acts, for example, to stabilize or to increase the absorption of the composition. Such physiologically acceptable
20 compounds include, for example, carbohydrates, such as glucose, sucrose or dextrans, antioxidants, such as ascorbic acid or glutathione, chelating agents, low molecular weight proteins or other stabilizers or excipients. One skilled in the art would know that the choice of a pharmaceutically acceptable carrier, including a physiologically acceptable compound, depends, for example, on the route of
25 administration of the composition. If desired, the pharmaceutical composition also can contain a second active agent such as a therapeutic agent.

One skilled in the art understands that a composition containing a human erythropoietin polypeptide variant of the invention can be administered to an individual by various routes including, for example, orally or parenterally, such
30 as intravenously, or by injection or intubation. In performing a therapeutic method as disclosed herein, an effective amount of the composition must be

administered to the subject. An effective amount is the amount of the conjugate that produces a desired effect and depends, for example, on the particular disease that is being treated.

The route of administration of the compositions of the invention will depend, in part, on the chemical structure of the erythropoietin polypeptide variants. Some polypeptides, for example, are not particularly useful when administered orally because they can be degraded in the digestive tract. However, methods for chemically modifying a polypeptide to render it less susceptible to degradation by endogenous proteases or more absorbable through the alimentary tract are well known in the art (see, for example, Blondelle et al., *supra*, 1995; Ecker and Crooke, *supra*, 1995; Goodman and Ro, *supra*, 1995). In addition, methods for preparing libraries of polypeptide analogs such as polypeptides containing D-amino acids; peptidomimetics consisting of organic molecules that mimic the structure of a polypeptide; or peptoids such as vinylogous peptoids, have been previously described above and can be used to identify erythropoietin polypeptide variants suitable for oral administration to an individual.

Compositions containing a human erythropoietin polypeptide variant of the invention can be delivered systemically in therapeutically or prophylactically effective amounts by pulmonary administration using a variety of pulmonary delivery devices, including nebulizers, metered dose inhalers and powder inhalers. Aerosol administration of compositions of the invention can result in significant elevation of red blood cell levels. Compositions of the invention can be administered in this manner to medically treat or prevent anemia, as well as to treat or prevent other maladies related to erythropoiesis.

Naffakh et al. examined whether the secretion of erythropoietin from genetically modified cells could represent an alternative to repeated injections of the recombinant hormone for treating chronic anemias responsive to erythropoietin (Naffakh et al., *Proc. Nat. Acad. Sci.* 92:3194-3198 (1995)). Primary mouse skin fibroblasts were transduced with a retroviral vector in which the murine cDNA was expressed under the control of the murine phosphoglycerate kinase promoter. 'Neo-organs' containing the genetically

modified fibroblasts embedded into collagen lattices were implanted into the peritoneal cavity of mice. Increased hematocrit and elevated serum erythropoietin concentration were observed in recipient animals over a 10-month observation period. The approach was considered applicable to the treatment of human
5 anemias and can be used with the compositions of the invention.

Osborne et al. investigated in rats the expression and biologic effects of transplanting autologous vascular smooth muscle cells transduced with a retroviral vector encoding rat erythropoietin cDNA (Osborne et al., Proc. Nat. Acad. Sci. 92:8055-8058 (1995)). Vector-derived erythropoietin secretion caused
10 increases in reticulocytes followed by clinically significant increases in hematocrit and hemoglobin for up to 11 weeks. There were no significant differences between control and treated animals in the number of white blood cells and platelets. Kidney and to a lesser extent liver are specific organs that synthesize Erythropoietin in response to tissue oxygenation. In the treated animals,
15 endogenous erythropoietin mRNA was largely downregulated in kidney and absent from liver. These results indicated that vascular smooth muscle cells can be genetically modified to provide treatment of anemias due to erythropoietin deficiency and suggest that this cell type may be targeted in the treatment of other diseases requiring systemic therapeutic protein delivery. Compositions of the
20 invention can be used in a like manner.

Similar experiments were performed by Kessler et al., who demonstrated that, following a single intramuscular administration of a recombinant adeno-associated virus (rAAV) vector containing the beta-galactosidase gene into adult mice, protein expression was detected in myofibers
25 for at least 32 weeks Kessler et al., Proc. Nat. Acad. Sci. 93:14082-14087 (1996)). Furthermore, a single intramuscular administration of an AAV vector containing a gene for human erythropoietin into mice resulted in dose-dependent secretion of erythropoietin and corresponding increases in red blood cell production that persisted for up to 40 weeks. Primary human myocytes transduced *in vitro* with
30 the AAV-Epo vector also showed dose-dependent production of erythropoietin.

The compositions and erythropoietin polypeptide variants of the invention are useful in modulating cell survival, proliferation and differentiation. For example, the compositions and polypeptides of the invention are useful in promoting erythroid precursor proliferation and can be used *in vivo*, *ex vivo*, *in situ*, or *in vitro*. For example, a composition containing a human erythropoietin polypeptide variant where the erythropoietin polypeptide variant is selected from SEQ ID NOS: 6, 14, 18, 26, 28, 40, 48, 60, 62, 74, 76, 82, 90, 92, 94, 96, 100, 102, 104, 112, 132, 134, 138, 152, 160, 166, 184, 188, 192, 206, 212, 218, 220, 222, 224, can be used to treat erythroid precursor cells derived from an individual *ex vivo* and then the increased proliferating cells can be administered back to the subject.

The invention provides a method for increasing erythrocytes in an individual by administering to the individual an effective amount of a composition that contains a human erythropoietin polypeptide variant containing an amino acid sequence selected from SEQ ID NOS: 2-212 and 218-224 EVEN and a pharmaceutically acceptable medium. The invention further provides a method for increasing erythrocytes in an individual by administering to the individual an effective amount of a composition that contains a human erythropoietin polypeptide variant containing an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 224 and a pharmaceutically acceptable medium.

The number of erythrocytes in an individual can be measured, for example, using a hematocrit. In one embodiment, the invention provides a method for providing increasing erythrocytes an individual by administering an effective amount of a composition containing a human erythropoietin polypeptide variant where the erythropoietin polypeptide variant is selected from SEQ ID NOS: 6, 14, 18, 26, 28, 40, 48, 60, 62, 74, 76, 82, 90, 92, 94, 96, 100, 102, 104, 112, 132, 134, 138, 152, 160, 166, 184, 188, 192, 206, 212, 218, 220, 222, 224,

and SEQ ID NOS: 4, 8, 68, 70, 150, 170, 174, 198. In one embodiment, the invention provides a method for increasing erythrocytes in an individual by administering an effective amount of a composition containing a human erythropoietin polypeptide variant where the erythropoietin polypeptide variant is
5 selected from SEQ ID NOS: 26, 70, 96, 112, 138, 152 and SEQ ID NOS: 8, 14, 28, 40, 48, 60, 62, 68, 74, 90, 94, 100, 104, 132, 150, 166, 174, 184, 206, 212.

The invention provides a method for increasing erythrocytes in an individual by administering to the individual an effective amount of a pharmaceutical composition containing a human erythropoietin polypeptide
10 variant where the erythropoietin polypeptide variant is selected from SEQ ID NOS: 2-212 and 218-224 EVEN, and where the individual is anemic. The invention provides a method for increasing erythrocytes in an individual by administering to the individual an effective amount of a pharmaceutical composition containing a human erythropoietin polypeptide variant where the
15 erythropoietin polypeptide variant is selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, and where the
20 individual is anemic. For example, a polypeptide variant or composition of the invention can be administered in an amount effective to increase the hematocrit level of an anemic subject. Anemia can be caused by several factors including diet and genetic factors as well as pathologies. For example, anemia can be caused by chronic renal failure or can be induced as a side-effect of chemotherapy
25 treatment for an individual who has cancer.

Chronic renal failure (CRF) almost invariable leads to anemia. In CRF, the main cause of renal anemia is loss of peritubular cells in the kidney which are responsible for the synthesis and secretion of erythropoietin. By the time subjects with CRF require dialysis, only about 3% have a normal
30 hemoglobin level. In most patients the level is 6-8 g/dl. Generally hemodialysis patients tend to have more severe anemia than those receiving peritoneal dialysis.

In addition to the treatment of anemia, the invention also contemplates the treatment of iron overload disorder. A subject having an iron overload disorder is administered an effective amount of a composition of the invention to increase red blood cell production and the subject is subsequently
5 phlebotomized to remove the excess red blood cells produced (see US. Patent No. 5,013,718).

The invention provides a method for reducing an effect of a neurological condition in an individual, by administering to the individual an effective amount of a composition containing a human erythropoietin polypeptide
10 variant having an amino acid sequence selected from SEQ ID NOS: 2-212 and 218-224 EVEN and a pharmaceutically acceptable medium. The invention further provides a method for reducing an effect of a neurological condition in an individual, by administering to the individual an effective amount of a composition containing a human erythropoietin polypeptide variant having an
15 amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, and a pharmaceutically acceptable
20 medium. For example a pharmaceutical composition of the invention can be administered prophylactically in individuals who are at risk for neurological conditions or can be used after an event such as a stroke or other neurological damage.

As described above, a neurological condition can be a pathological
25 condition affecting neuronal or glial cells in the nervous system. Pathological conditions affecting neuronal or glial cells include ischemia, apoptosis, necrosis, oxidative or free radical damage, and excitotoxicity. For example, neurological conditions include, without limitation, cerebral and spinal ischemia, acute brain injury, spinal cord injury, retinal disease, and neurodegenerative diseases such as
30 Alzheimer's disease, Parkinson's disease, Huntington's disease, and ALS.

In the central nervous system, neurons express erythropoietin receptor (EPOR) (see OMIM Entry 133171 for information regarding EPOR) and astrocytes produce erythropoietin. Erythropoietin has been shown to protect primary cultured neurons from NMDA receptor-mediated glutamate toxicity.

5 Sakanaka reported *in vivo* evidence that erythropoietin protects neurons against ischemia-induced cell death (Sakanaka, et al., Proc. Nat. Acad. Sci. 95:4635-4640 (1998)). They presented findings suggesting that erythropoietin may exert its neuroprotective effect by reducing the nitric oxide-mediated formation of free radicals or antagonizing their toxicity. Siren et al. presented data suggesting that
10 inhibition of neuronal apoptosis underlies short latency protective effects of erythropoietin after cerebral ischemia and other brain injuries (Siren et al. Proc. Nat. Acad. Sci. 98:4044-4049 (2001)). They suggested that evaluation of erythropoietin, a compound established as clinically safe, as neuroprotective therapy in acute brain injury is indicated.

15 In addition to its role as a kidney cytokine regulating hematopoiesis, erythropoietin is also produced in the brain after oxidative or nitrosative stress. The transcription factor HIF1 (see OMIM Entry 603348 for information regarding HIF1) up-regulates erythropoietin following hypoxic stimuli. Digicaylioglu and Lipton demonstrated that preconditioning with
20 erythropoietin protects neurons in models of ischemic and degenerative damage due to excitotoxins and consequent generation of free radicals, including nitric oxide (Digicaylioglu and Lipton, Nature 412:641-647, (2001)). Activation of neuronal erythropoietin receptors prevents apoptosis induced by NMDA or nitric oxide by triggering crosstalk between the signaling pathways JAK2 and NFkB
25 (see OMIM Entry 147796 for information regarding JAK2 and OMIM Entry 164011 for information regarding NFkB). Digicaylioglu and Lipton also demonstrated that erythropoietin receptor-mediated activation of JAK2 leads to phosphorylation of the inhibitor of NFkB (see I-kappa-B-alpha, OMIM Entry 164008), subsequent nuclear translocation of the transcription factor NFkB, and
30 NFkB-dependent transcription of neuroprotective genes (Digicaylioglu and Lipton, *supra* (2001)). Transfection of cerebrocortical neurons with a dominant interfering form of JAK2 or an I-kappa-B-alpha super-repressor blocks

Erythropoietin-mediated prevention of neuronal apoptosis. Thus, neuronal erythropoietin receptors activate a neuroprotective pathway that is distinct from previously well characterized JAK and NF κ B functions. Moreover, this erythropoietin effect may underlie neuroprotection mediated by hypoxic-ischemic preconditioning.

Celik et al. undertook studies in a rabbit model to determine whether exogenous erythropoietin might have a protective effect in injuries to the spinal cord (Celik, et al., Proc. Nat. Acad. Sci. 99:2258-2263 (2002)). Immunocytochemistry performed using human spinal cord sections showed abundant erythropoietin receptor immunoreactivity of capillaries, especially in white matter, and motor neurons within the ventral horn. Spinal cord ischemia was produced in rabbits by occlusion of the abdominal aorta. Recombinant human erythropoietin was administered intravenously immediately after the onset of reperfusion. The authors found both an acute and a delayed beneficial action of recombinant human Erythropoietin in ischemic spinal cord injury.

Erythropoietin is upregulated by hypoxia and provides protection against apoptosis of erythroid progenitors in bone marrow and also apoptosis of brain neurons (Siren et al., *supra*, 2001). Grimm et al. showed in the adult mouse retina that acute hypoxia dose-dependently stimulates expression of erythropoietin, fibroblast growth factor-2 (134920), and vascular endothelial growth factor (192240) via HIF1 stabilization (Grimm et al., Nature Med. 8:718-724 (2002)). Hypoxic preconditioning protects retinal morphology and function against light-induced apoptosis by interfering with caspase-1 (see OMIM Entry 147678) activation, a downstream event in the intracellular death cascade. In contrast, induction of activator protein-1 (see OMIM Entry 165160), an early event in the light-stressed retina, is not affected by hypoxia. The erythropoietin receptor, required for erythropoietin signaling, localizes to photoreceptor cells. The protective effect of hypoxic preconditioning is mimicked by systemically applied erythropoietin that crosses the blood-retina barrier and prevents apoptosis even when given therapeutically after light insult. Application of erythropoietin

may, through the inhibition of apoptosis, be beneficial for the treatment of different forms of retinal disease.

