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(54) **HLA CLASS II DEFICIENT CELLS, HLA
CLASS I DEFICIENT CELLS CAPABLE OF
EXPRESSING HLA CLASS II PROTEINS, AND
USES THEREOF**

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(57) **ABSTRACT**

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17, 2012.

The invention provides isolated primate cells preferably human cells that comprise a genetically engineered disruption in a human leukocyte antigen (HLA) class II-related gene, which results in deficiency in MHC class II expression and function. This invention also provides isolated cells further comprising a genetically engineered disruption in a beta-2 microglobulin (B2M) gene, which results in HLA class I/class II deficiency. Also provided are the method of using the cells for transplantation and treating a disease condition.

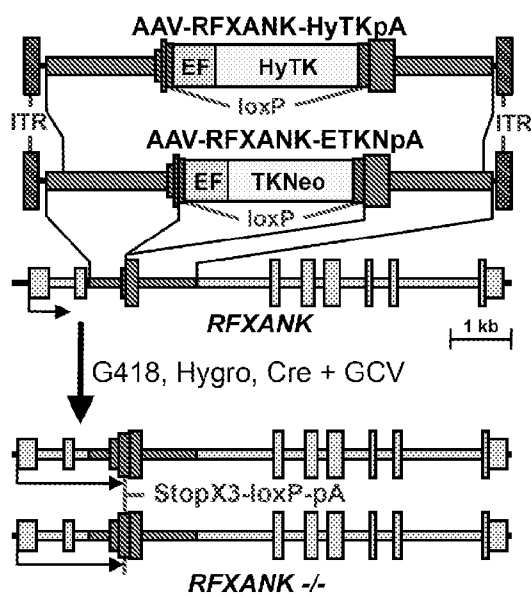


Figure 1

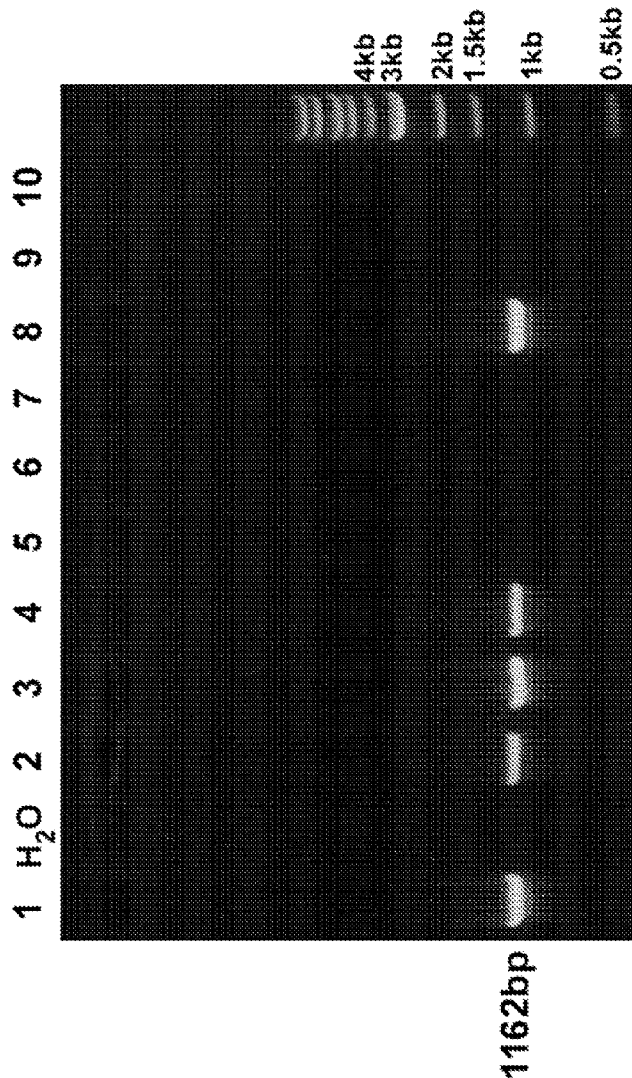
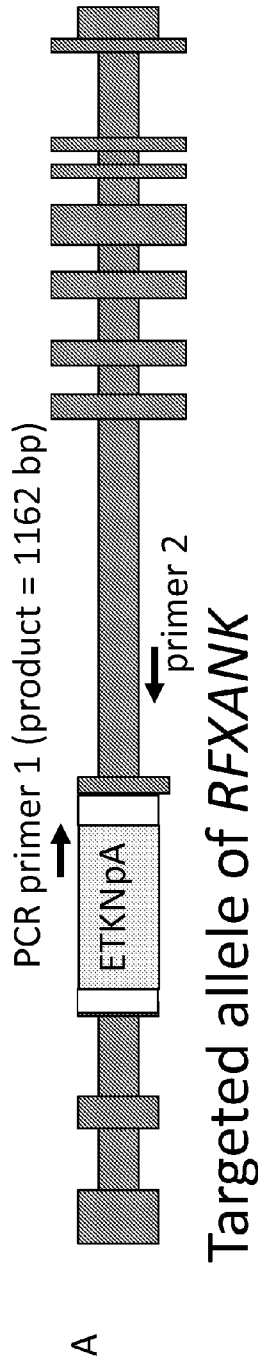


Figure 2

HLA CLASS II DEFICIENT CELLS, HLA CLASS I DEFICIENT CELLS CAPABLE OF EXPRESSING HLA CLASS II PROTEINS, AND USES THEREOF

CROSS REFERENCE

[0001] This application claims priority to U.S. provisional patent application Ser. No. 61/625,314 filed Apr. 17, 2012, incorporated by reference herein in its entirety.

STATEMENT OF GOVERNMENT RIGHTS

[0002] This invention was made with government support under grant numbers R01GM086497 and R01DK55759 awarded by the National Institutes of Health. The government has certain rights in the invention.

BACKGROUND OF THE INVENTION

[0003] Human pluripotent stem cells have the potential to treat diseases affecting almost every organ system. However, the clinical use of human pluripotent stem cells and their derivatives has a major limitation—rejection of transplanted cells by the recipient due to differences in the major histocompatibility complex.

[0004] The major histocompatibility complex (MHC) is a cell surface multi-component molecule found in all vertebrates that mediates interactions of leukocytes with other leukocytes or other cells. The MHC gene family is divided into three groups: class I, class II and class III. In humans, MHC is referred to as human leukocyte antigen (HLA). HLA class II molecules (HLA-II) are transmembrane protein found only on professional antigen-presenting cells (APCs) including macrophages, dendritic cells and B cells. In addition, solid organ may sometimes express HLA class II genes that participate in immune rejection. The HLA class I (HLA-I) protein is expressed on all nucleated cells and consists of an HLA class I heavy chain (or α chain) and β -2 microglobulin (B2M). HLA class I protein presents peptides on the cell surface to CD8⁺ cytotoxic T cells. Six HLA class I α chains have been identified to date, including three classical (HLA-A, HLA-B and HLA-C) and three non-classical (HLA-E, HLA-F and HLA-G) α chains. The specificity for peptide binding on the HLA class I molecule peptide binding cleft is determined by the α chain. Recognition by CD8⁺ T cells of the peptides presented by the HLA class I molecule mediates cellular immunity. HLA class II molecules and class I molecules are both heterodimers. Class I molecules consist of an α chain (or heavy chain) and β -2 microglobulin (B2M), whereas the class II molecules consist of two homologous subunits: the α subunit and β subunit.

[0005] HLA class II (HLA-II) molecules or proteins present on the cell surface peptide antigens from extracellular proteins including proteins of an extracellular pathogen, while HLA class I proteins present peptides from intracellular proteins or pathogens. Loaded HLA class II proteins on the cell surface interact with CD4⁺ helper T cells. The interaction leads to recruitment of phagocytes, local inflammation, and/or humoral responses through the activation of B cells. Several HLA class II gene loci have been identified to date, including HLA-DM (HLA-DMA and HLA-DMB that encode HLA-DM α chain and HLA-DM β chain, respectively), HLA-DO (HLA-DOA and HLA-DOB that encode HLA-DO α chain and HLA-DO β chain, respectively), HLA-DP (HLA-DPA and HLA-DPB that encode HLA-DP α chain

and HLA-DP β chain, respectively), HLA-DQ (HLA-DQA and HLA-DQB that encode HLA-DQ α chain and HLA-DQ β chain, respectively), and HLA-DR (HLA-DRA and HLA-DRB that encode HLA-DR α chain and HLA-DR β chain, respectively).

[0006] The HLA class I and/or class II proteins from an allogeneic source constitutes a foreign antigen in the context of transplantation. The recognition of non-self HLA class I and/or class II proteins is a major hurdle in using pluripotent cells for transplantation or replacement therapies.

[0007] Thus, although individualized stem cell preparations or HLA-diverse stem cell banks may address the current problem of transplantation, they require that multiple cell lines be characterized, differentiated into therapeutic cell products, and approved for human administration. This time-consuming, technically difficult, and expensive process is a major factor preventing stem cell-based therapies from entering clinical trials. Thus, there exists a need for a more effective and less expensive cell-based therapies that are not impeded by rejection.