In rats, Junk et al. conducted parallel studies of recombinant erythropoietin in a model of transient global retinal ischemia induced by raising intraocular pressure, which is a clinically relevant model for retinal diseases (Junk, et al., Proc. Nat. Acad. Sci. 99:10659-10664, (2002)). They observed abundant expression of EPOR throughout the ischemic retina. Neutralization of endogenous erythropoietin with soluble EPOR exacerbated ischemic injury, which supports a role for an endogenous EPO/EPOR system in the survival and recovery of neurons after an ischemic insult. Systemic administration of recombinant erythropoietin before or immediately after retinal ischemia not only reduced histopathologic damage, but also promoted functional recovery as assessed by electroretinography. Exogenous erythropoietin also significantly diminished terminal deoxynucleotidyltransferase-mediated dUTP end labeling of neurons in the ischemic retina, implying an antiapoptotic mechanism of action. These results further established Erythropoietin as a neuroprotective agent in acute neuronal ischemia.

To evaluate whether recombinant erythropoietin improves functional outcome if administered after spinal cord injury, Gorio et al. studied 2 rodent models (Gorio et al., Proc. Nat. Acad. Sci. 99:9450-9455 (2002)). In the first model, a moderate compression was produced by applying an aneurysm clip at level T3 and administering recombinant erythropoietin immediately after release of compression; partial recovery of motor function began within 12 hours after injury and was nearly complete by 28 days. In contrast, saline-treated animals exhibited only poor recovery. In the second model, recombinant erythropoietin administration given 1 hour after injury also produced a superior recovery of function compared with saline-treated controls after a contusion at level T9. In the latter model of more severe spinal cord injury, secondary inflammation was also markedly attenuated by recombinant erythropoietin administration and associated with reduced cavitation within the spinal cord. These authors suggested that erythropoietin provides early recovery of function,

especially after spinal cord compression, as well as longer-latency neuroprotective, antiinflammatory, and antiapoptotic functions.

It is understood that modifications which do not substantially affect the activity of the various embodiments of this invention are also included within the definition of the invention provided herein. Accordingly, the following examples are intended to illustrate but not limit the present invention.

EXAMPLE I

Generation of erythropoietin polypeptide variants

A version of human erythropoietin was designed which contains 10 optimized codons for expression in *E. coli*. This version of erythropoietin is called EgEpo 1.3 and is disclosed herein as SEQ ID NO:2. EgEpo1.3 contains the following changes with respect to human erythropoietin: the native leader sequence was removed and a met-asp-ile was added at the N-terminus. These three amino acids are designated as positions -3, -2, and -1 respectively so that the 15 rest of the EgEpo1.3 polypeptide correlates with the sequence of human erythropoietin from the literature. In addition, there is an ala to thr change at amino acid 79 and the deletion of TGDR at the carboxyl terminus.

The polypeptides of the invention, SEQ ID NOS: 2-212 and 218-224 EVEN, were generated using the Egea proprietary gene assembly method as 20 disclosed in PCT application No. WO 99/14318 and in U.S. Patent No. 6,521,427. Methods for automated synthesis and assembly similarly can be found described, for example, in the above patent publications as well as in WO 02/081490A2, all of which are incorporated herein by reference and described further above. For EgEpo1.3, a 564 base pair sequence was assembled. A 24 bp sequence for the 25 construct primers was added on the 5' and 3' ends for a construct size of 612 bp. The 24 bp primer at the 5' end is CAGGAATTCTGTTTGGAAGCTGTC (SEQ ID NO:215) and the primer at the 3' end is ACTCTCATACCATGGAAGCTTGCA (SEQ ID NO:216). In order to assemble the gene, 13 forward 50mer oligonucleotides were generated, 12 reverse 50mer

oligonucleotides were generated, and 2 terminal 25mer oligonucleotides were generated. The oligonucleotides were each purified and tested for quality.

The gene construct was designed with an upstream pelB leader sequence which directs the polypeptide to the periplasm. In addition, a stop codon 5 was also added at the end of the mature polypeptide sequence. Assembled products were cloned, transformed, and colonies were picked for DNA sequencing. The cloning vector was pCR-T7/NT-TOPO (Invitrogen). This vector contains an upstream T7 promoter, a ribosome binding site, start codon, 6xHis tag, an Xpress epitope, and an enterokinase cleavage site. Transformation of 10 topoisomerase ligated vector was done in BL21 host cells.

For the polypeptides listed in Figures 1 and 2, the following protocol was used. Targeted mutations at residues thought to be important for carbohydrate content, aggregation, and EPOR binding were generated. In particular the following amino acids were targeted: for N-linked carbohydrate 15 changes; A30, H32, P87, W88, and P90, for aggregation: N24, N38, N83, and for EPOR binding: T44, F48, N147 and L155. The oligonucleotides encoding these mutations were designed with an "N" at a single base of the targeted codon. The designation of "N" directs the oligonucleotide sequencer to add any of the four nucleotides, A, C, T, or G, at a desired position within the oligonucleotide. Genes 20 were synthesized, assembled, cloned, sequenced, and expressed as described above.

Variants identified to exhibit altered Epo activity were selected and modified for expression mammalian cells by substitution of the prokaryotic leader sequence with the eukaryotic leader sequence set forth in SEQ ID NO:226 and 25 encoded by the nucleotide sequence in SEQ ID NO:225. Substitution was performed by chemical synthesis of an encoding nucleic acid and ligation into the parent sequence devoid of the corresponding leader-containing fragment. Exemplary sequences modified to contain a mammalian leader sequence functioning to direct the human erythropoietin polypeptide variant into the 30 extracellular space include SEQ ID NOS: 218, 220, 222 and 224.

60

The position of the "N" within the codon was varied. The position was chosen based on two criteria: (1) a position was not selected if it could induce a stop codon when translated and (2) a position was selected based on the triplet coding for the greatest diversity of amino acid. For example, position 2 was chosen over position 3 in a codon if it translated a possible 2 amino acids rather than 1.

EXAMPLE II

Activities of erythropoietin polypeptide variants

Erythropoietin polypeptide variant clones generated in Example I, were individually expressed in *E. coli* using standard procedures and tested for activity using the protocol outlined below.

The human myeloid acute leukemia cell line UT-7 (DSMZ) which is known to differentiate and proliferate in response to erythropoietin was grown under standard culture conditions of 5%CO₂ at 37°C in 80% alpha – minimum essential media (AMEM)(Biosource) with 20% fetal bovine serum (FBS) (Biosource) and 5ng/ml of GM-CSF (Promega). UT-7 cells were equally distributed at approximately 1000 cells/100ml in a 96 well plate for each test and positive control well. The negative control wells contained 80% AMEM with 20% FBS. Once confluent, the cells were washed in 10% phosphate buffered saline and returned to standard culture conditions of 5%CO₂ at 37°C in 80% AMEM with 20% FBS for 48hr.

To each test well 5 µl of an erythropoietin polypeptide variant from an *E. coli* supernatant was added. In each well of a 96 well plate 10ul of alamarBlue™ (Biosource) was added. All plates were then incubated in 5%CO₂ at 37°C. At 24, 48, 72 and 96 hours after the initial addition of alamarBlue™, spectrophotometric readings (Spectramax) were recorded at 570nm and 600nm. From these two values the percentage reduction of alamarBlue™ was calculated as per the manufacturers directions. The percentage reduction of alamarBlue™ is a measure of cell proliferation in response to the erythropoietin polypeptide variant, where an increase in the reduction of alamarBlue™ is correlated to an

increase in cell proliferation. The same procedure was replicated using the TF1 cell line to confirm results obtained using the UT-7 cell line. Table I contains the erythroid precursor proliferation activity using the UT-7 cell line, and time of onset of activity for erythropoietin polypeptide variants of the invention.

5 Versions of the human erythropoietin polypeptide variants engineered for expression and secretion from mammalian cells were similarly produced and tested for cell proliferation in the alamarBlueTM assay described above. These versions correspond to SEQ ID NOS: 218, 220, 222 and 224. Briefly, the encoding nucleic acids referenced as SEQ ID NOS:217, 219, 221 and 10 223 were cloned into a mammalian expression vector and stably expressed in CHO K1 cells or transiently expressed in COS-7 cells following transfection. SEQ ID NOS:217, 219, 221 and 223 were modified to additionally encode a poly-His tag at the carboxyl terminus of each variant. These His tagged versions are identical to the human erythropoietin polypeptide variants shown as SEQ ID 15 NOS:218, 220, 222 and 224 and also included the addition of six His residues to the carboxyl terminus of each amino acid sequence. Following expression in CHO cells, the His-containing versions of SEQ ID NOS:218, 220, 222 and 224 were tested in the proliferation assay described previously.

Proliferation was tested for the His-containing human 20 erythropoietin polypeptide variants corresponding to SEQ ID NOS:218, 220, 222 and 224 either using supernatant of variant expressing cells or using purified forms of the variants. Supernatant activity was determined from both stably or transiently transfected cells for these variants and showed comparable results. Variants were purified from the stably transfected cells and the activity of these 25 isolated forms determined.

Purification was achieved the His tag of each variant and employing a purification kit obtained from Qiagen (Valencia, California). Briefly, Qiagen columns and buffers were used as supplied and procedures performed according the manufacturer's instructions. Cell culture medium was centrifuged 30 to remove cells. Supernatants were poured off and filtered through a 0.2 µm filter to remove any cells or cellular material. Nicle charged resin (Ni-NTA Agarose

beads) was added to the supernatant and mixed gently to create a slurry. The sample was incubated at 4°C for 4 hours to allow binding of the polypeptide-His tag to the agarose. The slurry was applied to a column and washed 6 times with 6 mls of Qiagen wash buffer (50 mM NaH₂PO₄.H₂O, 300 mM NaCl and 20mM 5 Imidazole). Bound polypeptide was subsequently eluted from the column with 3 x 1 ml washes using Qiagen elution buffer (50 mM NaH₂PO₄.H₂O, 300 mM NaCl and 250mM Imidazole). The polypeptide concentration resulting in the eluate was 0.01 ng/μl, which was used in the proliferation described above. The results of the proliferation assays for the variants shown as SEQ ID NOS: 218, 220, 222 10 and 224 is shown below in Table II.

Table I:

Clone Name	SEQ ID NO:	% reduction of alamar blue at 96hr	Time taken to reach maximum reduction of alamar blue (Hr) (Speed of activity)
P5H10	82	53.96	48
P5H5	76	54.54	48
P5G9	74	64.45	72
P5D8	132	69.02	72
P5E7	48	68.06	72
P1D7	18	87.94	48
P1B10	6	103.3	48
P5A4	90	86.77	72
P1B1	14	73.14	72
P1C8	4	51.44	48
P1C4	26	54.7	24
P5B8	104	86.58	72
P5A10	96	63.5	24
P5A8	94	95.25	72
P5B3	100	86.31	72
P5A5	92	87.5	48
P1D5	28	65.37	72
P5F9	60	59.27	72
P5F10	62	57.7	72
P6E5	184	55.89	72
P6B11	166	63.1	72
P6F9	198	44.34	48
P6F3	192	67.97	48
P6B1	152	68.63	24
P6H11	212	85.16	72
P5B7	102	58.8	48
P6A1	138	67.66	24
P5C6	112	53.53	24
P1B12	8	44.02	72
P6B6	160	64.82	48
P1A4	40	73.68	72
P5D9	134	63.49	48
P6E11	188	65.2	48
P5G2	68	51.68	72
P6A10	150	51.74	72
P6C6	170	51.13	48
P6D2	174	46.15	72
P5G5	70	48.54	24
P6H1	206	59.1	72
Tem-plate	2	52.93	48

TABLE II:

Clone Name	SEQ ID NO:	Supernatant Polypeptide		Purified polypeptide (0.01ng/ul)	
		% reduction of alamar blue 96hr	Time taken to reach max reduction of alamar blue (hr)	% reduction of alamar at 120hr	Time taken to reach max reduction of alamar blue (hr)
P5A4 B1	222	22.73	96	28.46	120
P5A4 B2	224	30.17	96	18.17	120
P1B10 B1	218	22.05	72	4.22	96
P1B10 B2	220	24.97	72	1.25	96

Throughout this application various publications have been referenced within parentheses. The disclosures of these publications in their entireties are hereby incorporated by reference in this application in order to more fully describe the state of the art to which this invention pertains.

Although the invention has been described with reference to the disclosed embodiments, those skilled in the art will readily appreciate that the specific experiments detailed are only illustrative of the invention. It should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

What is claimed is:

1. A human erythropoietin polypeptide variant comprising, a human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and an enhanced erythropoietin
5 activity, or a functional fragment thereof.
2. The human erythropoietin polypeptide variant of claim 1, further comprising an amino acid difference located outside an Epo-modification region.
3. The human erythropoietin polypeptide variant of claim 2,
10 wherein said amino acid difference is located at amino acid position 146.
4. The human erythropoietin polypeptide variant of claim 1, further comprising an amino acid difference in a third Epo-modification region.
5. The human erythropoietin polypeptide variant of claim 4, further comprising an amino acid difference located outside an Epo-modification
15 region.
6. The human erythropoietin polypeptide variant of claim 5, wherein said amino acid difference is located at amino acid position 146.
7. The human erythropoietin polypeptide variant of claim 1, wherein said enhanced erythropoietin activity comprises increased erythroid
20 precursor proliferation.
8. The human erythropoietin polypeptide variant of claim 1, wherein said enhanced erythropoietin activity comprises increased erythroid precursor differentiation.
9. The human erythropoietin polypeptide variant of claim 1,
25 wherein said enhanced erythropoietin activity comprises a faster time to reach a maximal level of an erythropoietin activity.