SUMMARY OF THE INVENTION

[0008] In a first aspect, the present invention provides isolated cells comprising a genetically engineered disruption in a human leukocyte antigen (HLA) class II-related gene, wherein the cell is a primate cell. In one embodiment, the HLA class II-related gene is selected from the group consisting of regulatory factor X-associated ankyrin-containing protein (RFXANK), regulatory factor 5 (RFX5), regulatory factor X-associated protein (RFXAP), class II transactivator (CIITA), HLA-DPA (α chain), HLA-DPB (β chain), HLA-DQA, HLA-DQB, HLA-DRA, HLA-DRB, HLA-DMA, HLA-DMB, HLA-DOA and HLA-DOB. In another embodiment, the cell comprises genetically engineered disruptions in at least two, at least three, or in all four of the HLA class II-related genes. In a further embodiment, the HLA class II-related gene is regulatory factor X-associated ankyrin-containing protein (RFXANK). In a still further embodiment, the cell comprises genetically engineered disruptions in all copies of the HLA class II-related gene. In another embodiment the cell further comprises one or more recombinant immunomodulatory genes, each capable of expressing an immunomodulatory polypeptide in the human cell. In a further embodiment, the one or more immunomodulatory genes comprise a polynucleotide capable of encoding an HLA II protein. In another embodiment, the one or more immunomodulatory genes comprise a polynucleotide capable of encoding a single chain fusion HLA class II protein. In a further embodiment, the cell further comprises a genetically engineered disruption in the β 2-microglobulin (B2M) gene.

[0009] In another aspect, the present invention provides isolated cells comprising (a) a genetically engineered disruption in a β 2-microglobulin (B2M) gene; and (b) one or more polynucleotides capable of encoding an HLA class II protein, or a single chain fusion HLA class II protein; wherein the cell is a primate cell.

[0010] In one embodiment of either of these aspects, the cell comprises genetically engineered disruptions of all copies of the B2M gene. In a further embodiment, the HLA II gene encodes an HLA protein selected from the group consisting of an HLA-DM α chain, an HLA-DM β chain, an HLA-DO α chain, an HLA-DO β chain, an HLA-DP α chain, an HLA-DP β chain, an HLA-DQ α chain, an HLA-DQ β chain, an HLA-DR α chain and an HLA-DR β chain.

[0011] In another embodiment, the single chain fusion HLA class II protein comprises at least a portion of an HLA class II gene α chain covalently linked to at least a portion of an HLA class II gene β chain, wherein the HLA class II gene is selected from the group consisting of HLA-DP, HLA-DQ, HLA-DR, HLA-DM, and HLA-DO. In a further embodiment, the single chain fusion HLA class II protein comprises a plurality of different single chain fusion HLA class II proteins. In another embodiment, the single chain fusion HLA class II protein comprises at least a portion of HLA-DQ α chain and at least a portion of HLA-DQ β chain. In a still further embodiment, the single chain fusion HLA class II protein comprises at least a portion of HLA-DQ α chain allele HLA-DQA1*01 and at least a portion of HLA-DQ β chain allele HLA-DQB1*02.

[0012] In a further embodiment of either aspect of the cells of the invention, the HLA protein or the single chain fusion HLA class II protein presents a first target peptide antigen on the cell surface. In one such embodiment, the first target peptide antigen is covalently linked to the single chain fusion HLA class II protein.

[0013] In another embodiment the cell further comprises a polynucleotide capable of encoding a single chain fusion HLA class I protein. In one such embodiment, the single chain fusion HLA class I protein comprises at least a portion of B2M covalently linked to at least a portion of an HLA class I α chain selected from the group consisting of HLA-A, HLA-B, HLA-C, HLA-E, HLA-F and HLA-G. In another such embodiment, the single chain fusion HLA class I protein comprises at least a portion of B2M covalently linked to at least a portion of HLA-A. In a further embodiment the single chain fusion HLA class I protein comprises at least a portion of B2M covalently linked to at least a portion of HLA-A0201. In another embodiment the cell further expresses a second target peptide antigen that is presented by the single chain fusion HLA class I protein on the cell surface. For example, the second target peptide antigen may be covalently linked to the single chain fusion HLA class I protein.

[0014] In another embodiment of either aspect of the cells of the invention, the cell further comprises one or more recombinant genes capable of encoding a suicide gene product. For example, the suicide gene product may comprise a protein selected from the group consisting of thymidine kinase and an apoptotic signaling protein.

[0015] The cells of either aspect of the may have a normal karyotype and may be non-transformed cells. The cells may be stem cells, such as hematopoietic stem cells, embryonic stem cells, pluripotent stem cells, induced pluripotent stem cells, liver stem cells, neural stem cells, pancreatic stem cells or mesenchymal stem cells. The stem cell may be differentiated, such as dendritic cells, pancreatic islet cells, liver cells, muscle cells, keratinocytes, neuronal cells, hematopoietic cells, lymphocytes, red blood cells, platelets, skeletal muscle cells, ocular cells, mesenchymal cells, fibroblasts, lung cells, gastrointestinal (GI) tract cells, vascular cells, endocrine cells, adipocytes or cardiomyocytes. The cells may be human cells.

[0016] In another aspect, the present invention provides vaccines comprising the cell of any one embodiment or combinations of embodiments of the cells of the present invention that include at least one target peptide antigen on the cell surface, wherein the vaccine is capable of eliciting in a primate an immune response specific for the target peptide antigen(s).

[0017] In a further aspect, the invention provides methods of transplantation in a patient in need thereof comprising the step of administering to the patient an effective amount of the cell or vaccine of any embodiment or combination of embodiments of the cells of the invention. In one such embodiment, the patient may be immune competent. In another embodiment, the cell or vaccine may comprise a differentiated cell.

DESCRIPTION OF THE FIGURES

[0018] FIG. 1 shows the structure of exemplary two adeno-associated virus (AAV) gene targeting vectors, designed to insert either a TKNeo (AAV-RFXANK-ETKNpA) or HyTK (AAV-RFXANK-HyTK) gene controlled by an EF1alpha promoter (EF) into exon 3 of the RFXANK gene, which is also shown below the vectors. Selection of vector-infected cells with G418 or hygromycin (Hygro) allows one to isolate cells targeted by the TKNeo or HyTK vectors respectively. Subsequent expression of Cre recombinase and selection with gancyclovir (GCV) then allows one to isolate clones that have removed the TKNeo or HyTK genes, leaving behind two inactivated RFXANK alleles with stop codons in all 3 reading frames, a loxP site, and a polyadenylation site (StopX3-loxP-pA). LoxP is the recombination site for Cre recombinase. ITR is a vector inverted terminal repeat. Similar vectors could be designed to target other genes.

[0019] FIG. 2 (A) Schematic depiction of targeting strategy for infection of human embryonic stem cells with construct AAV-RFXANK-ETKNpA. (B) Photograph of stained gel showing polymerase chain reaction (PCR) products obtained after infection of human embryonic stem cells with AAV-RFXANK-ETKNpA and PCR using a forward primer homologous to the neomycin sequence of the selection cassette and a reverse primer homologous to the RFXANK gene which was outside the targeting homology arm, as indicated by the arrows above.

DETAILED DESCRIPTION OF THE INVENTION

[0020] All references cited are herein incorporated by reference in their entirety. Within this application, unless otherwise stated, the techniques utilized may be found in any of several well-known references such as: *Molecular Cloning: A Laboratory Manual* (Sambrook, et al., 1989, Cold Spring Harbor Laboratory Press), *Gene Expression Technology* (Methods in Enzymology, Vol. 185, edited by D. Goeddel, 1991. Academic Press, San Diego, Calif.), "Guide to Protein Purification" in *Methods in Enzymology* (M. P. Deutscher, ed., (1990) Academic Press, Inc.); *PCR Protocols: A Guide to Methods and Applications* (Innis, et al. 1990. Academic Press, San Diego, Calif.), *Culture of Animal Cells: A Manual of Basic Technique*, 2nd Ed. (R. I. Freshney. 1987. Liss, Inc. New York, N.Y.), *Gene Transfer and Expression Protocols*, pp. 109-128, ed. E. J. Murray, The Humana Press Inc., Clifton, N.J.), and the Ambion 1998 Catalog (Ambion, Austin, Tex.).

[0021] As used herein, the singular forms "a", "an" and "the" include plural referents unless the context clearly dictates otherwise. "And" as used herein is interchangeably used with "or" unless expressly stated otherwise.

[0022] All embodiments of any aspect of the invention can be used in combination, unless the context clearly dictates otherwise.

[0023] In a first aspect, the present invention provides isolated cells comprising a genetically engineered disruption in

a human leukocyte antigen (HLA) class II-related gene, wherein the cell is a primate cell. The HLA class II related genes as used in the instant application broadly refer to genes that encode proteins involved in the HLA class II mediated immune responses. Thus, HLA class II related genes encompass genes that encode the HLA class II molecules such as HLA-DM (SEQ ID NO: 48, 50), HLA-DO (SEQ ID NO: 52, 54), HLA-DP (SEQ ID NO: 36, 38), HLA-DQ (SEQ ID NO: 40, 42), and HLA-DR (SEQ ID NO: 44, 46). The sequences of exemplary HLA class II genes/proteins can be found in publicly available database under GenBank or IMGT/HLA database numbers NM_033554.3 (SEQ ID NOs:36, 37) for HLA-DPA, HLA00514 (SEQ ID NOs:38, 39) for HLA-DPB, HLA00601 (SEQ ID NOs:40, 41) for HLA-DQA, HLA00622 (SEQ ID NOs:42, 43) for HLA-DQB, NM_019111 (SEQ ID NOs:44, 45) for HLA-DRA, HLA00664 (SEQ ID NOs:46, 47) for HLA-DRB, NM_006120 (SEQ ID NOs:48, 49) for HLA-DMA, NM_002118 (SEQ ID NOs:50, 51) for HLA-DMB, NM_002119 (SEQ ID NOs:52, 53) for HLA-DOA, and NM_002120 (SEQ ID NOs:54, 55) for HLA-DOB.