10. The human erythropoietin polypeptide variant of claim 9, wherein said enhanced erythropoietin activity comprises a faster time to reach a maximal level of erythroid precursor proliferation.
11. A human erythropoietin polypeptide variant comprising, a
5 human erythropoietin amino acid sequence having an amino acid difference in two or more different Epo-modification regions and a moderated erythropoietin activity, or a functional fragment thereof.
12. The human erythropoietin polypeptide variant of claim 11, further comprising an amino acid difference located outside an Epo-modification
10 region.
13. The human erythropoietin polypeptide variant of claim 12, wherein said amino acid difference is located at position 146.
14. The human erythropoietin polypeptide variant of claim 11, further comprising an amino acid difference in a third Epo-modification region.
15. 15. The human erythropoietin polypeptide variant of claim 14, further comprising an amino acid difference located outside an Epo-modification region.
16. The human erythropoietin polypeptide variant of claim 15, wherein said amino acid difference is located at position 146.
- 20 17. The human erythropoietin polypeptide variant of claim 11, wherein said moderated erythropoietin activity comprises decreased erythroid precursor proliferation.
18. The human erythropoietin polypeptide variant of claim 11, wherein said moderated erythropoietin activity comprises decreased erythroid
25 precursor differentiation.

19. The human erythropoietin polypeptide variant of claim 11, wherein said moderated erythropoietin activity comprises a slower time to reach a maximal level of an erythropoietin activity.
20. The human erythropoietin polypeptide variant of claim 19, wherein said moderated erythropoietin activity comprises a slower time to reach a maximal level of erythroid precursor proliferation.
21. A human erythropoietin polypeptide variant, having an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, or a functional fragment thereof.
22. An isolated nucleic acid molecule, comprising a nucleic acid sequence encoding a human erythropoietin polypeptide variant having an amino acid sequence selected from SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, or a functional fragment thereof.
23. A vector comprising the isolated nucleic acid molecule of claim 22.
24. A host cell comprising the vector of claim 23.
25. A method of producing a human erythropoietin polypeptide variant, comprising growing the host cell of claim 24 under conditions sufficient for expression of said erythropoietin polypeptide variant.
26. The method of claim 25, further comprising isolating said erythropoietin polypeptide variant from the host cell or host cell medium.

27. An antibody or functional binding fragment thereof comprising, a region that specifically binds to a human erythropoietin polypeptide variant comprising an amino acid sequence as shown in SEQ ID NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 5 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224.
28. A composition, comprising a human erythropoietin polypeptide variant comprising an amino acid sequence selected from SEQ ID
10 NOS: 4, 6, 8, 14, 16, 18, 26, 28, 30, 34, 36, 38, 40, 42, 44, 48, 50, 54, 56, 60, 62, 66, 68, 70, 72, 74, 76, 82, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 112, 116, 118, 120, 122, 124, 132, 134, 138, 144, 148, 150, 152, 160, 162, 164, 166, 170, 172, 174, 184, 188, 192, 194, 196, 198, 200, 206, 210, 212, 218, 220, 222, 224, and a pharmaceutically acceptable medium.
- 15 29. A method of increasing erythrocytes in an individual, comprising administering to said individual an effective amount of a composition of claim 28.
30. The method of claim 29, wherein said individual is anemic.
31. The method of claim 29, wherein said individual has
20 chronic renal failure.
32. The method of claim 29, wherein said individual has cancer.
33. A method for reducing an effect of a neurological condition in an individual, comprising administering to said individual an effective amount
25 of a composition of claim 29.

34. A method of measuring erythroid precursor proliferation activity of an erythropoietin polypeptide over time, comprising:

- (a) contacting an erythroid precursor cell line with said erythropoietin polypeptide and a non-toxic proliferation-sensitive dye under 5 conditions sufficient for cell viability, and
- (b) measuring a signal of said dye at various times after said contacting,

wherein changes in said signal of the dye correlate with erythroid precursor proliferation activity.

- 10 35. The method of claim 34, wherein said erythropoietin polypeptide further comprises a human erythropoietin polypeptide variant.

[illegible]

[illegible]

FIGURE 1 Continued

[illegible]

FIGURE 2 (CONTINUED)

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Evans, Glen A.

Jewell, Sally

Ware, Mark

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Methods of Use

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 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 9
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

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gtc aac att tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Ile Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50                      55                      60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65                      70                      75                      80

caa act tta ctg gta att tcc agt cag cct tgg gaa cta tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Leu Leu Gln Leu
                      85                      90                      95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
                      100                      105                      110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
                      115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
                      130                      135                      140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145                      150                      155                      160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
                      165

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<210> 10
<211> 165
<212> PRT
<213> Homo sapiens

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<400> 10
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35          40          45
Val Asn Ile Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65          70          75          80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Leu Leu Gln Leu
          85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115          120          125

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Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 11
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 11
 atg gat atc acc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Thr Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gta gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Val Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta att tcc agt cag cct tgg gaa cta tta cag ttg 288
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Leu Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480

Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga
 Gly Glu Ala Cys Arg *
 165

498

<210> 12

<211> 165

<212> PRT

<213> Homo sapiens

<400> 12

Met Asp Ile Thr Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Val Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Leu Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 13

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 13

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

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gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45

gtc aac ttt tat gct tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100              105              110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115              120              125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130              135              140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145              150              155              160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 14

<211> 165

<212> PRT

<213> Homo sapiens

<400> 14

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1              5              10              15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20              25              30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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- 12 -

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tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130                135                140

ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145                150                155                160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
    165

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<210> 16
 <211> 165
 <212> PRT
 <213> Homo sapiens

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<400> 16
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Ala Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
          20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35          40          45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65          70          75          80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Arg Glu Gln Leu Gln Leu
          85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130          135          140
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
          165

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<210> 17
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

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<400> 17
atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1	5	10	15	
aga tac ctg ttc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt				96
Arg Tyr Leu Phe Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
gca gaa cat tgc tca ctg aac gag att att act gta ccg gat ccg aaa				144
Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Pro Lys				
	35	40	45	
gtc aac ctt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg				192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt				240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg				288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu				
	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggt gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 18

<211> 165

<212> PRT

<213> Homo sapiens

<400> 18

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Phe Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Pro Lys				
	35	40	45	

Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 19
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 19
 atg gat atg gcc cgg ccc ggt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Met Ala Arg Pro Gly Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg caa ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

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cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                      135                      140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctt aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145                      150                      155                      160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 20
 <211> 165
 <212> PRT
 <213> Homo sapiens

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<400> 20
Met Asp Met Ala Arg Pro Gly Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35          40          45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65          70          75          80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100         105         110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115         120         125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130         135         140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145         150         155         160
Gly Glu Ala Cys Arg
      165

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<210> 21
 <211> 499
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS

<222> (2)...(499)

<400> 21

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c atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 49
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt   97
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20             25             30

gaa gaa tat tgc tca ctg aac gag att att act gta ccg gat tcg aaa   145
Glu Glu Tyr Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Ser Lys
      35             40             45

gtc aac ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg   193
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt   241
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65             70             75             80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg   289
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc   337
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100            105            110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc   385
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115            120            125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg   433
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130            135            140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg   481
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145            150            155            160

ggt gag gct tgt cgc tga
Gly Glu Ala Cys Arg *
      165

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<210> 22

<211> 165

<212> PRT

<213> Homo sapiens

<400> 22

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20           25           30
Glu Glu Tyr Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Ser Lys
      35           40           45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130          135          140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
      165

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<210> 23

<211> 499

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (2)...(499)

<400> 23

c atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 49

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15

```

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 97

Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys

```

      20           25           30

```

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat ccg aaa 145

Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Pro Lys

```

      35           40           45

```

gtc aac ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 193

Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val

```

      50           55           60

```

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 241

Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly

```

      65           70           75           80

```

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 289

Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				337
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				385
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				433
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				481
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggg gag gct tgt cgc tga				499
Gly Glu Ala Cys Arg *				
	165			

<210> 24
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 24

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Pro Lys				
	35	40	45	
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu				
	85	90	95	
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
Gly Glu Ala Cys Arg				
	165			

<210> 25
 <211> 499

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (2)...(499)

<400> 25

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c atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 49
  Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
    1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt   97
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
      20             25             30

gca gaa cat tgc tta ctg aac gag aat att act gta ccg gat acg aaa   145
Ala Glu His Cys Leu Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35             40             45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg   193
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt   241
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65             70             75             80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg   289
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc   337
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100            105            110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc   385
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115            120            125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg   433
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130            135            140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg   481
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
      145            150            155            160

ggg gag gct tgt cgc tga
Gly Glu Ala Cys Arg *
      165

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<210> 26

<211> 165

<212> PRT

<213> Homo sapiens

<400> 26

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
          20           25           30
Ala Glu His Cys Leu Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130          135          140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
          165

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<210> 27

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 27

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atg gat atc gtc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Val Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30

gta gaa gat tgc tca ctg aac gag aat att act gta ccg gat ccg aaa      144
Val Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Pro Lys
          35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg      192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt      240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag tct ggg gaa cga tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Gly Glu Arg Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct gga ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 28

<211> 165

<212> PRT

<213> Homo sapiens

<400> 28

Met Asp Ile Val Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Val Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Pro Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Gly Glu Arg Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 29
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 29

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1              5              10              15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20              25              30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ttt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Phe Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100              105              110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115              120              125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130              135              140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145              150              155              160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
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165

<210> 30
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 <213> Homo sapiens

<400> 30
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Phe Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 31
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 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(498)

<400> 31
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt agc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Ser Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 32
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 32
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
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 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Ser Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 33
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 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(498)

<400> 33
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aat gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca aca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Thr Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480

Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 34
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 34
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 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Thr Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 35
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 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1) ... (498)

<400> 35
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

aaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Lys Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggg gag gtt tgt cgc tga 498
 Gly Glu Val Cys Arg *
 165

<210> 36

<211> 165

<212> PRT

<213> Homo sapiens

<400> 36

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Lys Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Val Cys Arg
 165

<210> 37

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 37

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat tcg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
 35 40 45
 gtc aac tta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

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tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130                135                140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145                150                155                160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
    165

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<210> 38
<211> 165
<212> PRT
<213> Homo sapiens

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<400> 38
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
    20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
    35          40          45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65          70          75          80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
    85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
    100         105         110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115         120         125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130         135         140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145         150         155         160
Gly Glu Ala Cys Arg
    165

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<210> 39
<211> 498
<212> DNA
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<220>
<221> CDS
<222> (1)...(498)

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<400> 39
atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1	5	10	15	
aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt				96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
gca gaa cat tgc tca ctg aac gag att att act gta ccg gat acg aaa				144
Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys				
	35	40	45	
gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg				192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt				240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg				288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu				
	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca ggc ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg				480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr				
	145	150	155	160
ggt gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 40

<211> 165

<212> PRT

<213> Homo sapiens

<400> 40

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys				
	35	40	45	

Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 41
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 41
 atg gat atc gcc ccg tcc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Ser Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 gga gaa aat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Gly Glu Asn Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct ggg gaa cta tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Gly Glu Leu Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 42
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 42
 Met Asp Ile Ala Pro Ser Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 Gly Glu Asn Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Gly Glu Leu Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 43
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS

<222> (1)...(498)

<400> 43

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
      20             25             30

gaa gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Glu Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35             40             45

gtc aac ttt tat gcc cgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65             70             75             80

caa act tta ctg gta aat tcc agt cag gct cgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Arg Glu Pro Leu Gln Leu
      85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130             135             140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
      145             150             155             160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 44

<211> 165

<212> PRT

<213> Homo sapiens

<400> 44

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
20           25           30
Glu Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
35           40           45
Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Arg Glu Pro Leu Gln Leu
85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
130          135          140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
165

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<210> 45

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 45

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
20           25           30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat gcg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
35           40           45

gtc aac tta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80

caa act tta ctg gta aat tcc agt cag act ggg gaa caa tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Gly Glu Gln Leu Gln Leu

```

	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr				
	145	150	155	160
ggt gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 46
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 46

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys				
	35	40	45	
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Gly Glu Gln Leu Gln Leu				
	85	90	95	
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr				
	145	150	155	160
Gly Glu Ala Cys Arg				
	165			

<210> 47
 <211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 47

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1                5                10                15

aga tac ctg ctt gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
      20                25                30

gca gaa gat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35                40                45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50                55                60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65                70                75                80

caa act tta ctg gta aat tcc agt cag tct cgg gaa cga tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Arg Glu Arg Leu Gln Leu
      85                90                95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100                105                110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                120                125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                135                140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145                150                155                160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 48

<211> 165

<212> PRT

<213> Homo sapiens

<400> 48

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
             20             25             30
Ala Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
             35             40             45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
             50             55             60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65             70             75             80
Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Arg Glu Arg Leu Gln Leu
             85             90             95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
             100            105            110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
             115            120            125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
             130            135            140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145            150            155            160
Gly Glu Ala Cys Arg
             165

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<210> 49

<211> 503

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 49

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atg gat atc gcc ccg ccc' cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
             20             25             30

gta gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa      144
Val Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
             35             40             45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg      192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
             50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt      240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt ttt ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Phe Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga actct 503
 Gly Glu Ala Cys Arg *
 165

<210> 50

<211> 165

<212> PRT

<213> Homo sapiens

<400> 50

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 Val Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Phe Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 51
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 51
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat gcg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
 35 40 45
 gtc aac ttt tat gcc cgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *

165

<210> 52
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 52
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
 35 40 45
 Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 53
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 53
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gta gaa gat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Val Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

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gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50                      55                      60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65                      70                      75                      80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
    85                      90                      95

cac gtg gat aag acg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Thr Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
    100                      105                      110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130                      135                      140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
    145                      150                      155                      160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
    165

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<210> 54

<211> 165

<212> PRT

<213> Homo sapiens

<400> 54

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20          25          30
Val Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35          40          45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65          70          75          80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85          90          95
His Val Asp Lys Thr Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
115          120          125

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Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 55
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 55
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta agt tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt ttt ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Phe Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480

Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 56
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 56
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Phe Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 57
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1) ... (498)

<400> 57
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

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gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg gaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Glu
      35              40              45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130             135             140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
      145             150             155             160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 58

<211> 165

<212> PRT

<213> Homo sapiens

<400> 58

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20           25           30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Glu
      35           40           45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 59