[0024] In addition, HLA class II related genes also include genes that encode HLA class II regulatory proteins that regulate the expression of HLA class II molecules, including without limitation regulatory factor X-associated ankyrin-containing protein (RFXANK), regulatory factor 5 (RFX5), regulatory factor X-associated protein (RFXAP), and class II transactivator (CIITA). For example, regulatory factor X-associated ankyrin-containing protein (RFXANK) together with regulatory factor X-associated protein and regulatory factor-5 form a complex that binds to the X box motif of HLA class II gene promoters and activates transcription of the HLA class II genes. The sequences of exemplary HLA class II-related genes that regulate the expression of HLA class II molecules can be found in publicly available database under GenBank Accession Numbers NM_134440.1 (SEQ ID NOs: 24, 25) and NM_003721.2 (SEQ ID NOs:26, 27) for RFX-ANK, NM_000449.3 (SEQ ID NOs:28, 29) and NM_001025603.1 (SEQ ID NOs:30, 31) for RFX5, NM_000538.3 (SEQ ID NOs:32, 33) for RFXAP and NM_000246.3 (SEQ ID NOs:34, 35) for CIITA. All the sequences disclosed under these GenBank Accession Numbers are herein incorporated by reference.

[0025] In certain embodiments, the invention provides an isolated primate preferably human cell that comprises a genetically engineered disruption in at least one HLA class II-related gene as defined herein. In certain particular embodiments, the cell comprises genetically engineered disruptions of all copies of the at least one HLA class II-related gene. In certain other embodiments, the cell comprises a plurality of genetically engineered disruptions in a plurality of HLA class II-related genes.

[0026] In certain embodiments, the HLA class II-related gene is selected from the group consisting of regulatory factor X-associated ankyrin-containing protein (RFXANK), regulatory factor 5 (RFX5), regulatory factor X-associated protein (RFXAP), and class II transactivator (CIITA). In certain particular embodiments, the cell comprises at least one genetically engineered disruption in at least one, at least two, at least three, or all of the HLA class II-related genes selected from the group consisting of regulatory factor X-associated ankyrin-containing protein (RFXANK), regulatory factor 5 (RFX5), regulatory factor X-associated protein (RFXAP), and class II transactivator (CIITA). Any combinations of

these four HLA class II-related genes as target for genetic disruption to create HLA class II deficient cell are within the scope of the invention.

[0027] In certain other embodiments, the cell comprises at least one genetically engineered disruption of an HLA class II-related genes selected from the group consisting of regulatory factor X-associated ankyrin-containing protein (RFX-ANK) (SEQ ID NO: 24-27), regulatory factor 5 (RFX5) (SEQ ID NO: 28-31), regulatory factor X-associated protein (RFXAP) (SEQ ID NO: 32, 33), class II transactivator (CIITA) (SEQ ID NO: 34, 35), HLA-DPA (α chain) (SEQ ID NO: 36, 37), HLA-DPB (β chain) (SEQ ID NO: 38, 39), HLA-DQA (SEQ ID NO: 40, 41), HLA-DQB (SEQ ID NO: 42, 43), HLA-DRA (SEQ ID NO: 44, 45), HLA-DRB (SEQ ID NO: 46-47), HLA-DMA (SEQ ID NO: 48, 49), HLA-DMB (SEQ ID NO: 50, 51), HLA-DOA (SEQ ID NO: 52, 53) and HLA-DOB (SEQ ID NO: 54, 55).

[0028] The genetically engineered disruptions include without limitation deletions, insertions, substitutions and truncations of a target HLA class II-related gene that result in no expression of the target gene or expression of a truncated or mutated protein with no function or much reduced function as compared to the wild type protein. In certain embodiments, the genetically engineered disruption of a HLA class II-related gene leads to the expression of a truncated HLA class II-related protein. In certain particular embodiments, the HLA class II-related gene is RFXANK (SEQ ID NO: 24-27). In certain other particular embodiments, the HLA-related gene is selected from the group consisting of HLA-DPA (α chain) (SEQ ID NO: 36, 37), HLA-DPB (β chain) (SEQ ID NO: 38, 39), HLA-DQA (SEQ ID NO: 40, 41), HLA-DQB (SEQ ID NO: 42, 43), HLA-DRA (SEQ ID NO: 44, 45), HLA-DRB (SEQ ID NO: 46-47), HLA-DMA (SEQ ID NO: 48, 49), HLA-DMB (SEQ ID NO: 50, 51), HLA-DOA (SEQ ID NO: 52, 53) and HLA-DOB (SEQ ID NO: 54, 55). In certain further embodiments the cell comprises genetically engineered disruptions in all copies of the HLA class II-related gene.

[0029] In another aspect, the invention provides HLA class I and HLA class II deficient cells. In certain embodiments, the invention provides a primate cell, preferably a human cell that comprises a genetically engineered disruption in an HLA class II-related gene and further comprises a genetically engineered disruption in the β 2-microglobulin (B2M) gene (SEQ ID NO: 1). In other particular embodiments, the cell further comprises genetically engineered disruptions of all copies of the B2M gene (SEQ ID NO: 1). In certain embodiments, the genetic disruptions in the B2M (SEQ ID NO: 1) gene result in defective or no expression of the B2M protein (SEQ ID NO: 2). In other particular embodiments, the cell further comprises genetically engineered disruptions of all copies of the B2M gene. In certain embodiments, the genetic disruptions in the B2M gene result in defective or no expression of the B2M protein. Since B2M is a common component of all HLA class I proteins, the disruptions preclude the expression of all natural HLA class I proteins on the cell surface. Thus, in this aspect of the invention an HLA class I/class II deficient cell is provided. The B2M coding sequence is shown in SEQ ID NO:1 (GenBank Accession Number NM_004048) and the B2M protein sequence is shown in SEQ ID NO:2. There may be many single nucleotide polymorphisms (SNPs) in the gene; as will be understood by those of skill in the art, the human cells and methods of the invention are applicable to any such B2M gene and SNPs.

[0030] Any suitable technique for introducing a genetically engineered disruption (in an HLA class II-related gene, in B2M gene or any other suitable gene) can be used; exemplary techniques for gene disruptions are disclosed throughout the application and are within the level of skill in the art based on the teachings herein and the teachings known in the art. Other exemplary techniques can be found, for example, in U.S. Patent Application Publication Number US2008/0219956, published Sep. 11, 2008, and incorporated by reference herein in its entirety. These techniques may optionally include steps to remove non-human DNA sequences from the cells after disruption of an HLA class II-related gene and optionally disruption of B2M gene.

[0031] One such techniques employs an adeno-associated virus gene targeting vector, optionally including removing the transgene used for targeting via techniques such as those described below, or by removing the transgene used for targeting by Cre-mediated loxP recombination, or other suitable recombination techniques. See Khan et al. 2011, Protocol, 6:482-501, which is incorporated by reference in its entirety. Exemplary targeting vectors and exemplary vector diagrams are also disclosed herein. It is within the level of those of skill in the art, based on the teachings herein and known in the art, to utilize a variety of techniques for making the HLA class II, preferably human cells, of the invention.

[0032] In certain embodiments, the cell genome of HLA class II deficient cells may comprise no more than 100, no more than 50 or no more than 30 nucleotides of non-human DNA sequences. In certain other embodiments, the cell genome may comprise 6, 5, 4, 3, 2, 1, or 0 nucleotides of non-human DNA sequences. Exemplary strategy for genetically disrupting the RFXANK gene is shown in FIG. 1. The non-human DNA sequences can be removed by a second round of targeting to delete the HyTK or TKNeo transgenes in the first vectors or by the Cre-mediated loxP recombination.

[0033] In certain other embodiments, the HLA class II or HLA class I/class II deficient cells further comprise one or more recombinant immunomodulatory genes. Suitable immunomodulatory genes include without limitation a gene encoding a viral protein that inhibits antigen presentation, a microRNA gene, a gene that encodes an HLA class II protein, or a gene that encodes a single chain (SC) fusion HLA class II protein. The term “single chain fusion HLA class II protein,” “single chain fusion HLA class II molecule” or “single chain fusion HLA class II antigen” refers to a fusion protein comprising at least a portion of the HLA class II α chain covalently linked, either directly or via a linker sequence, to at least a portion of an HLA class II β chain or a class II α or β chain linked to a peptide antigen, or linked class II α and β chains also linked to a peptide antigen. On the other hand, the term “HLA class II protein,” “HLA class II molecule” or “HLA class II antigen” refers to a non-covalently associated heterodimer of an HLA class II α chain and an HLA β chain expressed on the surface of a wild type cell. In embodiments wherein the gene encodes an HLA class II protein (as opposed to a single chain fusion HLA class II protein), the gene is under control of a promoter not involved in normal class II expression in the cell. In one embodiment, the gene is episomally expressed; in another embodiment, the gene is integrated into the cell's genome. In either embodiment, the gene is operatively linked (i.e.: under transcriptional control) to a promoter not involved in normal class II expression in the cell. Any suitable promoter may be used, as may be deter-

mined by one of skill in the art based on the specific intended design and use of the constructs and cells.

[0034] In another aspect, the present invention provides isolated cells comprising (a) a genetically engineered disruption in a beta-2 microglobulin (B2M) gene; and (b) one or more polynucleotides capable of encoding an HLA II protein (alpha or beta chains) or a single chain fusion HLA class II protein; wherein the cell is a primate cell. Cells according to this aspect of the invention are HLA class I deficient cells.

[0035] HLA class II deficient cells, HLA class I deficient cells, or HLA class I/class II deficient cells can be used as universal donor cells. In certain particular embodiments, the HLA class II deficient cells, HLA class I deficient cells, or HLA class I/class II deficient cells are hematopoietic cells or dendritic cells for use in transplantation. In addition, solid organ cells may sometimes express HLA class II genes that participate in immune rejection. Thus, in certain advantageous embodiments, the invention provides HLA class II, HLA class I deficient cells, or HLA class I/class II deficient cells for transplantation for treatment of diseases or injuries associated with solid organs.

[0036] In certain particular embodiments of any of the cells of the present invention, the HLA α and β chains are selected from the group consisting of α and β chains of HLA-DM, HLA-DR, HLA-DP, HLA-DQ, and HLA-DO. The α and β chains can be but do not have to be from the same HLA class II gene. For example, an HLA class II protein or a single chain fusion HLA class II protein may comprise at least a portion of an HLA-DQ α chain and at least a portion of an HLA-DQ β chain (also referred to as a dimeric construct). HLA class II proteins and single chain fusion HLA class II proteins comprising mismatching HLA class II alleles are also contemplated. In certain particular embodiments, an HLA class II protein or a single chain fusion HLA class II protein may comprise at least a portion of the HLA-DQ α chain allele HLA-DQA1*01 (SEQ ID NO:41) and at least a portion of the HLA-DQ β chain allele HLA-DQB1*02 (SEQ ID NO:43). In certain preferred embodiments, the leader sequence (or signal peptide) of the second portion of the fusion protein is removed in the fusion construct. For example, in a single chain fusion HLA class II protein that comprises at least a portion of HLA-DQA1*01 (SEQ ID NO: 41) at the N-terminus covalently linked to at least a portion of HLA-DQB1*02 (SEQ ID NO: 43) at the C-terminus, the HLA-DQA1*01 (SEQ ID NO: 41) leader sequence is left in, and the HLA-DQB1*02 (SEQ ID NO: 43) leader sequence is removed from the construct. In certain other embodiments, the cell further expresses at least two, at least three, or at least four or more different single chain fusion HLA class II proteins. In certain particular embodiments, the HLA class II protein or single chain fusion HLA class II protein also comprises a first target peptide antigen that occupies the peptide binding site of the HLA class II protein or single chain fusion HLA class II protein, wherein the peptide antigen is covalently linked to the HLA class II protein or single chain fusion HLA class II protein (also referred to as a trimeric construct). In certain other embodiments, the covalently linked peptide antigen is cleaved via a built-in protease cleavage site, and the cleaved peptide antigen can bind to the peptide binding site of the single chain fusion HLA-II protein for presentation.

[0037] Thus, HLA class II, HLA class I deficient cells, or HLA class I/class II deficient cells also encompass cells having genetically engineered disruptions in all copies of an HLA class II gene (e.g., disruptions in all copies of HLA-DQ

a and/or β chain), wherein one HLA class II allele is genetically engineered to express, instead of the wild type HLA class II protein, an HLA class II protein of interest or a single chain fusion HLA class II protein (i.e., genetically targeted knockin in one HLA-II allele). Take HLA-DQ as an example, in certain embodiments, HLA-DQ^{-/-} cells express HLA-DQ protein only in the context of a single chain fusion HLA-DQ protein from an HLA-DQ genetic locus. In certain advantageous embodiments, the expression of the single chain fusion HLA class II protein is regulated by the endogenous HLA-DQ regulatory sequence located at the HLA-DQ locus.

[0038] In related embodiments, HLA class II, HLA class I deficient cells, or HLA class I/class II deficient cells further encompass cells having genetically engineered disruptions in all copies of a certain HLA-II gene, wherein all alleles of the specific HLA-II gene are genetically engineered to express, instead of the wild type HLA-II protein, single chain fusion HLA class II proteins (i.e., genetically targeted knockin in all HLA-II alleles). HLA class II, HLA class I deficient cells, or HLA class I/class II deficient cells with such genetic disruptions express a particular HLA-II protein only in the context of single chain fusion HLA class II proteins from the genetic loci of all the alleles of the particular HLA-II gene.

[0039] HLA class II proteins and single chain fusion HLA class II proteins comprising sequence variants and fragments of HLA class II α chains and β chains are contemplated by the instant invention, wherein such HLA class II proteins or single chain fusion constructs nevertheless possess normal HLA class II functions, e.g., forming proper secondary structure of the heterodimer on the cell surface, presenting peptides in the peptide binding site, interacting with CD4⁺ helper T cells and triggering HLA class II-mediated immune responses. In certain embodiments, the variants share at least 75%, 78%, 80%, 81%, 85%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or complete sequence homology with the naturally occurring HLA class II α or β chain sequences, wherein the variants possess normal HLA class II functions. In certain other embodiments, the variants share at least 75%, 80%, 81%, 85%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or complete sequence homology with the sequences of HLA class II α or β chains as shown in SEQ ID NOs:37, 39, 41, 43, 45, 47, 49, 51, 53 and 55.

[0040] Further, the HLA class II, HLA class I deficient cells, or HLA class I/class II deficient cells can be engineered to recombinantly express a single chain fusion HLA class I protein in a B2M^{-/-} genetic background. The HLA class I deficient cells or HLA class I/class II deficient cells recombinantly expressing a single chain fusion HLA class I protein are nevertheless deficient in normal B2M function in that the cells do not express wild type B2M protein (SEQ ID NO:2) that can form a non-covalently associated heterodimer with any HLA class I α chain on the cell surface.

[0041] The term “single chain fusion HLA class I protein,” “single chain fusion HLA class I molecule” or “single chain fusion HLA class I antigen” refers to a fusion protein comprising at least a portion of the B2M protein covalently linked, either directly or via a linker sequence, to at least a portion of an HLA-I α chain. On the other hand, the term “HLA class I protein,” “HLA class I molecule” or “HLA class I antigen” refers to a non-covalently associated heterodimer of B2M and an HLA α chain expressed on the surface of a wild type cell.

[0042] As used herein, the term “HLA class I α chain” or “HLA-I heavy chain” refers to the α chain of the HLA class

I heterodimer. HLA class I heavy chain includes without limitation HLA class I α chains HLA-A, HLA-B, HLA-C, HLA-E, HLA-F, and HLA-G. Representative DNA and protein sequences are provided for HLA-A (GenBank No. K02883.1, SEQ ID NO:3; UniProt No. P01892, SEQ ID NO:4), HLA-B (NM_005514, SEQ ID NO:5; NP_005505; SEQ ID NO:6), HLA-C (NM_002117, SEQ ID NO:7; NP_002108, SEQ ID NO:8), HLA-E (NM_005516, SEQ ID NO:9; NP_005507, SEQ ID NO:10), HLA-F (NM_018950, SEQ ID NO:11; NP_061823, SEQ ID NO:12), and HLA-G (NM_002127, SEQ ID NO:13; NP_002118, SEQ ID NO:14).

[0043] In addition, although the term “HLA class I or II protein/molecule” is known to refer to the MHC class I or II protein/molecule in human, the terms HLA and MHC are sometimes used interchangeably throughout this application: for example, the term HLA class I or HLA class II protein can also be used to refer to the primate equivalent to the HLA class I protein or HLA class II protein, respectively, in a primate. One of skill in the art will be able to discern the meaning of the term based on the content.

[0044] Thus, HLA class I deficient cells or HLA class I/class II deficient cells also encompass cells having genetically engineered disruptions in all copies of the B2M gene, wherein one B2M allele is genetically engineered to express, instead of the wild type B2M protein, a single chain fusion HLA class I protein (i.e., genetically targeted knockin in one B2M allele). B2M^{-/-} cells with such genetic background express B2M only in the context of the single chain fusion HLA class I protein from a B2M genetic locus. In certain advantageous embodiments, the expression of the single chain fusion HLA class I protein is regulated by the endogenous B2M regulatory sequence located at the B2M locus.

[0045] In related embodiments, HLA class I deficient cells or HLA class I/class II deficient cells further encompass cells having genetically engineered disruptions in all copies of the B2M gene, wherein all B2M alleles are genetically engineered to express, instead of the wild type B2M protein, single chain fusion HLA class I proteins (i.e., genetically targeted knockin in all B2M alleles). HLA class I deficient cells or HLA class I/class II deficient cells with such genetic disruptions express B2M only in the context of single chain fusion HLA class I proteins from the genetic loci of all the alleles of the B2M gene. In certain embodiments, the cells are genetically engineered to express the same type of single chain fusion HLA class I protein from the genetic loci of all alleles of the B2M gene; while in other embodiments, the cells are genetically engineered to express different types of single chain fusion HLA class I proteins from different genetic loci of the B2M gene.

[0046] In certain embodiments, the single chain fusion HLA class I protein comprises at least a portion of B2M (SEQ ID NO: 2) and at least a portion of HLA-A (SEQ ID NO: 4), HLA-B (SEQ ID NO: 6), HLA-C (SEQ ID NO: 8), HLA-E (SEQ ID NO: 10), HLA-F (SEQ ID NO: 12) or HLA-G (SEQ ID NO: 14) (also referred to as a dimeric construct). In certain preferred embodiments, the HLA α chain contained in the single chain fusion HLA class I protein does not contain the leader sequence (or signal sequence) of the HLA class I α chain (leaderless HLA α chain). In certain other embodiments, the single chain fusion HLA class I protein comprises at least a portion of B2M (SEQ ID NO: 2) and at least a portion of HLA-C (SEQ ID NO: 8), HLA-E (SEQ ID NO: 10) or HLA-G (SEQ ID NO: 14). In certain further embodiments,

the single chain fusion HLA class I protein comprises at least a portion of B2M (SEQ ID NO: 2) and at least a portion of HLA-A (SEQ ID NO: 4), HLA-E (SEQ ID NO: 10) or HLA-G (SEQ ID NO: 14). In certain preferred embodiments, the single chain fusion HLA class I protein comprises a leader sequence (or signal peptide) covalently linked to at least a portion of B2M and at least a portion of an HLA α chain to ensure proper folding of the single chain fusion on the cell surface. The leader sequence can be the leader sequence of the B2M protein, the leader sequence of an HLA α chain protein or the leader sequence of other secretory proteins. In certain particular embodiments, the single chain fusion HLA class I protein comprises a B2M protein with its leader sequence removed. In certain other particular embodiments, the single chain fusion HLA class I protein comprises an HLA α chain protein with its leader sequence removed. Certain HLA class I α chains are highly polymorphic. As will be understood by those of skill in the art, the human cells and methods of the invention are applicable to any such HLA α chains and polymorphism thereof.