<211> 498

<212> DNA /

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 59

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg tta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag att att act gta ccg gat ccg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Pro Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160

ggc gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 60

<211> 165

<212> PRT

<213> Homo sapiens

<400> 60

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Pro Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 61

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 61

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc atc aca ggc tgt   96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Ile Thr Gly Cys
           20           25           30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa   144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
           35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg   192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
           50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt   240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
           65           70           75           80

caa act tta ctg gta aat tcc agt cag act tgg gaa caa tta cag ttg   288
Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Trp Glu Gln Leu Gln Leu
           85           90           95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc   336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
           100           105           110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc   384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
           115           120           125

tca gca gcg ctg tta cgc act att aca gcc gat acc ttc cgt aaa ctg   432
Ser Ala Ala Leu Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
           130           135           140

ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg   480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
           145           150           155           160

ggt gag gct tgt cgc tga
Gly Glu Ala Cys Arg *   498
           165

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<210> 62

<211> 165

<212> PRT

<213> Homo sapiens

<400> 62

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Ile Thr Gly Cys
           20           25           30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
           35           40           45

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Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Trp Glu Gln Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Leu Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 63

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 63

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

gaa gtt tgg cag gga ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta act tcc agt cag gct cgg gaa cga tta cag ttg 288
 Gln Thr Leu Leu Val Thr Ser Ser Gln Ala Arg Glu Arg Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

```

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                      120                      125

tca gca gcg ccg tta cgc act att acg gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                      135                      140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145                      150                      155                      160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 64
<211> 165
<212> PRT
<213> Homo sapiens

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<400> 64
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35          40          45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65          70          75          80
Gln Thr Leu Leu Val Thr Ser Ser Gln Ala Arg Glu Arg Leu Gln Leu
      85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100         105         110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115         120         125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130         135         140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145         150         155         160
Gly Glu Ala Cys Arg
      165

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<210> 65
<211> 498
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS

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<222> (1) ... (498)

<400> 65

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30

gga gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Gly Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65           70           75           80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85           90           95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115          120          125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130          135          140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg 480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
          145          150          155          160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 66

<211> 165

<212> PRT

<213> Homo sapiens

<400> 66

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
20           25           30
Gly Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
35           40           45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
130          135          140
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
165

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<210> 67

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 67

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
20           25           30

gca gaa cat tgc tca ctg aac gag agt att act gta ccg gat gcg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ala Lys
35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80

caa act tta ctg gta aat tcc agt cag gct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Trp Glu Pro Leu Gln Leu

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	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggg gag gct tgt ccc tga				498
Gly Glu Ala Cys Pro *				
	165			

<210> 68
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 68
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ala Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Pro
 165

<210> 69
 <211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1) ... (498)

<400> 69

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35             40             45

gtc aac gtc tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65             70             75             80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130             135             140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
      145             150             155             160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 70

<211> 165

<212> PRT

<213> Homo sapiens

<400> 70

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
             20             25             30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
             35             40             45
Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
             50             55             60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65             70             75             80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
             85             90             95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
             100            105            110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
             115            120            125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
             130            135            140
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
145            150            155            160
Gly Glu Ala Cys Arg
             165

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<210> 71

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 71

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
             20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa     144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
             35             40             45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg     192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
             50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt     240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta agt tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgt act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 72

<211> 165

<212> PRT

<213> Homo sapiens

<400> 72

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 73
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1) ... (498)

<400> 73
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gaa gaa aat tgc tca ctg aac gag agt att act gta ccg gat acg aaa 144
 Glu Glu Asn Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta att tcc agt cag tct cgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Ile Ser Ser Gln Ser Arg Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *

165

<210> 74
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 74
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Glu Glu Asn Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Ser Arg Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 75
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 75
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgt tca ctg aac gag aat att act gta ccg gat tcg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
 35 40 45

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gtc aac ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50                      55                      60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65                      70                      75                      80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
                      85                      90                      95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
    100                      105                      110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130                      135                      140

ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
    145                      150                      155                      160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
    165

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<210> 76
<211> 165
<212> PRT
<213> Homo sapiens

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<400> 76
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
    20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
    35          40          45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65          70          75          80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
    85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
    100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115          120          125

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Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 77

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 77

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

gta gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Val Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta aat tcc agt cag gct agg gaa caa tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Arg Glu Gln Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca acg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Thr Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480

Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 78
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 78
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Val Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Arg Glu Gln Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Thr Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 79
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 79
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

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gga gaa cat tgc tca ctg aac gag act att act gta ccg gat acg aaa 144
Gly Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
    35                40                45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50                55                60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65                70                75                80

caa act tta ctg gta act tcc agt cag tct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Thr Ser Ser Gln Ser Trp Glu Pro Leu Gln Leu
    85                90                95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
    100                105                110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115                120                125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130                135                140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
    145                150                155                160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
    165

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<210> 80

<211> 165

<212> PRT

<213> Homo sapiens

<400> 80

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
    20          25          30
Gly Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
    35          40          45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65          70          75          80
Gln Thr Leu Leu Val Thr Ser Ser Gln Ser Trp Glu Pro Leu Gln Leu

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<400> 81																
atg	gat	atc	gcc	ccg	ccc	cgt	ctg	att	tgc	gac	agc	agg	gtg	cta	gaa	48
Met	Asp	Ile	Ala	Pro	Pro	Arg	Leu	Ile	Cys	Asp	Ser	Arg	Val	Leu	Glu	
1			5			10			15							
aga	tac	ctg	ctc	gaa	gcg	aaa	gag	gct	gaa	act	atc	acc	aca	ggc	tgt	96
Arg	Tyr	Leu	Leu	Glu	Ala	Lys	Glu	Ala	Glu	Thr	Ile	Thr	Thr	Gly	Cys	
			20			25			30							
gca	gaa	cat	tgc	tca	ctg	aac	gag	aat	att	act	gta	ccg	gat	acg	aaa	144
Ala	Glu	His	Cys	Ser	Leu	Asn	Glu	Asn	Ile	Thr	Val	Pro	Asp	Thr	Lys	
35			40			45										
gtc	aac	ttt	tat	gcc	tgg	aaa	cga	atg	gaa	gtt	gga	caa	cag	gcg	gtg	192
Val	Asn	Phe	Tyr	Ala	Trp	Lys	Arg	Met	Glu	Val	Gly	Gln	Gln	Ala	Val	
50			55			60										
gaa	gtt	tgg	cag	ggg	ctt	gcc	ctg	ttg	tcg	gag	gca	gtc	ctg	cgg	ggg	240
Glu	Val	Trp	Gln	Gly	Leu	Ala	Leu	Leu	Ser	Glu	Ala	Val	Leu	Arg	Gly	
65			70			75			80							
caa	act	tta	ctg	gta	aat	tcc	agt	cag	tct	tgg	gaa	cca	tta	cag	ttg	288
Gln	Thr	Leu	Leu	Val	Asn	Ser	Ser	Gln	Ser	Trp	Glu	Pro	Leu	Gln	Leu	
			85			90			95							
cac	gtg	gat	aag	gcg	gtt	tct	ggc	ctg	cgc	agc	ctt	acc	acg	ctg	ctc	336
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Arg	Ser	Leu	Thr	Thr	Leu	Leu	
100			105			110										
cgt	gca	ctg	ggg	gcc	caa	aaa	gaa	gct	atc	tcg	ccg	cct	gac	gcg	gcc	384
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala	
115			120			125										

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 82
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 82
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 83
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 83
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
aga tac ctg ttc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Phe Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30

gaa gaa aat tgc tca ctg aac gag agt att act gta ccg gat acg aaa 144
Glu Glu Asn Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys
          35           40           45

gtc aac ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65           70           75           80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cta tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Leu Leu Gln Leu
          85           90           95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100           105           110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115           120           125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130           135           140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145           150           155           160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 84

<211> 165

<212> PRT

<213> Homo sapiens

<400> 84

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15
Arg Tyr Leu Phe Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30
Glu Glu Asn Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys
          35           40           45

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Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Leu Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 85

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 85

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc act aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat gcg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
 35 40 45

gtc aac cta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

aaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Lys Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

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cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc      384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                      120                      125

tca gca gcg ccg tta tgc act att aca gcc gat acc ttc cgt aaa ctg      432
Ser Ala Ala Pro Leu Cys Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                      135                      140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg      480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145                      150                      155                      160

ggt gag gct tgt cgc tga                                          498
Gly Glu Ala Cys Arg *
      165

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<210> 86
<211> 165
<212> PRT
<213> Homo sapiens

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<400> 86
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
      20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
      35          40          45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50          55          60
Lys Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65          70          75          80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100         105         110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115         120         125
Ser Ala Ala Pro Leu Cys Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130         135         140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145         150         155         160
Gly Glu Ala Cys Arg
      165

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<210> 87
<211> 498
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS

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<222> (1) ... (498)

<400> 87

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30

gca gaa tat tgc tca ctg aac gag act att act gta ccg gat tcg aaa 144
Ala Glu Tyr Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Ser Lys
          35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65           70           75           80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85           90           95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100           105           110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115           120           125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130           135           140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145           150           155           160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 88

<211> 165

<212> PRT

<213> Homo sapiens

<400> 88

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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      1             5             10             15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20             25             30
Ala Glu Tyr Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Ser Lys
      35             40             45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50             55             60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65             70             75             80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85             90             95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100            105            110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115            120            125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130            135            140
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145            150            155            160
Gly Glu Ala Cys Arg
      165

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<210> 89

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 89

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
      1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
      20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat tcg aaa      144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
      35             40             45

gtc aac atg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg      192
Val Asn Met Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt      240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65             70             75             80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg      288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggt gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 90
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 90
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
 35 40 45
 Val Asn Met Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 91
 <211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 91

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1              5              10              15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
              20              25              30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa     144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
              35              40              45

gtt aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg     192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
              50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt     240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
              65              70              75              80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg     288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
              85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc     336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
              100              105              110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc     384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
              115              120              125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg     432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
              130              135              140

ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg     480
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
              145              150              155              160

ggg gag gct tgt cgc tga
Gly Glu Ala Cys Arg *
              165

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<210> 92

<211> 165

<212> PRT

<213> Homo sapiens

<400> 92

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
           20           25           30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
           35           40           45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
           50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
           85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
           100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
           115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
           130          135          140
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
           165

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<210> 93

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 93

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa   48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15

aga cac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt   96
Arg His Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
           20           25           30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat tcg aaa   144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
           35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg   192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
           50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt   240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat aca 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 94
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 94
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
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 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 95
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(498)

<400> 95
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa aat tgc tca ctg aac gag att att act gta ccg gat acg aaa 144
 Ala Glu Asn Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag act tgg gaa caa tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Trp Glu Gln Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *

165

<210> 96
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 96
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 1 5 10 15
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 20 25 30
 Ala Glu Asn Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Trp Glu Gln Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

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 <212> DNA
 <213> Homo sapiens

<220>
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 <222> (1)...(498)

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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 98
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 98
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 99
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 <213> Homo sapiens

<220>
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 <222> (1)...(498)

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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta cca gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480

Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 100
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 100
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
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 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

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<220>
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 <222> (1)...(498)

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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

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gta gaa cat tgc tca ctg aac gag att att act gta ccg gat ccg aaa 144
Val Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Pro Lys
      35              40              45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130             135             140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145             150             155             160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 102

<211> 165

<212> PRT

<213> Homo sapiens

<400> 102

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1      5      10      15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20      25      30
Val Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Pro Lys
      35      40      45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50      55      60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65      70      75      80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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				85					90					95					
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Arg	Ser	Leu	Thr	Thr	Leu	Leu				
			100					105						110					
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala				
		115					120						125						
Ser	Ala	Ala	Pro	Leu	Arg	Thr	Ile	Thr	Ala	Asp	Thr	Phe	Arg	Lys	Leu				
		130				135						140							
Phe	Arg	Val	Tyr	Ser	Asn	Phe	Leu	Arg	Gly	Lys	Leu	Lys	Leu	Tyr	Thr				
145					150					155					160				
Gly	Glu	Ala	Cys	Arg															
				165															

<210> 103

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 103

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Met	Asp	Ile	Ala	Pro	Pro	Arg	Leu	Ile	Cys	Asp	Ser	Arg	Val	Leu	Glu	
1			5					10					15			
aga	tac	ctg	ctc	gaa	gcg	aaa	gag	gct	gaa	agt	atc	acc	aca	ggc	tgt	96
Arg	Tyr	Leu	Leu	Glu	Ala	Lys	Glu	Ala	Glu	Ser	Ile	Thr	Thr	Gly	Cys	
		20					25					30				
gta	gaa	cat	tgc	tca	ctg	aac	gag	act	att	act	gta	ccg	gat	acg	aaa	144
Val	Glu	His	Cys	Ser	Leu	Asn	Glu	Thr	Ile	Thr	Val	Pro	Asp	Thr	Lys	
		35				40						45				
gtc	aac	ttt	tat	gcc	tgg	aaa	cga	atg	gaa	gtt	gga	caa	cag	gcg	gtg	192
Val	Asn	Phe	Tyr	Ala	Trp	Lys	Arg	Met	Glu	Val	Gly	Gln	Gln	Ala	Val	
	50					55				60						
gaa	gtt	tgg	cag	ggg	ctt	gcc	ctg	ttg	tcg	gag	gca	gtc	ctg	cgg	ggt	240
Glu	Val	Trp	Gln	Gly	Leu	Ala	Leu	Leu	Ser	Glu	Ala	Val	Leu	Arg	Gly	
	65				70				75					80		
caa	act	tta	ctg	gta	agt	tcc	agt	cag	cct	tgg	gaa	cca	tta	cag	ttg	288
Gln	Thr	Leu	Leu	Val	Ser	Ser	Ser	Gln	Pro	Trp	Glu	Pro	Leu	Gln	Leu	
			85					90					95			
cac	gtg	gat	aag	gcg	gtt	tct	ggc	ctg	tgc	agc	ttt	acc	acg	ctg	ctc	336
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Cys	Ser	Phe	Thr	Thr	Leu	Leu	
		100					105						110			
cgt	gca	ctg	ggt	gcc	caa	aaa	gaa	gct	atc	tcg	ccg	cct	gac	gcg	gcc	384
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala	
		115					120					125				

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 104
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 104
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30
 Val Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Cys Ser Phe Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 105
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 105
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

1	5	10	15	
aga tac ctg ctc	gaa gcg aaa gag gct	gaa aat atc acc	aca ggc tgt	96
Arg Tyr Leu Leu	Glu Ala Lys Glu	Ala Glu Asn Ile	Thr Thr Gly Cys	
	20	25	30	
gca gaa aat tgc	tca ctg aac gag att	att act gta ccg	gat tcg aaa	144
Ala Glu Asn Cys	Ser Leu Asn Glu	Ile Ile Thr Val	Pro Asp Ser Lys	
	35	40	45	
gtc aac ttt tat	gcc tgg aaa cga atg	gaa gtt gga caa	cag gcg gtg	192
Val Asn Phe Tyr	Ala Trp Lys Arg	Met Glu Val Gly	Gln Gln Ala Val	
	50	55	60	
gaa gtt tgg cag	ggg ctt gcc ctg	ttg tcg gag gca	gtc ctg cgg ggt	240
Glu Val Trp Gln	Gly Leu Ala Leu	Leu Ser Glu Ala	Val Leu Arg Gly	
	65	70	75	80
caa act tta ctg	gta aat tcc agt	cag cct ggg gaa	cta tta cag ttg	288
Gln Thr Leu Leu	Val Asn Ser Ser	Gln Pro Gly Glu	Leu Leu Gln Leu	
	85	90	95	
cac gtg gat aag	gcg gtt tct ggc	ctg cgc agc ctt	acc acg ctg ctc	336
His Val Asp Lys	Ala Val Ser Gly	Leu Arg Ser Leu	Thr Thr Leu Leu	
	100	105	110	
cgt gca ctg ggt	gcc caa aaa gaa	gct atc tcg ccg	cct gac gcg gcc	384
Arg Ala Leu Gly	Ala Gln Lys Glu	Ala Ile Ser Pro	Pro Asp Ala Ala	
	115	120	125	
tca gca gcg ccg	tta cgc act att	aca gcc gat acc	ttc cgt aaa ctg	432
Ser Ala Ala Pro	Leu Arg Thr Ile	Thr Ala Asp Thr	Phe Arg Lys Leu	
	130	135	140	
ttt cgc gtc tac	tcc aac ttc ttg	cgt ggc aaa ctg	aaa ctt tat acg	480
Phe Arg Val Tyr	Ser Asn Phe Leu	Arg Gly Lys Leu	Lys Leu Tyr Thr	
	145	150	155	160
ggt gag gct tgt	cgc tga			498
Gly Glu Ala Cys	Arg *			
	165			

<210> 106

<211> 165

<212> PRT

<213> Homo sapiens

<400> 106

Met Asp Ile Ala	Pro Pro Arg Leu	Ile Cys Asp Ser	Arg Val Leu Glu
1	5	10	15
Arg Tyr Leu Leu	Glu Ala Lys Glu	Ala Glu Asn Ile	Thr Thr Gly Cys
	20	25	30
Ala Glu Asn Cys	Ser Leu Asn Glu	Ile Ile Thr Val	Pro Asp Ser Lys
	35	40	45

Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Gly Glu Leu Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 107

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 107

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30

gga gaa gat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Gly Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 108

<211> 165

<212> PRT

<213> Homo sapiens

<400> 108

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30
 Gly Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 109

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 109

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa   48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt   96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
             20             25             30

gaa gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa  144
Glu Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
             35             40             45

gtc agc ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg  192
Val Ser Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
             50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt  240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
             65             70             75             80

caa act tta ctg gta aat tcc agt cag cct ggg gaa cta tta cag ttg  288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Gly Glu Leu Leu Gln Leu
             85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc  336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
             100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc  384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
             115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg  432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
             130             135             140

ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg  480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
             145             150             155             160

ggg gag gct tgt cgc tga
Gly Glu Ala Cys Arg  *
             165

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<210> 110

<211> 165

<212> PRT

<213> Homo sapiens

<400> 110

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
          20           25           30
Glu Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45
Val Ser Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Gly Glu Leu Leu Gln Leu
          85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130          135          140
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
          165

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<210> 111

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1) ... (498)

<400> 111

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
          20           25           30

gga gaa gat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Gly Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65           70           75           80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg				480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr				
	145	150	155	160
ggg gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 112
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 112
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
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 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 Gly Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 113
 <211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 113

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
          20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35             40             45

gtc aac ctt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65             70             75             80

caa act tta ctg gta agt tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100             105             110

cgt gca ctg ggt gcc caa aaa gaa gtt atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Val Ile Ser Pro Pro Asp Ala Ala
          115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130             135             140

ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145             150             155             160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 114

<211> 165

<212> PRT

<213> Homo sapiens

<400> 114

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
          20           25           30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Val Ile Ser Pro Pro Asp Ala Ala
          115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130          135          140
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
          165

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<210> 115

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 115

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa   48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt   96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
          20           25           30

gta gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa  144
Val Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg  192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60

gaa gtt tgg caa ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt  240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag gct ggg gaa cga tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Gly Glu Arg Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 116

<211> 165

<212> PRT

<213> Homo sapiens

<400> 116

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30
 Val Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Gly Glu Arg Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 117

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 117

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa	48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu	
1 5 10 15	
aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt	96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys	
20 25 30	
gga gaa cat tgc tca ctg aac gag act att act gta ccg gat tcg aaa	144
Gly Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Ser Lys	
35 40 45	
gtc aac gtt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg	192
Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val	
50 55 60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt	240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly	
65 70 75 80	
caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg	288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu	
85 90 95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc	336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu	
100 105 110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc	384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala	
115 120 125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg	432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu	
130 135 140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg	480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr	
145 150 155 160	
ggt gag gct tgt cgc tga	498
Gly Glu Ala Cys Arg *	

165

<210> 118
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 118
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30
 Gly Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Ser Lys
 35 40 45
 Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 119
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 119
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag agt att act gta ccg gat tcg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ser Lys
 35 40 45

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gtc aac ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50                      55                      60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65                      70                      75                      80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
                      85                      90                      95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
                      100                      105                      110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130                      135                      140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
    145                      150                      155                      160

ggt gag gct tgt cgc tga
Gly Glu Ala Cys Arg * 498
                      165

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<210> 120

<211> 165

<212> PRT

<213> Homo sapiens

<400> 120

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1                      5                      10                      15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
    20                      25                      30
Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ser Lys
    35                      40                      45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50                      55                      60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
    65                      70                      75                      80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
    85                      90                      95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
    100                      105                      110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115                      120                      125