[0047] Single chain fusion HLA class I proteins comprising sequence variants and fragments of B2M and/or HLA α chains are contemplated by the instant invention, wherein such single chain fusion constructs nevertheless possess normal HLA class I functions, e.g., forming proper secondary structure of the heterodimer on the cell surface, presenting peptides in the peptide binding cleft and engaging the inhibitory receptors on the surface of NK cells. In certain embodiments, the variants share at least 75%, 80%, 81%, 85%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or complete sequence homology with the naturally occurring HLA heavy chains and B2M sequences, wherein the variants possess normal HLA class I functions. In certain other embodiments, the variants share at least 75%, 80%, 81%, 85%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or complete sequence homology with the sequences of B2M or HLA heavy chains as shown in SEQ ID NOs: 2, 4, 6, 8, 10, 12 or 14.

[0048] In certain particular embodiments, the HLA-A variants share at least 85%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or complete sequence homology with SEQ ID NO: 4. In certain other particular embodiments, the HLA-B variants share at least 81%, 83%, 85%, 88%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or complete sequence homology with SEQ ID NO: 6. In certain further embodiments, the HLA-C variants share at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or complete sequence homology with SEQ ID NO: 8. In yet other embodiments, the HLA-E variants share at least 97%, 98%, 99%, or complete sequence homology with SEQ ID NO: 10. In certain particular embodiments, the HLA-F variants share at least 99%, or complete sequence homology with SEQ ID NO: 12. In certain other embodiments, the HLA-G variants share at least 98%, 99%, or complete sequence homology with SEQ ID NO: 14.

[0049] In certain other embodiments, the single chain fusion HLA class I protein comprises full-length B2M (SEQ ID NO: 2) (including its leader sequence) and an HLA α chain without the leader sequence (leaderless HLA α chain); while in certain other embodiments, the single chain fusion HLA class I protein comprises B2M (SEQ ID NO: 2) protein without the leader sequence. It is understood that B2M^{-/-} cells expressing two, three or more different types of single chain fusion HLA class I protein in any combination, for example,

expressing SC fusion comprising HLA-A (SEQ ID NO: 4) (or a leaderless HLA-A) and SC fusion comprising HLA-C (SEQ ID NO: 8) (or a leaderless HLA-C), expressing SC fusion comprising HLA-A (SEQ ID NO: 4) (or a leaderless HLA-A) and SC fusion comprising HLA-E (SEQ ID NO: 10) (or a leaderless HLA-E), or expressing SC fusion comprising HLA-B (SEQ ID NO: 6) (or a leaderless HLA-B), SC fusion comprising HLA-E (SEQ ID NO: 10) (or a leaderless HLA-E) and SC fusion comprising HLA-G (SEQ ID NO: 14) (or a leaderless HLA-G), etc., are all contemplated by the invention and fall within the scope of the invention.

[0050] Natural killer (NK) cells are part of the innate immune response. Several pathogens can down regulate HLA class I protein expression in infected cells. The NK cells monitor infection by recognizing and inducing apoptosis in cells that do not express HLA class I proteins. The inhibitory receptors on the NK cell surface recognize HLA class I α chain alleles thereby preventing NK-mediated apoptosis in uninfected normal cells. Thus, in certain particular embodiments, the single chain fusion HLA-I protein inhibits NK cell-mediated killing of cells that do not express endogenous HLA class I proteins by binding to the inhibitory receptors on the NK cells. For example, HLA-E is a ligand for the CD94/NKG2 receptor of NK cells that inhibits NK cell-mediated apoptosis. Thus, in certain particular embodiments, the B2M^{-/-} cell expresses the single chain fusion HLA class I protein comprising at least a portion of B2M and at least a portion of HLA-E. In addition, HLA-G is normally expressed on the surface of placental cytotrophoblasts that do not express HLA-A, B or C, and it protects these cells from NK cell-mediated lysis by interacting with the inhibitory ILT2 (LIR1) receptor on NK cells (Pazmany et al., 1996, Science 274, 792-795). Thus, in certain other preferred embodiments, the B2M^{-/-} cell expresses the single chain fusion HLA class I protein comprising at least a portion of B2M and at least a portion of HLA-G.

[0051] In certain particular embodiments, the single chain fusion HLA class I protein comprises at least a portion of B2M and at least a portion of HLA-A0201. HLA-A0201 (SEQ ID NO: 4) is a common HLA class I allele found in a large percentage of the population in the United States. Thus, in certain advantageous embodiments, the isolated cell expresses the single chain fusion HLA class I protein comprising at least a portion of B2M and at least a portion of HLA-A0201 in a B2M^{-/-} genetic background, wherein the isolated cell is immune compatible with a large percentage of the human population in the United States. Other suitable common alleles that can be used include without limitation HLA-A0101, HLA-A0301, HLA-B0702, HLA-B0801, HLA-00401, HLA-00701, and HLA-00702. In certain preferred embodiments, the HLA allele comprises at least a portion of HLA-A0201 (SEQ ID NO: 4), HLA-B0702 (SEQ ID NO: 6) or HLA-00401 (SEQ ID NO: 8).

[0052] In certain further embodiments, the single chain fusion HLA class I protein also comprises a second target peptide antigen that occupies the peptide binding cleft of the single chain fusion HLA class I protein, wherein the peptide antigen is covalently linked to the single chain fusion HLA class I protein (also referred to as a trimeric construct). An example of the trimeric construct is shown in FIG. 2. The HLA-bGBE construct of FIG. 2 comprises B2M and HLA-E covalently linked to a peptide antigen (such as, but not limited to, the HLA-G signal peptide as illustrated in the figure) (SEQ ID NO: 23) designed to occupy the peptide binding cleft of the

single chain fusion HLA class I protein. In certain other embodiments, the covalently linked peptide antigen is cleaved via a built-in protease cleavage site, and the cleaved peptide antigen can bind to the peptide binding cleft of the single chain fusion HLA-I protein for presentation.

[0053] In certain alternative embodiments, the peptide antigen occupying the peptide binding cleft of the single chain fusion HLA class I protein is produced by the intracellular antigen processing pathway, in which the peptide antigen is produced by proteasome, transported to and loaded onto the single chain fusion HLA class I protein in the endoplasmic reticulum. In certain particular embodiments, the peptide antigen comprises a peptide of a tumor antigen. In certain other embodiments, the peptide antigen comprises a peptide of a protein from a pathogen including without limitation a bacterium, a virus, a fungus and a parasite. In further embodiments, the peptide antigen comprises a peptide of a tumor antigen. In certain particular embodiments, the HLA class I deficient cell or HLA class I/class II deficient cell expresses a single chain fusion HLA class I protein that is covalently linked to a peptide that does not comprise an auto-antigen or neo-antigen to the patient. It is within the ability of a skilled person to design the single chain fusion HLA class I protein and the peptide antigen presented thereon to modulate the immune response that may be elicited in a recipient.

[0054] The isolated HLA class II deficient cells, HLA class I deficient cells, or HLA class I/class II deficient cells expressing an HLA class II protein or a single chain fusion HLA class II protein optionally a single chain fusion HLA class I protein comprising a specific peptide antigen either covalently or non-covalently bound to the single chain fusion proteins can be used, for example, for administration to a recipient to elicit an immune response. Accordingly, in a related aspect, the invention provides a vaccine comprising the isolated cell of the invention, wherein the vaccine is capable of eliciting in a recipient an immune response specific for the target peptide antigen. The immune response includes without limitation a cellular immune response and/or a humoral immune response. The vaccine may comprise a stem cell or a differentiated cell; in certain particular embodiments, the cell is a differentiated dendritic cell. In certain other embodiments, the cell further expresses a cytokine. Any suitable cytokine can be used; in certain particular embodiments, the cytokine is IL2 or IFN- γ . In certain preferred embodiments, the cell is a human cell and the recipient is a human. Thus, in a further aspect, the invention provides kits comprising the vaccines of the invention and optionally an immune adjuvant.

[0055] The single chain fusion HLA class I protein, HLA class II protein, or single chain fusion HLA class II protein can be expressed from an expression vector that allows either transient or more preferably, stable expression of the protein in a cell. Exemplary suitable expression vectors are known in the art. One such example is a retroviral vector, which is capable of integrating into the cellular genome to provide long-term, stable expression of an exogenous gene. In certain particular embodiments, the viral vector is derived from human foamy virus, a type of retrovirus. Other suitable viral vectors include without limitation vectors derived from retrovirus, adenoviral virus, adeno-associated virus, lentivirus, herpes simplex virus, vaccinia virus, and pox virus.

[0056] In certain preferred embodiments, the polynucleotide capable of encoding a single chain fusion HLA class I or class II protein or an HLA class II protein is integrated into the chromosome of the cells, preferably into the B2M or the HLA

class II loci, for stable expression. Thus, in certain preferred embodiments, the B2M loci are disrupted by inserting in the B2M loci the polynucleotide capable of encoding a single chain fusion HLA class I protein to replace the expression of the endogenous wild type B2M protein. Thus, in certain other preferred embodiments, certain HLA-II loci are disrupted by inserting in the HLA-II loci the polynucleotide capable of encoding an HLA class II protein or a single chain fusion HLA class II protein to replace the expression of the endogenous wild type HLA-II protein. The result of such gene targeting precludes formation of wild type HLA class I proteins and specific HLA class II proteins but permits expression of a predetermined HLA class II protein or single chain fusion HLA class I or class II protein of choice on the surface of the otherwise HLA class II deficient cells. Other expression vectors are also contemplated and the selection of suitable expression vector is within the ability of one ordinary skill in the art.

[0057] The "isolated cell" can be any suitable cell type for a given purpose. For example, the cell can be a pluripotent stem cell or a differentiated cell. "A stem cell" broadly encompasses any cells that are capable of further differentiation. "A pluripotent stem cell" refers to a stem cell that has the potential to differentiate into any of the three germ layers: endoderm, mesoderm or ectoderm. "An adult stem cell," on the other hand, is multipotent in that it can produce only a limited number of cell types. "An embryonic stem (ES) cell" refers to a pluripotent stem cell derived from the inner cell mass of the blastocyst, an early-stage embryo. "Induced pluripotent stem cells (iPS cells)" are pluripotent stem cell artificially derived from a non-pluripotent cell, typically an adult somatic cell, by artificially inducing expression of certain genes.

[0058] In another aspect, the invention provides a method of transplantation in a patient in need thereof comprising the step of administering to the patient an effective amount of the cells of the invention for transplantation. Because the HLA class II deficient cells and/or HLA class I deficient cells do not express wild type HLA class II protein (and optionally also HLA class I protein) on the cell surface, the cells when administered to a patient elicit minimal or no immune responses in the patient. Thus, transplantation using the HLA class II deficient cells and/or HLA class I deficient cells limits the need for taking immune suppressant therapies. Thus, in certain preferred embodiments, the patient is immune competent. In certain other embodiments, the cell is an isogeneic cell; while in other embodiments, the cell is an allogeneic cell.

[0059] In certain further embodiments, the cells of the invention are pluripotent stem cells; while in other embodiments, the cells of the invention are differentiated cells. In certain preferred embodiments, the cell is a human cell and the patient is a human patient. In certain particular embodiments, the method of transplantation comprises administering to a human an effective amount of the pluripotent stem cells or differentiated cells. In certain preferred embodiments, the cells of the invention further express one or more engineered single chain fusion HLA class II proteins and optionally also a single chain fusion HLA class I protein. In certain other embodiments, the cells are able to escape NK cell-mediated killing and elicit minimal or no immune response in the recipient after transplantation.

[0060] Transplantation therapy, replacement therapy or regenerative therapy refers to therapies for a disease condition by administering to a patient cells or tissues to replenish

or replace defective cellular functions in a target organ. In certain particular embodiments, the need for transplantation arises as a result of physical or pathological injuries to a tissue or organ. In certain other particular embodiments, the need for transplantation arises as a result of one or more genetic defect or mutation in the patient and the transplantation of the cells of the invention replenishes or replaces defective cellular functions in the patient without the need for gene therapy to correct the underlying genetic mutation of the patient. In certain further embodiments, the transplantation includes without limitation hematopoietic stem cell transplantation, or transplantation of cells that are incorporated into an organ such as liver, kidney, pancreas, lung, brain, muscle, heart, gastrointestinal tract, nervous system, skin, bones, bone marrow, fat, connective tissue, immune system, or blood vessels. In certain particular embodiments, the target organ is a solid organ.

[0061] In certain particular embodiments, the cells administered to the recipient may or may not be incorporated into an organ in need of such therapy. In certain embodiments, the cells of the invention are differentiated into the desired cell type, either before or after transplantation, and provide the necessary cellular function without itself being incorporated into the tissue at the site of transplantation. For example, in certain embodiments for treating diabetes, the cells of the invention either as pluripotent stem cells or differentiated pancreatic beta islet cells are transplanted to a diabetic patient. The transplanted cells need not reconstitute a functioning pancreas: they just need to secrete insulin in response to glucose levels. In certain particular embodiments, the cells are transplanted into an ectopic location and are not fully incorporated into the pancreas. Transplantation of pluripotent cells of the invention, differentiated cells of the invention, or a tissue differentiated and developed ex vivo from the cells of the invention are all contemplated by the invention. In certain preferred embodiments, the cell is a human cell and the patient is a human patient. In certain other preferred embodiments, the cells of the invention express one or more single chain fusion HLA class II proteins and optionally also single chain fusion HLA class I proteins.

[0062] In a further aspect, the invention provides a method of treating a disease condition in a patient in need thereof comprising the step of administering to the patient an effective amount of the cell of the invention to treat the disease condition, wherein the disease condition is diabetes, an autoimmune disease, cancer, infection, anemia, cytopenia, myocardial infarction, heart failure, skeletal or joint condition, osteogenesis imperfecta or burns. In certain particular embodiments, the disease condition results from pathological or physical injuries to a tissue or organ. In certain embodiments, the cells of the invention are stem cells; while in other embodiments, the cells of the invention are differentiated cells. In certain preferred embodiments, the cell is a human cell and the patient is a human patient. In certain particular embodiments, the human cell is a differentiated cell. Transplantation of a tissue developed ex vivo from the cells of the invention is also contemplated by the invention. In certain preferred embodiments, the cells of the invention further express one or more single chain fusion HLA class II proteins and optionally also one or more single chain fusion HLA class I proteins. In certain embodiments, the cell is an isogeneic cell; while in other embodiments, the cell is an allogeneic cell.

[0063] In certain particular embodiments, the cell is a differentiated cell including without limitation a dendritic cell,

lymphocyte, red blood cell, platelet, hematopoietic cell, pancreatic islet cell, liver cell, muscle cell, keratinocyte, cardiomyocyte, neuronal cell, skeletal muscle cell, ocular cell, mesenchymal cell, fibroblast, lung cell, GI tract cell, vascular cell, endocrine cell and adipocyte. In certain other particular embodiments, the invention provides a method of treating a disease condition in a solid organ. In certain embodiments, the cells of the invention used in treating a disease condition express one or more single chain fusion HLA class I proteins and optionally also one or more single chain fusion HLA class I proteins.

[0064] “Treating” a patient having a disease or disorder means accomplishing one or more of the following: (a) reducing the severity of the disease; (b) arresting the development of the disease or disorder; (c) inhibiting worsening of the disease or disorder; (d) limiting or preventing recurrence of the disease or disorder in patients that have previously had the disease or disorder; (e) causing regression of the disease or disorder; (f) improving or eliminating the symptoms of the disease or disorder; and (f) improving survival. In certain preferred embodiments, the disease or disorder is a disease or disorder that can be treated by transplantation of tissues or cells.

[0065] The effective amount of the isolated cells of the invention for transplantation or for treating a disease condition depends on a number of factors, such as the type of tissue, the severity of the disease condition, the transplantation reaction, the reason for transplantation, and the age and general health of the patient. The effective amount can be determined by a skilled researcher or clinician by routine practice. Due to the reduced immunogenicity of the transplanted cells, relative large amount of cells can be tolerated by a patient to achieve the desired therapeutic effects. Alternatively, the cells can be repeatedly transplanted at intervals until a desired therapeutic effect is achieved.

[0066] The route for administration of the cells of the invention is not limited in any particular way. Exemplary delivery routes include without limitation intravenous, intramuscular, subdermal, intraperitoneal, transcutaneous, intracutaneous, and subcutaneous route. The cells of the present invention can also be administered topically by injection. For example, the cells can be injected into an injured joint, a fractured bone, an infarct site, an ischemic site or their periphery.

[0067] In certain particular embodiments, the cells are administered via a delivery device including without limitation a syringe. For example, the cells can be suspended in a solution or a pharmaceutical composition contained in such a delivery device. The “solution” or “pharmaceutical composition” comprises a physiological compatible buffer and optionally a pharmaceutically acceptable carrier or diluent in which the cells of the invention remain viable. The use of such carriers and diluents is well known in the art. The solution includes without limitation physiologically compatible buffers such as Hank’s solution, Ringer’s solution, or physiologically buffered saline. The cells can be kept in the solution or pharmaceutical composition for short term storage without losing viability. In certain particular embodiments, the cells are frozen for long term storage without losing viability according to cryopreservation methods well-known in the art.

[0068] Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran, but still fluid to the extent that can be easily delivered by syringe

injection. The solution is preferably sterile, stable under the conditions of manufacture and storage and is free of micro-organism contamination through the use of, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, and the like. The cells contained in the solution can be stem cells or differentiated cells as described herein, in a pharmaceutically acceptable carrier or diluent and, as required, other ingredients indicated above.

[0069] The cells may be administered systemically (e.g., intravenously) or locally (e.g., directly into a myocardial defect under the guidance of echocardiogram, or by direct application to damaged tissues or organs accessible during open surgery). For injections, the cells may be in an injectable liquid suspension preparation or in a biocompatible medium which is injectable in liquid form and becomes semi-solid at the site of damaged tissue. A syringe, a controllable endoscopic delivery device or other similar devices can be used so long as the needle lumen is of sufficient diameter (e.g. at least 30 gauge or larger) to avoid physical damages to the cells during delivery.

[0070] In certain other embodiments, the cells can be transplanted via a solid support, e.g., a planar surface or three-dimensional matrix. The matrix or planar surface is surgically implanted into the appropriate site in a patient. For example, a patient needing a pancreatic graft can have differentiated cells on a solid support surgically implanted in the pancreas tissue. Exemplary solid support includes without limitation a patch, a gel matrix (such as GELFOAM® from Pharmacia-Upjohn), polyvinyl alcohol sponge (PVA)-collagen gel implants (such as IVALON, Unipoint Industries, High Point, N.C.) and other similar or equivalent devices. A variety of other encapsulation technologies can be used with the cells of the invention, for example, WO 91/10470; WO 91/10425; U.S. Pat. No. 5,837,234; U.S. Pat. No. 5,011,472; U.S. Pat. No. 4,892,538).