```

Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 121
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 121
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa gat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480

Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga
 Gly Glu Ala Cys Arg *
 165

498

<210> 122
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 122
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 123
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 123
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30

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gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80

caa act tta ctg gta aat tcc agt cag cct cgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Arg Glu Pro Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130             135             140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145             150             155             160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 124

<211> 165

<212> PRT

<213> Homo sapiens

<400> 124

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1              5              10              15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
      20              25              30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Arg Glu Pro Leu Gln Leu

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<400> 125																			
atg	gat	atc	gcc	tcg	ccc	cgt	ctg	att	tgc	gac	agc	agg	gtg	cta	gaa	48			
Met	Asp	Ile	Ala	Ser	Pro	Arg	Leu	Ile	Cys	Asp	Ser	Arg	Val	Leu	Glu				
1				5			10						15						
aga	tac	ctg	ctc	gaa	gcg	aaa	gag	gct	gaa	agt	atc	acc	aca	ggc	tgt	96			
Arg	Tyr	Leu	Leu	Glu	Ala	Lys	Glu	Ala	Glu	Ser	Ile	Thr	Thr	Gly	Cys				
				20			25						30						
gta	gaa	gat	tgc	tca	ctg	aac	gag	aat	att	act	gta	ccg	gat	acg	aaa	144			
Val	Glu	Asp	Cys	Ser	Leu	Asn	Glu	Asn	Ile	Thr	Val	Pro	Asp	Thr	Lys				
35				40						45									
gtc	aac	ttt	tat	gcc	tgg	aaa	cga	atg	gaa	gtt	gga	caa	cag	gcg	gtg	192			
Val	Asn	Phe	Tyr	Ala	Trp	Lys	Arg	Met	Glu	Val	Gly	Gln	Gln	Ala	Val				
50				55						60									
gaa	gtt	tgg	cag	ggg	ctt	gcc	ctg	ttg	tcg	gag	gca	gtc	ctg	cgg	ggg	240			
Glu	Val	Trp	Gln	Gly	Leu	Ala	Leu	Leu	Ser	Glu	Ala	Val	Leu	Arg	Gly				
65				70						75						80			
caa	act	tta	ctg	gta	agt	tcc	agt	cag	cct	tgg	gaa	cca	tta	cag	ttg	288			
Gln	Thr	Leu	Leu	Val	Ser	Ser	Ser	Gln	Pro	Trp	Glu	Pro	Leu	Gln	Leu				
				85			90						95						
cac	gtg	gat	aag	gcg	gtt	tct	ggc	ctg	cgc	agc	ctt	acc	acg	ctg	ctc	336			
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Arg	Ser	Leu	Thr	Thr	Leu	Leu				
100				105						110									
cgt	gca	ctg	ggg	gcc	caa	aaa	gaa	gct	atc	tcg	ccg	cct	gac	gcg	gcc	384			
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala				
115				120						125									

```

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130                135                140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145                150                155                160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
    165

```

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<210> 126
<211> 165
<212> PRT
<213> Homo sapiens

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<400> 126
Met Asp Ile Ala Ser Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1      5      10      15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
    20      25      30
Val Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
    35      40      45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
    50      55      60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65      70      75      80
Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
    85      90      95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
    100     105     110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
    115     120     125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
    130     135     140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145     150     155     160
Gly Glu Ala Cys Arg
    165

```

```

<210> 127
<211> 498
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS
<222> (1)...(498)

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<400> 127
atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1	5	10	15	
aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt				96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys				
	20	25	30	
gca gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa				144
Ala Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys				
	35	40	45	
gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg				192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt				240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg				288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu				
	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa att tat acg				480
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr				
	145	150	155	160
ggt gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 128

<211> 165

<212> PRT

<213> Homo sapiens

<400> 128

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys				
	35	40	45	

```

Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65          70          75          80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100         105         110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115         120         125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130         135         140
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
      165

```

<210> 129

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 129

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20          25          30

gta gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa      144
Val Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35          40          45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg      192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50          55          60

gaa gtt tgg caa ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt      240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65          70          75          80

caa act tta ctg gta act tcc agt cag cct tgg gaa tca tta cag ttg      288
Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Ser Leu Gln Leu
      85          90          95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc      336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100         105         110

```