[0071] The cells of the invention can be differentiated into various cell types of all three lineages, including without limitation hematopoietic, mesenchymal, pancreatic endoderm, cardiac and keratinocytes cells. In certain embodiments, the differentiated cell further expresses an HLA class II protein or a single chain fusion HLA class II protein and optionally also a single chain fusion HLA class I protein. In general, each cell type can be analyzed for HLA class II and optionally also class I protein expression, reactivity with human T cells and NK cells, appropriate differentiation markers, and xenotransplantation in immunodeficient mice to examine in vivo developmental potential. A brief discussion of each differentiated cell type follows.

[0072] In certain embodiments, the cells of the invention can be differentiated to hematopoietic cells for treating various hematopoietic diseases currently treated by bone marrow transplantation. Patients receiving transfusion can become refractory to platelet transfusions due to HLA mismatches. Anemic or cytopenic patients can be treated by delivering the cells of the invention-derived erythrocytes, platelets or neutrophils to treat bleeding or infection.

[0073] Further, stem cells of the invention-derived dendritic cells are antigen-presenting cells that can be used as cellular vaccines when properly engineered. In certain embodiments, the cells of the invention engineered to express an HLA class II protein or a single chain fusion HLA class II protein and optionally also a single chain fusion HLA class I protein and a unique peptide antigen are used to vaccinate against specific pathogen or tumor antigens. In certain other

embodiments, differentiated HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient cytotoxic lymphocytes with HLA-restricted reactivity against specific antigens are used to eliminate infected cells or tumor cells.

[0074] To obtain hematopoietic cells, the pluripotent cells are first allowed to form embryoid bodies, thereafter non-adherent cells were cultured in the presence of hematopoietic cytokines to develop into specific cell lineages. The differentiation of hematopoietic cells from the cells of the invention that express an HLA class II protein or a single chain fusion HLA class II protein and optionally also a single chain fusion HLA class I protein can be analyzed by flow cytometry and colony assays. The different cell populations are sorted based on their surface markers, and used to monitor the expression of HLA genes and reactivity with human NK cells and T cells as measured by Elispot, mixed lymphocyte reactions, and cytotoxicity assays. The effectiveness of the single chain fusion HLA constructs on suppression of NK cell-mediated killing can be examined at different stages of differentiation and transplantation. See Bix et al., 1991, *Nature* 349, 329-331. The hematopoietic stem cells can also be assayed using xenotransplantation models in, for example, immunodeficient mice (SCID-repopulating cells or SRCs).

[0075] The cells of the invention can be differentiated into hematopoietic cell either before or after the cells are administered to a patient. In certain preferred embodiments, the cell is a human cell and the patient is a human. In vitro hematopoietic differentiation can be performed according to established protocols. See for example, Slukvin et al., 2006, *J Immunol* 176:2924-32, and Chang et al., 2006, *Blood* 108: 1515-23.

[0076] In certain other embodiments, the cells of the invention can be differentiated into mesenchymal stem cells. In certain embodiments, the cells of the invention express one or more HLA class II protein or single chain fusion HLA class II proteins and optionally also one or more single chain fusion HLA class I proteins. MSCs have the potential to form several differentiated cell types, including marrow stromal cells, adipocytes, osteoblasts, and chondrocytes. Thus, inducing pluripotent stem cells to form MSCs (iMSCs) is useful in treating skeletal and joint conditions. The iMSCs can be further differentiated into osteoblasts and formed bone in vivo. Deyle et al., 2012, *Mol. Ther.* 20(1):204-13. Cellular responses of T cells and NK cells to ESCs, iMSCs, and their more terminally differentiated derivatives such as osteoblasts can be examined.

[0077] In certain particular embodiments, the mesenchymal stem cells are capable of differentiating into non-limiting examples of cell types such as marrow stromal cells, adipocytes, osteoblasts, osteocytes and chondrocytes. The cells of the invention are differentiated into mesenchymal stem cells either before or after the cells are administered to a patient. In certain preferred embodiments, the cell is a human cell and the patient is a human. In vitro mesenchymal differentiation can be performed according to established protocols. See for example, Deyle et al., *supra*.

[0078] In yet other particular embodiments, the cells of the invention can be differentiated into insulin-producing pancreatic islet cells. In certain embodiments, the cells of the invention express one or more HLA class II proteins or single chain fusion HLA class II proteins and optionally also one or more single chain fusion HLA class I proteins. The cells of the invention can be used to treat insulin-dependent diabetes mellitus. Advantageously, the transplanted cells do not need

to reconstitute a functioning pancreas: they just need to secrete insulin in response to glucose levels. Therefore the treatment can succeed with different cell doses, with cells that are not perfectly differentiated into adult cell types, and when cells are transplanted into an ectopic location. Specific auto-antigens such as those derived from GAD65 or Insulin can cause autoimmune destruction of β cells in diabetes (Di Lorenzo et al., 2007, Clin Exp Immunol 148, 1-16). Thus, HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient cells expressing single chain fusion HLA protein presenting a predetermined peptide antigen provide additional advantages in that they do not present these auto-antigens and can avoid autoimmune rejection and prevent a relapse of diabetes after transplantation.

[0079] The cells of the invention can be differentiated into pancreatic cells as described previously, which employs exposure of cells to different cytokines and drugs to promote sequential formation of mesendoderm, definitive endoderm, and pancreatic progenitors (Kroon et al., 2008, Nat Biotechnol 26, 443-452). These cells can be further cultured in implants in immunodeficient mice. The wild-type cells and cells of the invention with or without expressing one or more single chain fusion HLA class II proteins or both one or more single chain fusion HLA class II proteins and optionally also one or more single chain HLA class I proteins can be analyzed at different developmental stages for their reactivity with T cells and NK cells.

[0080] The cells of the invention are differentiated into pancreatic islet cell either before or after patient administration. In certain preferred embodiments, the cell is a human cell and the patient is a human. In vitro hematopoietic differentiation can be performed according to established protocols. See for example, Kroon et al., 2008, Nat Biotechnol 26, 443-452.

[0081] In certain other particular embodiments, the cells of the invention can be differentiated into cardiomyocytes. In certain embodiments, the cells of the invention further express one or more HLA class II proteins or single chain fusion HLA class II proteins and optionally also one or more single chain fusion HLA class I proteins. The common clinical problems of myocardial infarction and congestive heart failure can be treated by transplanting healthy stem cell-derived cardiomyocytes that engraft and re-establish functional myocardium. The cells of the invention-derived cardiomyocytes allow these treatments to proceed with pre-packaged cells and avoid the immunosuppression currently required for allogeneic heart transplants. Physiologically relevant tests can be performed on the cardiomyocytes derived from the cells of the invention, such as electrical conduction and contraction studies. HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient stem cells or differentiated cardiomyocytes with or without expressing a single chain fusion HLA class I protein can be tested to determine their immunological reactivity when expressing cardiomyocyte genes, and to establish which HLA modifications minimize these immune responses.

[0082] The cells of the invention can be differentiated into cardiomyocytes either before or after the cells are administered to a patient. In certain preferred embodiments, the cell is a human cell and the patient is a human. In certain embodiments, the cells of the invention are differentiated into cardiomyocytes for treating diseases including without limitation myocardial infarction and congestive heart failure. In vitro cardiomyocyte differentiation can be performed according to

established protocols. See for example, Laflamme et al., 2007, Nat Biotechnol 25, 1015-1024.

[0083] In yet other particular embodiments, the cells of the invention can be differentiated into keratinocytes. In certain embodiments, the cells of the invention used for differentiation into keratinocytes express one or more single chain fusion HLA class II proteins and optionally also one or more HLA class II proteins or single chain fusion HLA class I proteins. Severe burns and genetic skin conditions require treatment with skin grafts, and this is currently done with a variety of cell sources such as porcine skin grafts and cultured autologous human keratinocytes. Keratinocytes derived from the cells of the invention can provide a major clinical advance, since burns could be treated as an emergency with pre-packaged cells, and genetic diseases such as epidermolysis bullosa can be treated with otherwise normal HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient cells that do not require correction of the responsible genetic mutations. In many cases the cells only need to engraft long enough for neighboring host cells to repopulate the affected area. For in vivo differentiation, the cells of the invention can be embedded in polyvinyl alcohol sponge (PVA)-collagen gel implants for transplantation into a recipient. The cells of the invention can be differentiated into keratinocytes either before or after transplantation. In certain preferred embodiments, the cell is a human cell and the patient is a human.

[0084] In yet another aspect, the invention provides a use of the cells of the invention for the preparation for a medicament for transplantation. In a related aspect, the invention provides a use of the cells of the invention for the preparation for a medicament for treating a disease condition.

[0085] Further, the cells of the invention can serve as a research tool to provide a system for studying the functions of immunoregulatory proteins in a HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient genetic background. In certain embodiments, the cells of the invention further express one or more HLA class II proteins or single chain fusion HLA class II proteins and optionally also one or more single chain fusion HLA class I proteins. Accordingly, in a related aspect, the invention provides a method of determining the function of an immunoregulatory protein comprising the steps of introducing one or more immunoregulatory genes into the cells of the invention of the invention and assaying for the activities of the immunoregulatory genes. In certain preferred embodiments, the cell is a human cell. For example, the cells of the invention can be used to study the function of an immune regulatory gene, or to study an immune response, in the absence of unwanted HLA class II antigens or HLA class I/class II antigens. In a further related aspect, the invention provides a method of identifying a compound or molecule that modulates the function of the immunoregulatory protein comprising the steps of contacting the HLA class II deficient cells, HLA class I deficient cells, or HLA class I/class II deficient cells comprising the one or more immunoregulatory genes with a compound or molecule of interest and assaying for the activities of the immunoregulatory genes. In certain preferred embodiments, the cell is a human cell.