```

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                      135                      140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145                      150                      155                      160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

```

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<210> 130
<211> 165
<212> PRT
<213> Homo sapiens

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```

<400> 130
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1      5      10      15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20      25      30
Val Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35      40      45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50      55      60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65      70      75      80
Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Ser Leu Gln Leu
      85      90      95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100     105     110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115     120     125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130     135     140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145     150     155     160
Gly Glu Ala Cys Arg
      165

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<210> 131
<211> 498
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS

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<222> (1)...(498)

<400> 131

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1 5 10 15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
20 25 30

gaa gaa tat tgc tca ctg aac gag aat att act gta ccg gat gcg aaa 144
Glu Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65 70 75 80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145 150 155 160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
165

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<210> 132

<211> 165

<212> PRT

<213> Homo sapiens

<400> 132

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
                20           25           30
Glu Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
                35           40           45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
                50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
                85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
                100           105           110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
                115           120           125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
                130           135           140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145           150           155           160
Gly Glu Ala Cys Arg
                165

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<210> 133

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 133

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
                20           25           30

gca gaa gat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
                35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
                50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cggt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg				480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr				
	145	150	155	160
ggg gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 134
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 134
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 135
 <211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 135

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20             25             30

gca gaa tat tgc tca ctg aac gag agt att act gta ccg gat tcg aaa     144
Ala Glu Tyr Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ser Lys
          35             40             45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg     192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt     240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65             70             75             80

caa act tta ctg gta agt tcc agt cag cct ggg gaa caa tta cag ttg     288
Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Gly Glu Gln Leu Gln Leu
          85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc     336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100            105            110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc     384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115            120            125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg     432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130            135            140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg     480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145            150            155            160

ggt gag gct tgt cgc tga                                           498
Gly Glu Ala Cys Arg *
          165

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<210> 136

<211> 165

<212> PRT

<213> Homo sapiens

<400> 136

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1              5              10              15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
              20              25              30
Ala Glu Tyr Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ser Lys
              35              40              45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
              50              55              60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65              70              75              80
Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Gly Glu Gln Leu Gln Leu
              85              90              95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
              100             105             110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
              115             120             125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
              130             135             140
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145             150             155             160
Gly Glu Ala Cys Arg
              165

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<210> 137

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 137

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc aag gtg cta gaa   48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Lys Val Leu Glu
 1              5              10              15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt   96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
              20              25              30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa  144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
              35              40              45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg  192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
              50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt  240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag act tgg gaa cta tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Trp Glu Leu Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 138

<211> 165

<212> PRT

<213> Homo sapiens

<400> 138

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Lys Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Ile Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Thr Trp Glu Leu Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 139
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 139
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gta gaa gat tgc tca ctg aac gag act att act gta ccg gat acg aaa 144
 Val Glu Asp Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta act tcc agt cag gct cgg gaa caa tta cag ttg 288
 Gln Thr Leu Leu Val Thr Ser Ser Gln Ala Arg Glu Gln Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *

165

<210> 140
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 140
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Val Glu Asp Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Thr Ser Ser Gln Ala Arg Glu Gln Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 141
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 141
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag agt att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg' gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 142
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 142
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 143

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 143

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15

aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc cgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta act tcc agt cag gct tgg gaa cga tta cag ttg 288
 Gln Thr Leu Leu Val Thr Ser Ser Gln Ala Trp Glu Arg Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg 480

Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga
 Gly Glu Ala Cys Arg *
 165

498

<210> 144
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 144
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Thr Ser Ser Gln Ala Trp Glu Arg Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 145
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 145
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30

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gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100              105              110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115              120              125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130              135              140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145              150              155              160

ggt gag gct tgt cgc tga
Gly Glu Ala Cys Arg * 498
      165

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<210> 146

<211> 165

<212> PRT

<213> Homo sapiens

<400> 146

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1              5              10              15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
      20              25              30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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<400> 147																
atg	gat	atc	gcc	cgc	ccc	cgt	ctg	att	tgc	gac	agc	agg	gtg	cta	gaa	48
Met	Asp	Ile	Ala	Pro	Pro	Arg	Leu	Ile	Cys	Asp	Ser	Arg	Val	Leu	Glu	
1			5			10			15							
aga	tac	ctg	ctc	gaa	gcg	aaa	gag	gct	gaa	aat	atc	acc	aca	ggc	tgt	96
Arg	Tyr	Leu	Leu	Glu	Ala	Lys	Glu	Ala	Glu	Asn	Ile	Thr	Thr	Gly	Cys	
			20			25			30							
gta	gaa	cat	tgc	tca	ctg	aac	gag	aat	att	act	gta	ccg	gat	acg	aaa	144
Val	Glu	His	Cys	Ser	Leu	Asn	Glu	Asn	Ile	Thr	Val	Pro	Asp	Thr	Lys	
35			40			45										
gtc	aac	ttt	tat	gcc	tgg	aaa	cga	atg	gaa	gtt	gga	caa	cag	gcg	gtg	192
Val	Asn	Phe	Tyr	Ala	Trp	Lys	Arg	Met	Glu	Val	Gly	Gln	Gln	Ala	Val	
50			55			60										
gaa	gtt	tgg	cag	ggg	ctt	gcc	ctg	ttg	tgc	gag	gca	gtc	ctg	cag	ggg	240
Glu	Val	Trp	Gln	Gly	Leu	Ala	Leu	Leu	Ser	Glu	Ala	Val	Leu	Gln	Gly	
65			70			75			80							
caa	act	tta	ctg	gta	aat	tcc	agt	cag	cct	tgg	gaa	cta	tta	cag	ttg	288
Gln	Thr	Leu	Leu	Val	Asn	Ser	Ser	Gln	Pro	Trp	Glu	Leu	Leu	Gln	Leu	
			85			90			95							
cac	gtg	gat	aag	gcg	gtt	tct	ggc	ctg	cgc	agc	ctt	acc	acg	ctg	ctc	336
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Arg	Ser	Leu	Thr	Thr	Leu	Leu	
			100			105			110							
cgt	gca	ctg	ggg	gcc	caa	aaa	gaa	gct	atc	tgc	ccg	cct	gac	gcg	gcc	384
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala	
115			120			125										

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 148

<211> 165

<212> PRT

<213> Homo sapiens

<400> 148

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Val Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Gln Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Leu Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 149

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 149

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

1	5	10	15	
aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt				96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
gca gaa cat tgc tca ctg aac gag agt att act gta ccg gat acg aaa				144
Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys				
	35	40	45	
gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg				192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt				240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg				288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu				
	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggg gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 150

<211> 165

<212> PRT

<213> Homo sapiens

<400> 150

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys				
	35	40	45	

Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 151
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 151
 atg gat atc gcc ccg cdc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat gcg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
 35 40 45
 gtc aac gta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag tct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

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cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                120                125

tca gca gcg ccg tta cac act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu His Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                135                140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145                150                155                160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 152
<211> 165
<212> PRT
<213> Homo sapiens

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<400> 152
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1      5      10      15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
      20      25      30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
      35      40      45
Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50      55      60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65      70      75      80
Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Trp Glu Pro Leu Gln Leu
      85      90      95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100     105     110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115     120     125
Ser Ala Ala Pro Leu His Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130     135     140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145     150     155     160
Gly Glu Ala Cys Arg
      165

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<210> 153
<211> 498
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS

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<222> (1)...(498)

<400> 153

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1 5 10 15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
20 25 30

gca gaa cat tgc tca ctg aac gag att att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys
35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65 70 75 80

caa act tta ctg gta aat tcc agt cag gct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Trp Glu Pro Leu Gln Leu
85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
130 135 140

ttt cgc gtc tac tcc aac ttt ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145 150 155 160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
165

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<210> 154

<211> 165

<212> PRT

<213> Homo sapiens

<400> 154

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
                20           25           30
Ala Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys
                35           40           45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
                50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Asn Ser Ser Gln Ala Trp Glu Pro Leu Gln Leu
                85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
                100           105           110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
                115           120           125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
                130           135           140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145           150           155           160
Gly Glu Ala Cys Arg
                165

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<210> 155

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 155

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
                20           25           30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat tcg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
                35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
                50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
        65           70           75           80

caa act tta ctg gta att tcc agt cag cct ggg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Gly Glu Pro Leu Gln Leu

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	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggt gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 156

<211> 165

<212> PRT

<213> Homo sapiens

<400> 156

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1 5 10 15				
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
20 25 30				
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys				
35 40 45				
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val				
50 55 60				
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
65 70 75 80				
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Gly Glu Pro Leu Gln Leu				
85 90 95				
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
100 105 110				
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
115 120 125				
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
130 135 140				
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
145 150 155 160				
Gly Glu Ala Cys Arg				
165				

<210> 157

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 157

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa      144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35             40             45

gtc aac gta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg      192
Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt      240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65             70             75             80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg      288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc      336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc      384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg      432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130             135             140

ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg      480
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145             150             155             160

ggt gag gct tgt cgc tga                                          498
Gly Glu Ala Cys Arg  *
          165

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<210> 158

<211> 165

<212> PRT

<213> Homo sapiens

<400> 158

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45
Val Asn Val Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85           90           95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130          135          140
Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
          165

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<210> 159

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 159

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30

gaa gaa tat tgc tca ctg aac gag act att act gta ccg gat acg aaa      144
Glu Glu Tyr Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
          35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cgg gcg gtg      192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Arg Ala Val
          50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt      240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta att tcc agt cag tct agg gaa cga tta cag ttg 288
 Gln Thr Leu Leu Val Ile Ser Ser Gln Ser Arg Glu Arg Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 160

<211> 165

<212> PRT

<213> Homo sapiens

<400> 160

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Glu Glu Tyr Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Arg Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Ser Arg Glu Arg Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 161

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 161

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20             25             30

gca gaa cat tgc tca ctg aac gag act att act gta ccg gat acg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
          35             40             45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65             70             75             80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130             135             140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145             150             155             160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
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165

<210> 162
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 162
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 163
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 163
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gaa gaa cat tgc tca ctg aac gag att att act gta ccg gat acg aaa 144
 Glu Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys
 35 40 45

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gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg   192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50                      55                      60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt   240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65                      70                      75                      80

caa act tta ctg gta act tcc agt cag cct agg gaa caa tta cag ttg   288
Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Arg Glu Gln Leu Gln Leu
                      85                      90                      95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc   336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
                      100                      105                      110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc   384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
                      115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg   432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
                      130                      135                      140

ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg   480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
      145                      150                      155                      160

ggg gag gct tgt cgc tga                                           498
Gly Glu Ala Cys Arg *
                      165

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<210> 164

<211> 165

<212> PRT

<213> Homo sapiens

<400> 164

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1                      5                      10                      15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20                      25                      30
Glu Glu His Cys Ser Leu Asn Glu Ile Ile Thr Val Pro Asp Thr Lys
      35                      40                      45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50                      55                      60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65                      70                      75                      80
Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Arg Glu Gln Leu Gln Leu
      85                      90                      95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100                      105                      110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                      120                      125

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Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 165
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 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 165
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gta gaa gat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Val Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480

Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga
 Gly Glu Ala Cys Arg *
 165

498

<210> 166
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 166
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Val Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 167
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 167
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30

gca aaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Lys His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 168

<211> 165

<212> PRT

<213> Homo sapiens

<400> 168

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 Ala Lys His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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      85              90              95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100              105              110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115              120              125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130              135              140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145              150              155              160
Gly Glu Ala Cys Arg
      165

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<210> 169
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

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<400> 169
atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1              5              10              15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20              25              30

gca gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu Tyr Cys Ser Leu Asn Glu Ala Asn Ile Thr Val Pro Asp Thr Lys
      35              40              45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg ctg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Leu Gly
      65              70              75              80

caa act tta ctg gta act tcc agt cag cct tgg gaa tca tta cag ttg 288
Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Ser Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100              105              110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115              120              125

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tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggc gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 170
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 170
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Leu Gly
 65 70 75 80
 Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Ser Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 171
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 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 171
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

1	5	10	15	
aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt				96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa				144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys				
	35	40	45	
gtc aac ttt tat gcc cgg aaa cga atg gaa gtt gga caa cag gcg gtg				192
Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt				240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
cca act tta ctg gta act tcc agt cag cct tgg gaa cca tta cag ttg				288
Pro Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu				
	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggt gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 172

<211> 165

<212> PRT

<213> Homo sapiens

<400> 172

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys				
	35	40	45	

Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Pro Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 173
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 173
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag act att act gta ccg gat tcg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Ser Lys
 35 40 45
 gtc aac cta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa aat tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Asn Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

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cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                      120                      125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                      135                      140

ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aat ctt tat acg 480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Asn Leu Tyr Thr
      145                      150                      155                      160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 174
 <211> 165
 <212> PRT
 <213> Homo sapiens

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<400> 174
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
      20          25          30
Ala Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Ser Lys
      35          40          45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65          70          75          80
Gln Asn Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100         105         110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115         120         125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130         135         140
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Asn Leu Tyr Thr
      145         150         155         160
Gly Glu Ala Cys Arg
      165

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<210> 175
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
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<222> (1) ... (498)

<400> 175

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
          20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat tcg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
          35             40             45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65             70             75             80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130             135             140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
          145             150             155             160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 176

<211> 165

<212> PRT

<213> Homo sapiens

<400> 176

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
                20           25           30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
                35           40           45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
                50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
                85           90           95
His Val Asp Lys, Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
                100           105           110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
                115           120           125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
                130           135           140
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
145           150           155           160
Gly Glu Ala Cys Arg
                165

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<210> 177

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 177

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
                20           25           30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat gcg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
                35           40           45

gtc aac cta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
                50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80

caa act tta ctg gta aat tcc agt cag tct tgg gaa cga tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Trp Glu Arg Leu Gln Leu

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85										90										95										
cac	gtg	gat	aag	gcg	gtt	tct	ggc	ctg	cg	agc	ctt	acc	acg	ctg	ctc	336														
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Arg	Ser	Leu	Thr	Thr	Leu	Leu															
100					105					110																				
cg	t	gca	ctg	gg	t	gcc	caa	aaa	gaa	gct	atc	tcg	ccg	cct	gac	gcg	gcc	384												
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala															
115					120					125																				
tca	gca	gcg	ccg	tta	cg	c	act	att	aca	gcc	gat	acc	ttc	cg	t	aaa	ctg	432												
Ser	Ala	Ala	Pro	Leu	Arg	Thr	Ile	Thr	Ala	Asp	Thr	Phe	Arg	Lys	Leu															
130					135					140																				
ttt	cg	c	gtc	tac	tcc	aac	ttc	ttg	cg	t	ggc	aaa	ctg	aaa	ctt	tat	acg	480												
Phe	Arg	Val	Tyr	Ser	Asn	Phe	Leu	Arg	Gly	Lys	Leu	Lys	Leu	Tyr	Thr															
145					150					155					160															
gg	t	gag	gct	tgt	cg	c	tga											498												
Gly	Glu	Ala	Cys	Arg	*																									
165																														

<210> 178

<211> 165

<212> PRT

<213> Homo sapiens

<400> 178

Met	Asp	Ile	Ala	Pro	Pro	Arg	Leu	Ile	Cys	Asp	Ser	Arg	Val	Leu	Glu			
1				5					10					15				
Arg	Tyr	Leu	Leu	Glu	Ala	Lys	Glu	Ala	Glu	Asn	Ile	Thr	Thr	Gly	Cys			
		20						25					30					
Ala	Glu	His	Cys	Ser	Leu	Asn	Glu	Asn	Ile	Thr	Val	Pro	Asp	Ala	Lys			
		35				40						45						
Val	Asn	Leu	Tyr	Ala	Trp	Lys	Arg	Met	Glu	Val	Gly	Gln	Gln	Ala	Val			
	50					55					60							
Glu	Val	Trp	Gln	Gly	Leu	Ala	Leu	Leu	Ser	Glu	Ala	Val	Leu	Arg	Gly			
65					70					75					80			
Gln	Thr	Leu	Leu	Val	Asn	Ser	Ser	Gln	Ser	Trp	Glu	Arg	Leu	Gln	Leu			
			85					90						95				
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Arg	Ser	Leu	Thr	Thr	Leu	Leu			
		100						105					110					
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala			
		115					120						125					
Ser	Ala	Ala	Pro	Leu	Arg	Thr	Ile	Thr	Ala	Asp	Thr	Phe	Arg	Lys	Leu			
	130					135					140							
Phe	Arg	Val	Tyr	Ser	Asn	Phe	Leu	Arg	Gly	Lys	Leu	Lys	Leu	Tyr	Thr			
145					150					155					160			
Gly	Glu	Ala	Cys	Arg														
				165														

<210> 179

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 179

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
          20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat tcg aaa 144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
          35             40             45

gtc aac atc tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Ile Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65             70             75             80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85             90             95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130             135             140

ttt cgc gtc tac tcc aac ttc ttg cgt ggt aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145             150             155             160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 180

<211> 165

<212> PRT

<213> Homo sapiens

<400> 180

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
          20             25             30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ser Lys
          35             40             45
Val Asn Ile Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65             70             75             80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85             90             95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100            105            110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115            120            125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130            135            140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145            150            155            160
Gly Glu Ala Cys Arg
          165

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<210> 181

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 181

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
          20             25             30

gca gaa cat tgt tca ctg aac gag aat att act gta ccg gat gcg aaa      144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
          35             40             45

gtc aac ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg      192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt      240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag tct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 182

<211> 165

<212> PRT

<213> Homo sapiens

<400> 182

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Ala Lys
 35 40 45
 Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 183
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 183
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30
 gga gaacat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Gly Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg 480
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *

165

<210> 184
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 184
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30
 Gly Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 185
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 185
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gta gaa aat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Val Glu Asn Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

caa act tta ctg gta aat tcc agt cag tct agg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Arg Glu Pro Leu Gln Leu
 85 90 95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg 480
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 186

<211> 165

<212> PRT

<213> Homo sapiens

<400> 186

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15

Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30

Val Glu Asn Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45

Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60

Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80

Gln Thr Leu Leu Val Asn Ser Ser Gln Ser Arg Glu Pro Leu Gln Leu
 85 90 95

His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 187
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 187
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa act atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta agt tcc agt cag cct cgg gaa cga tta cag ttg 288
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Arg Glu Arg Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg 480

Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga
 Gly Glu Ala Cys Arg *
 165

498

<210> 188
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 188
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Thr Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Arg Glu Arg Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 189
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 189
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30

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gaa gaa gat tgc tca ctg aac gag aat att act gta ccg gat ccg aaa 144
Glu Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Pro Lys
      35              40              45

gtc aac atg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Met Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65              70              75              80

caa act tta ctg gta att tcc agt cag tct agg gaa cta tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Ser Arg Glu Leu Leu Gln Leu
      85              90              95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100              105              110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115              120              125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130              135              140

ttt cgc gtc tac acc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Thr Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145              150              155              160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
      165

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<210> 190

<211> 165

<212> PRT

<213> Homo sapiens

<400> 190

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1      5      10      15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
      20      25      30
Glu Glu Asp Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Pro Lys
      35      40      45
Val Asn Met Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50      55      60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65      70      75      80
Gln Thr Leu Leu Val Ile Ser Ser Gln Ser Arg Glu Leu Leu Gln Leu

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<400> 191																	
atg	gat	atc	gcc	ccg	ccc	cgt	ctg	att	tgc	gac	agc	agg	gtg	cta	gaa	48	
Met	Asp	Ile	Ala	Pro	Pro	Arg	Leu	Ile	Cys	Asp	Ser	Arg	Val	Leu	Glu		
1				5			10						15				
aga	tac	ctg	ctc	gaa	gcg	aaa	gag	gct	gaa	aat	atc	acc	aca	ggc	tgt	96	
Arg	Tyr	Leu	Leu	Glu	Ala	Lys	Glu	Ala	Glu	Asn	Ile	Thr	Thr	Gly	Cys		
20				25						30							
gca	gaa	cat	tgc	tca	ctg	aac	gag	act	att	act	gta	ccg	gat	gcg	aaa	144	
Ala	Glu	His	Cys	Ser	Leu	Asn	Glu	Thr	Ile	Thr	Val	Pro	Asp	Ala	Lys		
35				40						45							
gtc	aac	att	tat	gcc	tgg	aaa	cga	atg	gaa	gtt	gga	caa	cag	gcg	gtg	192	
Val	Asn	Ile	Tyr	Ala	Trp	Lys	Arg	Met	Glu	Val	Gly	Gln	Gln	Ala	Val		
50				55						60							
gaa	gtt	tgg	cag	ggg	ctt	gcc	ctg	ttg	tcg	gag	gca	gtc	ctg	cgg	ggg	240	
Glu	Val	Trp	Gln	Gly	Leu	Ala	Leu	Leu	Ser	Glu	Ala	Val	Leu	Arg	Gly		
65				70						75						80	
caa	act	tta	ctg	gta	att	tcc	agt	cag	cct	tgg	gaa	cca	tta	cag	ttg	288	
Gln	Thr	Leu	Leu	Val	Ile	Ser	Ser	Gln	Pro	Trp	Glu	Pro	Leu	Gln	Leu		
85				90						95							
cac	gtg	gat	aag	gcg	gtt	tct	ggc	ctg	cgc	agc	ctt	acc	acg	ctg	ctc	336	
His	Val	Asp	Lys	Ala	Val	Ser	Gly	Leu	Arg	Ser	Leu	Thr	Thr	Leu	Leu		
100				105						110							
cgt	gca	ctg	ggg	gcc	caa	aaa	gaa	gct	atc	tgc	ccg	cct	gac	gcg	gcc	384	
Arg	Ala	Leu	Gly	Ala	Gln	Lys	Glu	Ala	Ile	Ser	Pro	Pro	Asp	Ala	Ala		
115				120						125							

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggc gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 192

<211> 165

<212> PRT

<213> Homo sapiens

<400> 192

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Thr Ile Thr Val Pro Asp Ala Lys
 35 40 45
 Val Asn Ile Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 193

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 193

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

1	5	10	15	
aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt				96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa				144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys				
	35	40	45	
gtc aac ttt tat gcc cgg aaa cga atg gaa gtt gga caa cag gcg gtg				192
Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val				
	50	55	60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt				240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly				
	65	70	75	80
caa act tta ctg gta act tcc agt cag cct tgg gaa cca tta cag ttg				288
Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu				
	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr				
	145	150	155	160
ggg gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 194

<211> 165

<212> PRT

<213> Homo sapiens

<400> 194

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu				
1	5	10	15	
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys				
	20	25	30	
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys				
	35	40	45	

Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Thr Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 195
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

<400> 195
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 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta agt tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125

tca gca gcg cca tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 196
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 196
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ser Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 197
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS

<222> (1)...(498)

<400> 197

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg tta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
  1             5             10             15

aga tac ctg ttc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Phe Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20             25             30

gca gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35             40             45

gtc aac ttt tat gcc cgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65             70             75             80

caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85             90             95

cac gtg gat aag tcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ser Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100             105             110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115             120             125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130             135             140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
          145             150             155             160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 198

<211> 165

<212> PRT

<213> Homo sapiens

<400> 198

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu

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1           5           10           15
Arg Tyr Leu Phe Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
20           25           30
Ala Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
35           40           45
Val Asn Phe Tyr Ala Arg Lys Arg Met Glu Val Gly Gln Gln Ala Val
50           55           60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80
Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
85           90           95
His Val Asp Lys Ser Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
100          105          110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
115          120          125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
130          135          140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
145          150          155          160
Gly Glu Ala Cys Arg
165

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<210> 199
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(498)

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<400> 199
atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
1           5           10           15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
20           25           30

gca gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Ala Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
35           40           45

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65           70           75           80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

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	85	90	95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc				336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu				
	100	105	110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc				384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala				
	115	120	125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg				432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu				
	130	135	140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg				480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr				
	145	150	155	160
ggg gag gct tgt cgc tga				498
Gly Glu Ala Cys Arg *				
	165			

<210> 200
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 200
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 201
 <211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 201

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1           5           10          15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20           25           30

gga gaa tat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
Gly Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35           40           45

gtc aac gta tat gcc tgg gaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Val Tyr Ala Trp Glu Arg Met Glu Val Gly Gln Gln Ala Val
          50           55           60

gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
          65           70           75           80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
          85           90           95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100          105          110

cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115          120          125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130          135          140

ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
          145          150          155          160

ggg gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
          165

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<210> 202

<211> 165

<212> PRT

<213> Homo sapiens

<400> 202

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1              5              10              15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
              20              25              30
Gly Glu Tyr Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
              35              40              45
Val Asn Val Tyr Ala Trp Glu Arg Met Glu Val Gly Gln Gln Ala Val
              50              55              60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65              70              75              80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
              85              90              95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
              100             105             110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
              115             120             125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
              130             135             140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
145             150             155             160
Gly Glu Ala Cys Arg
              165

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<210> 203

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 203

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1              5              10              15

aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
              20              25              30

gca gaa cat tgc tta ctg aac gag att att act gta ccg gat tcg aaa      144
Ala Glu His Cys Leu Leu Asn Glu Ile Ile Thr Val Pro Asp Ser Lys
              35              40              45

gtc aac ttg tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg      192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
              50              55              60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt      240

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Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa ttt tat acg 480
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 204

<211> 165

<212> PRT

<213> Homo sapiens

<400> 204

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Leu Leu Asn Glu Ile Ile Thr Val Pro Asp Ser Lys
 35 40 45
 Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Phe Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg

165

<210> 205

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 205

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa	48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu	
1 5 10 15	
aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt	96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys	
20 25 30	
gca gaa cat tgc tca ctg aac gag agt att act gta ccg gat acg aaa	144
Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys	
35 40 45	
gtc aac cta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg	192
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val	
50 55 60	
gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt	240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly	
65 70 75 80	
caa act tta ctg gta agt tcc agt cag tct agg gaa caa tta cag ttg	288
Gln Thr Leu Leu Val Ser Ser Ser Gln Ser Arg Glu Gln Leu Gln Leu	
85 90 95	
cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc	336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu	
100 105 110	
cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc	384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala	
115 120 125	
tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg	432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu	
130 135 140	
ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa gtt tat acg	480
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr	
145 150 155 160	
ggt gag gct tgt cgc tga	498
Gly Glu Ala Cys Arg *	

165

<210> 206
 <211> 165
 <212> PRT
 <213> Homo sapiens

<400> 206

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Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1             5             10             15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
          20             25             30
Ala Glu His Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Thr Lys
          35             40             45
Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
          50             55             60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
65             70             75             80
Gln Thr Leu Leu Val Ser Ser Ser Gln Ser Arg Glu Gln Leu Gln Leu
          85             90             95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
          100            105            110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
          115            120            125
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
          130            135            140
Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Val Tyr Thr
145            150            155            160
Gly Glu Ala Cys Arg
          165

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<210> 207
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 207

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atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gta      48
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Val
 1             5             10             15

aga tac ctg ctc gaa gcg aaa gag gct gaa att atc acc aca ggc tgt      96
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
          20             25             30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa      144
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
          35             40             45

```

```

gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50                55                60

gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65                70                75                80

caa act tta ctg gta aat tcc agt cag cct tgg gaa cca tta cag ttg 288
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
              85                90                95

cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
              100                105                110

cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115                120                125

tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
      130                135                140

ttt cgc gtc tac gcc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
      145                150                155                160

ggt gag gct tgt cgc tga 498
Gly Glu Ala Cys Arg *
              165

```

<210> 208
 <211> 165
 <212> PRT
 <213> Homo sapiens

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<400> 208
Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Val
 1          5          10          15
Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ile Ile Thr Thr Gly Cys
      20          25          30
Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
      35          40          45
Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
      50          55          60
Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
      65          70          75          80
Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
      85          90          95
His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
      100         105         110
Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
      115         120         125

```

Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ala Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 209
 <211> 498
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1) ... (498)

<400> 209
 atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa aat atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 gca gaa gat tgc tca ctg aac gag agt att act gta ccg gat tcg aaa 144
 Ala Glu Asp Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ser Lys
 35 40 45
 gtc aac tta tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tcg gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta aat tcc agt cag cct ggg gaa caa tta cag ttg 288
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Gly Glu Gln Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tcg ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac tcc aac ttc ttg cgt ggc aaa ctg aaa att tat acg 480

Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160

ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 210

<211> 165

<212> PRT

<213> Homo sapiens

<400> 210

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu Asp Cys Ser Leu Asn Glu Ser Ile Thr Val Pro Asp Ser Lys
 35 40 45
 Val Asn Leu Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Asn Ser Ser Gln Pro Gly Glu Gln Leu Gln Leu
 85 90 95
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Ile Tyr Thr
 145 150 155 160
 Gly Glu Ala Cys Arg
 165

<210> 211

<211> 498

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)...(498)

<400> 211

atg gat atc gcc ccg ccc cgt ctg att tgc gac agc agg gtg cta gaa 48
 Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 aga tac ctg ctc gaa gcg aaa gag gct gaa agt atc acc aca ggc tgt 96
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30

gca gaa cat tgc tca ctg aac gag aat att act gta ccg gat acg aaa 144
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 gtc aac ttt tat gcc tgg aaa cga atg gaa gtt gga caa cag gcg gtg 192
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 gaa gtt tgg cag ggg ctt gcc ctg ttg tgc gag gca gtc ctg cgg ggt 240
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 caa act tta ctg gta att tcc agt cag cct tgg gaa cca tta cag ttg 288
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu
 85 90 95
 cac gtg gat aag gcg gtt tct ggc ctg cgc agc ctt acc acg ctg ctc 336
 His Val Asp Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu
 100 105 110
 cgt gca ctg ggt gcc caa aaa gaa gct atc tgc ccg cct gac gcg gcc 384
 Arg Ala Leu Gly Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala
 115 120 125
 tca gca gcg ccg tta cgc act att aca gcc gat acc ttc cgt aaa ctg 432
 Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu
 130 135 140
 ttt cgc gtc tac ccc aac ttc ttg cgt ggc aaa ctg aaa ctt tat acg 480
 Phe Arg Val Tyr Pro Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr
 145 150 155 160
 ggt gag gct tgt cgc tga 498
 Gly Glu Ala Cys Arg *
 165

<210> 212

<211> 165

<212> PRT

<213> Homo sapiens

<400> 212

Met Asp Ile Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu
 1 5 10 15
 Arg Tyr Leu Leu Glu Ala Lys Glu Ala Glu Ser Ile Thr Thr Gly Cys
 20 25 30
 Ala Glu His Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys
 35 40 45
 Val Asn Phe Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val
 50 55 60
 Glu Val Trp Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly
 65 70 75 80
 Gln Thr Leu Leu Val Ile Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu

- 165 -

act ctg ctt cgg gct ctg cga gcc cag aag gaa gcc atc tcc cct cca 628
 Thr Leu Leu Arg Ala Leu Arg Ala Gln Lys Glu Ala Ile Ser Pro Pro
 110 115 120

gat gcg gcc tca gct gct cca ctc cga aca atc act gct gac act ttc 676
 Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe
 125 130 135

cgc aaa ctc ttc cga gtc tac tcc aat ttc ctc cgg gga aag ctg aag 724
 Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys
 140 145 150

ctg tac aca ggg gag gcc tgc agg aca ggg gac aga tga ccaggtgtgt 773
 Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp Arg *
 155 160 165

ccacctgggc atatccacca cctccctcac caacattgct tgtgccacac cctccccgc 833
 cactcctgaa ccccgctcag gggctctcag ctcagcgcca gcctgtccca tggacactcc 893
 agtgccagca atgacatctc aggggccaga ggaactgtcc agagagcaac tctgagatct 953
 aaggatgtca cagggccaac ttgagggcc agagcaggaa gcattcagag agcagcttta 1013
 aactcaggga cagagccatg ctgggaagac gcctgagctc actcggcacc ctgcaaaatt 1073
 tgatgccagg acacgctttg gaggcgattt acctgttttc gcacctacca tcagggacag 1133
 gatgacctgg agaacttagg tggcaagctg tgacttctcc aggtctcacg ggcattgggca 1193
 ctcccttggt ggcaagagcc cccttgacac cggggtggtg ggaaccatga agacaggatg 1253
 ggggctggcc tctggctctc atggggtcca agttttgtgt attcttcaac ctcattgaca 1313
 agaactgaaa ccaccaaaaa aaaaaaaaaa 1342

<210> 214
 <211> 166
 <212> PRT
 <213> Homo sapiens

<400> 214
 Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu
 1 5 10 15
 Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His
 20 25 30
 Cys Ser Leu Asn Glu Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe
 35 40 45
 Tyr Ala Trp Lys Arg Met Glu Val Gly Gln Gln Ala Val Glu Val Trp
 50 55 60
 Gln Gly Leu Ala Leu Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu
 65 70 75 80
 Leu Val Asn Ser Ser Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp
 85 90 95
 Lys Ala Val Ser Gly Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu
 100 105 110
 Arg Ala Gln Lys Glu Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala
 115 120 125
 Pro Leu Arg Thr Ile Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val
 130 135 140
 Tyr Ser Asn Phe Leu Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala
 145 150 155 160
 Cys Arg Thr Gly Asp Arg
 165

<210> 215
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 215
 caggaattct gtttggaac tgtc

24

<210> 216
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 216
 actctcatcac catggaagct tgca

24

<210> 217
 <211> 567
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(567)

<400> 217
 atg ggc gtg cac gag tgc ccc gcc tgg ctg tgg ctg ctg ctg agc ctg 48
 Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
 1 5 10 15
 ctg agc ctg ccc ctg ggc ctg ccc gtg ctg ggc gcc ccc ccc cgg ctg 96
 Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
 20 25 30
 atc tgc gac agc cgg gtg ctg gag cgg tac ctg ctg gag gcc aag gag 144
 Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
 35 40 45
 gcc gag acc atc acc acc ggc tgc gtg gag gac tgc agc ctg aac gag 192
 Ala Glu Thr Ile Thr Thr Gly Cys Val Glu Asp Cys Ser Leu Asn Glu
 50 55 60
 aac atc acc gtg ccc gac acc aag gtg aac ttc tac gcc cgg aag cgg 240
 Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Arg Lys Arg
 65 70 75 80
 atg gag gtg ggc cag cag gcc gtg gag atc tgg cag gcc ctg gcc ctg 288

Met Glu Val Gly Gln Gln Ala Val Glu Ile Trp Gln Gly Leu Ala Leu
85 90 95

ctg agc gag gcc gtg ctg cgg ggc cag acc ctg ctg gtg atc agc agc 336
Leu Ser Glu Ala Val Leu Arg Gly Gln Thr Leu Leu Val Ile Ser Ser
100 105 110

cag ccc tgg gag ccc ctg cag ctg cac gtg gac aag gcc gtg agc ggc 384
Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
115 120 125

ctg cgg agc ctg acc acc ctg ctg cgg gcc ctg ggc gcc cag aag gag 432
Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu
130 135 140

gcc atc agc ccc ccc gac gcc gcc agc gcc gcc ccc ctg cgg acc atc 480
Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
145 150 155 160

acc gcc gac acc ttc cgg aag ctg ttc cgg gtg tac agc aac ttc ctg 528
Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu
165 170 175

cgg ggc aag ctg aag ctg tac acc ggc gag gcc tgc cgg 567
Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg
180 185

<210> 218

<211> 189

<212> PRT

<213> Homo sapiens

<400> 218

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
1 5 10 15

Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
20 25 30

Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
35 40 45

Ala Glu Thr Ile Thr Thr Gly Cys Val Glu Asp Cys Ser Leu Asn Glu
50 55 60

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Arg Lys Arg
65 70 75 80

Met Glu Val Gly Gln Gln Ala Val Glu Ile Trp Gln Gly Leu Ala Leu
85 90 95

Leu Ser Glu Ala Val Leu Arg Gly Gln Thr Leu Leu Val Ile Ser Ser
100 105 110

Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
115 120 125

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu
130 135 140

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
145 150 155 160

Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu

165 170 175
 Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg
 180 185

<210> 219
 <211> 567
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(567)

<400> 219
 atg ggc gtg cac gag tgc ccc gcc tgg ctg tgg ctg ctg ctg agc ctg 48
 Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
 1 5 10 15
 ctg agc ctg ccc ctg ggc ctg ccc gtg ctg ggc gcc ccc ccc cgg ctg 96
 Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
 20 25 30
 atc tgc gac agc cgg gtg ctg gag cgg tac ctg ctg gag gcc aag gag 144
 Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
 35 40 45
 gcc gag acc atc acc acc ggc tgc gtg gag gac tgc agc ctg aac gag 192
 Ala Glu Thr Ile Thr Thr Gly Cys Val Glu Asp Cys Ser Leu Asn Glu
 50 55 60
 aac atc acc gtg ccc gac acc aag gtg aac ttc tac gcc cgg aag cgg 240
 Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Arg Lys Arg
 65 70 75 80
 atg gag gtg ggc cag cag gcc gtg gag atc tgg cag ggc ctg gcc ctg 288
 Met Glu Val Gly Gln Gln Ala Val Glu Ile Trp Gln Gly Leu Ala Leu
 85 90 95
 ctg agc gag gcc gtg ctg cgg ggc cag acc ctg ctg gtg atc agc agc 336
 Leu Ser Glu Ala Val Leu Arg Gly Gln Thr Leu Leu Val Ile Ser Ser
 100 105 110
 cag gtg aac gag acc ctg cag ctg cac gtg gac aag gcc gtg agc ggc 384
 Gln Val Asn Glu Thr Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
 115 120 125
 ctg cgg agc ctg acc acc ctg ctg cgg gcc ctg ggc gcc cag aag gag 432
 Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu
 130 135 140
 gcc atc agc ccc ccc gac gcc gcc agc gcc gcc ccc ctg cgg acc atc 480
 Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
 145 150 155 160
 acc gcc gac acc ttc cgg aag ctg ttc cgg gtg tac agc aac ttc ctg 528

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<210> 220
<211> 189
<212> PRT
<213> Homo sapiens
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```
<210> 221
<211> 567
<212> DNA
<213> Homo sapiens
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<220>  
<221> CDS  
<222> (1) ... (567)
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<400> 221
atg ggc gtg cac gag tgc ccc gcc tgg ctg tgg ctg ctg ctg agc ctg      48
Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
      1              5              10              15

ctg agc ctg ccc ctg ggc ctg ccc gtg ctg ggc gcc ccc ccc cgg ctg      96
Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu

```

20	25	30	
atc tgc gac agc cgg gtg ctg gag cgg tac ctg ctg gag gcc aag gag			144
Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu			
35	40	45	
gcc gag agc atc acc acc ggc tgc gcc gag cac tgc agc ctg aac gag			192
Ala Glu Ser Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu			
50	55	60	
aac atc acc gtg ccc gac agc aag gtg aac atg tac gcc tgg aag cgg			240
Asn Ile Thr Val Pro Asp Ser Lys Val Asn Met Tyr Ala Trp Lys Arg			
65	70	75	80
atg gag gtg ggc cag cag gcc gtg gag gtg tgg cag ggc ctg gcc ctg			288
Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu			
85	90	95	
ctg agc gag gcc gtg ctg cgg ggc cag acc ctg ctg gtg aac agc agc			336
Leu Ser Glu Ala Val Leu Arg Gly Gln Thr Leu Leu Val Asn Ser Ser			
100	105	110	
cag ccc tgg gag ccc ctg cag ctg cac gtg gac aag gcc gtg agc ggc			384
Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly			
115	120	125	
ctg cgg agc ctg acc acc ctg ctg cgg gcc ctg ggc gcc cag aag gag			432
Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu			
130	135	140	
gcc atc agc ccc ccc gac gcc gcc agc gcc gcc ccc ctg cgg acc atc			480
Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile			
145	150	155	160
acc gcc gac acc ttc cgg aag ctg ttc cgg gtg tac agc aac ttc ctg			528
Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu			
165	170	175	
cgg ggc aag ctg aag ctg tac acc ggc gag gcc tgc cgg			567
Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg			
180	185		

<210> 222

<211> 189

<212> PRT

<213> Homo sapiens

<400> 222

Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu			
1	5	10	15
Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu			
20	25	30	
Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu			
35	40	45	

Ala Glu Ser Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu
 50 55 60
 Asn Ile Thr Val Pro Asp Ser Lys Val Asn Met Tyr Ala Trp Lys Arg
 65 70 75 80
 Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu
 85 90 95
 Leu Ser Glu Ala Val Leu Arg Gly Gln Thr Leu Leu Val Asn Ser Ser
 100 105 110
 Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
 115 120 125
 Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu
 130 135 140
 Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
 145 150 155 160
 Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu
 165 170 175
 Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg
 180 185

<210> 223
 <211> 567
 <212> DNA
 <213> Homo sapiens

<220>
 <221> CDS
 <222> (1)...(567)

<400> 223
 atg ggc gtg cac gag tgc ccc gcc tgg ctg tgg ctg ctg ctg agc ctg 48
 Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
 1 5 10 15
 ctg agc ctg ccc ctg ggc ctg ccc gtg ctg ggc gcc ccc ccc cgg ctg 96
 Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
 20 25 30
 atc tgc gac agc cgg gtg ctg gag cgg tac ctg ctg gag gcc aag gag 144
 Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
 35 40 45
 gcc gag agc atc acc acc ggc tgc gcc gag cac tgc agc ctg aac gag 192
 Ala Glu Ser Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu
 50 55 60
 aac atc acc gtg ccc gac agc aag gtg aac atg tac gcc tgg aag cgg 240
 Asn Ile Thr Val Pro Asp Ser Lys Val Asn Met Tyr Ala Trp Lys Arg
 65 70 75 80
 atg gag gtg ggc cag cag gcc gtg gag gtg tgg cag gcc ctg gcc ctg 288
 Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu
 85 90 95
 ctg agc gag gcc gtg ctg cgg gcc cag acc ctg ctg gtg aac agc agc 336
 Leu Ser Glu Ala Val Leu Arg Gly Gln Thr Leu Leu Val Asn Ser Ser

100	105	110	
cag gtg aac gag acc ctg	cag ctg cac gtg gac aag gcc	gtg agc ggc	384
Gln Val Asn Glu Thr Leu	Gln Leu His Val Asp Lys Ala	Val Ser Gly	
115	120	125	
ctg cgg agc ctg acc acc	ctg ctg cgg gcc ctg ggc gcc	cag aag gag	432
Leu Arg Ser Leu Thr Thr	Leu Leu Arg Ala Leu Gly Ala	Gln Lys Glu	
130	135	140	
gcc atc agc ccc ccc gac	gcc gcc agc gcc gcc ccc	ctg cgg acc atc	480
Ala Ile Ser Pro Pro Asp	Ala Ala Ser Ala Ala Pro	Leu Arg Thr Ile	
145	150	155	160
acc gcc gac acc ttc	cgg aag ctg ttc cgg	gtg tac agc aac ttc	528
Thr Ala Asp Thr Phe Arg	Lys Leu Phe Arg Val Tyr	Ser Asn Phe Leu	
165	170	175	
cgg ggc aag ctg aag	ctg tac acc ggc gag gcc	tgc cgg	567
Arg Gly Lys Leu Lys Leu	Tyr Thr Gly Glu Ala Cys	Arg	
180	185		

<210> 224

<211> 189

<212> PRT

<213> Homo sapiens

<400> 224

Met Gly Val His Glu Cys Pro Ala Trp	Leu Trp Leu Leu Leu Ser Leu
1	5 10 15
Leu Ser Leu Pro Leu Gly Leu Pro Val	Leu Gly Ala Pro Pro Arg Leu
20	25 30
Ile Cys Asp Ser Arg Val Leu Glu Arg	Tyr Leu Leu Glu Ala Lys Glu
35	40 45
Ala Glu Ser Ile Thr Thr Gly Cys Ala	Glu His Cys Ser Leu Asn Glu
50	55 60
Asn Ile Thr Val Pro Asp Ser Lys Val	Asn Met Tyr Ala Trp Lys Arg
65	70 75 80
Met Glu Val Gly Gln Gln Ala Val Glu	Val Trp Gln Gly Leu Ala Leu
85	90 95
Leu Ser Glu Ala Val Leu Arg Gly Gln	Thr Leu Leu Val Asn Ser Ser
100	105 110
Gln Val Asn Glu Thr Leu Gln Leu His	Val Asp Lys Ala Val Ser Gly
115	120 125
Leu Arg Ser Leu Thr Thr Leu Leu Arg	Ala Leu Gly Ala Gln Lys Glu
130	135 140
Ala Ile Ser Pro Pro Asp Ala Ala Ser	Ala Ala Pro Leu Arg Thr Ile
145	150 155 160
Thr Ala Asp Thr Phe Arg Lys Leu Phe	Arg Val Tyr Ser Asn Phe Leu
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Arg Gly Lys Leu Lys Leu Tyr Thr Gly	Glu Ala Cys Arg
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Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly
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Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly
20 25