[0086] In a related aspect, the invention provides kits that comprise the HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient cells of the invention and an implant, wherein the implant comprises the cells of the invention.

[0087] In yet another aspect, the invention provides an in vivo research tool in a mammal, particular in a non-human primate, that are administered the cells of the invention, for studying the functions of immunoregulatory genes, or identifying a compound that modulates the function of an immunoregulatory gene in the administered cells in an HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient genetic background. In certain embodiments, the cells of the invention further express one or more HLA class II proteins or single chain fusion HLA class II proteins and optionally also one or more single chain fusion HLA class I proteins.

[0088] Mice, especially immune deficient mice, have been used as a model system for studying human cells in vivo. Human stem cells can behave differently in mice. In addition, the mouse and human immune systems have different HLA class II genes, NK cell receptors and non-classical MHC class I genes (e.g. HLA-E, F and G). Therefore, a *Macaca nemestrina* (Mn, pigtailed macaque) model can be developed to study the cells of the invention. The *Macaca mulatta* genome has been sequenced, which is highly homologous to the *nemestrina* genome. Further, the organization of macaque MHC loci is similar to human HLA, including the non-classical genes. Homologs of the human HLA-E and HLA-G genes have been identified in macaques. The macaque MHC loci also contain homologs of many human NK cell receptors. Human and Mn HLA class II deficient, HLA class I deficient, or HLA class I/class II deficient ESCs can be used for transplantation in macaques.

[0089] MHC class II-deficient of MHC class I/class II-deficient macaque ESCs can be developed using the same AAV-mediated gene targeting strategy described for human cells. Mn versions of the single chain fusion HLA class II proteins and optionally single chain fusion HLA class I proteins are expressed in the HLA class II or HLA class II/class I deficient macaques ESCs using the analogous viral vectors as described above.

[0090] Cells can be expanded in vitro and labeled with a vector expressing GFP for subsequent identification of transplanted cells. The cells can be embedded in polyvinyl alcohol sponge (PVA)-collagen gel implants, and placed subdermally into macaques. The implants can be harvested, sectioned and

stained to determine the cell types that are present. Specific antibodies can be used to identify the differentiated cell types formed by the transplanted cells.

[0091] Any and every embodiment described above applies to any and every aspect of the invention, unless the context clearly indicates otherwise. All embodiments within and between different aspects can be combined unless the context clearly dictates otherwise.

EXAMPLES

Example 1

Construction of Human Embryonic Stem Cells with Knockout Mutation in RFXANK Gene

[0092] FIG. 1 shows the structure of exemplary two adeno-associated virus (AAV) gene targeting vectors, designed to insert either a TKNeo (AAV-RFXANK-ETKNpA) or HyTK (AAV-RFXANK-HyTK) gene controlled by an EF1alpha promoter (EF) into exon 3 of the RFXANK gene, which is also shown below the vectors. Selection of vector-infected cells with G418 or hygromycin (Hygro) allows one to isolate cells targeted by the TKNeo or HyTK vectors respectively. Subsequent expression of Cre recombinase and selection with gancyclovir (GCV) then allows one to isolate clones that have removed the TKNeo or HyTK genes, leaving behind two inactivated RFXANK alleles with stop codons in all 3 reading frames, a loxP site, and a polyadenylation site (StopX3-loxP-pA). LoxP is the recombination site for Cre recombinase. ITR is a vector inverted terminal repeat. Similar vectors could be designed to target other genes.

[0093] The AAV-RFXANK-ETKNpA vector (SEQ ID NO: 56) was used to create a knockout mutation in a first allele of the RFXANK gene. Human embryonic stem cells were infected with AAV-RFXANK-ETKNpA and screened for targeting by PCR using a forward primer homologous to the neomycin sequence of the selection cassette and a reverse primer homologous to the RFXANK gene which was outside the targeting homology arm, as indicated by the arrows above. As shown in FIG. 2, 5 positive clones of the correct size are shown above out of 40 clones screened yielding a targeting frequency of 12.5%.

SEQUENCE LISTING

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<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

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<221> NAME/KEY: CDS

<222> LOCATION: (61)..(420)

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Met Ser Arg Ser Val Ala Leu Ala Val Leu Ala Leu Leu Ser Leu Ser
1 5 10 15

ggc ctg gag gct atc cag cgt act cca aag att cag gtt tac tca cgt 156
Gly Leu Glu Ala Ile Gln Arg Thr Pro Lys Ile Gln Val Tyr Ser Arg
20 25 30

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His Pro Ala Glu Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser	
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Gly Phe His Pro Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu	
50 55 60	
aga att gaa aaa gtg gag cat tca gac ttg tct ttc agc aag gac tgg	300
Arg Ile Glu Lys Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp	
65 70 75 80	
tct ttc tat ctc ttg tac tac act gaa ttc acc ccc act gaa aaa gat	348
Ser Phe Tyr Leu Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp	
85 90 95	
gag tat gcc tgc cgt gtg aac cat gtg act ttg tca cag ccc aag ata	396
Glu Tyr Ala Cys Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile	
100 105 110	
gtt aag tgg gat cga gac atg taa gcagcatcat ggaggtttga agatgccgca	450
Val Lys Trp Asp Arg Asp Met	
115	
tttgatttg atgaattcca aattctgctt gcttgctttt taatattgat atgcttatac	510
acttacactt tatgcacaaa atgtagggtt ataataatgt taacatggac atgatcttct	570
ttataattct actttgagtg ctgtctccat gtttgatgta tctgagcagg ttgctccaca	630
ggtagctcta ggagggttg caacttagag gtggggagca gagaattctc ttaaccaaca	690
tcaacatctt ggtcagattt gaactcttca atctcttgca ctcaaagctt gttaagatag	750
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tagaaatata attgacagga ttattggaaa tttgttataa tgaatgaaac attttgtcat	870
ataagattca tatttacttc ttatacattt gataaagtaa ggcatggttg tggtaaatct	930
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<212> TYPE: PRT	
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20 25 30	
His Pro Ala Glu Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser	
35 40 45	
Gly Phe His Pro Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu	
50 55 60	
Arg Ile Glu Lys Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp	
65 70 75 80	
Ser Phe Tyr Leu Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp	
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Glu Tyr Ala Cys Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile	
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Val Lys Trp Asp Arg Asp Met	
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<212> TYPE: DNA
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<220> FEATURE:
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<222> LOCATION: (85)..(1182)

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tcagattctc cccagacgcc gagg atg gcc gtc atg gcg ccc cga acc ctc      111
                Met Ala Val Met Ala Pro Arg Thr Leu
                1                5

ctc ctg cta ctc tgc ggg gcc ctg gcc ctg acc cag acc tgg gcg ggc      159
Leu Leu Leu Leu Ser Gly Ala Leu Ala Leu Thr Gln Thr Trp Ala Gly
10                15                20                25

tcc cac tcc atg agg tat ttc ttc aca tcc gtg tcc cgg ccc ggc cgc      207
Ser His Ser Met Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly Arg
                30                35                40

ggg gag ccc cgc ttc atc gcc gtg ggc tac gtg gac gac acg cag ttc      255
Gly Glu Pro Arg Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln Phe
                45                50                55

gtg cgg ttc gac agc gac gcc gcg agc cag aag atg gag ccg cgg gcg      303
Val Arg Phe Asp Ser Asp Ala Ala Ser Gln Lys Met Glu Pro Arg Ala
                60                65                70

ccg tgg ata gag cag gag ggg ccg gag tat tgg gac cag gag aca ccg      351
Pro Trp Ile Glu Gln Glu Gly Pro Glu Tyr Trp Asp Gln Glu Thr Arg
                75                80                85

aat atg aag gcc cac tca cag act gac cga gcg aac ctg ggg acc ctg      399
Asn Met Lys Ala His Ser Gln Thr Asp Arg Ala Asn Leu Gly Thr Leu
90                95                100                105

cgc gcc tac tac aac cag agc gag gac ggt tct cac acc atc cag ata      447
Arg Gly Tyr Tyr Asn Gln Ser Glu Asp Gly Ser His Thr Ile Gln Ile
                110                115                120

atg tat ggc tgc gac gtg ggg ccg gac ggg cgc ttc ctc cgc ggg tac      495
Met Tyr Gly Cys Asp Val Gly Pro Asp Gly Arg Phe Leu Arg Gly Tyr
                125                130                135

cgg cag gac gcc tac gac gcc aag gat tac atc gcc ctg aac gag gac      543
Arg Gln Asp Ala Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Asn Glu Asp
                140                145                150

ctg cgc tct tgg acc gcg gcg gac atg gca gct cag atc acc aag cgc      591
Leu Arg Ser Trp Thr Ala Ala Asp Met Ala Ala Gln Ile Thr Lys Arg
                155                160                165

aag tgg gag gcg gtc cat gcg gcg gag cag cgg aga gtc tac ctg gag      639
Lys Trp Glu Ala Val His Ala Ala Glu Gln Arg Arg Val Tyr Leu Glu
170                175                180                185

ggc cgg tgc gtg gac ggg ctc cgc aga tac ctg gag aac ggg aag gag      687
Gly Arg Cys Val Asp Gly Leu Arg Arg Tyr Leu Glu Asn Gly Lys Glu
                190                195                200

acg ctg cag cgc acg gac ccc ccc aag aca cat atg acc cac cac ccc      735
Thr Leu Gln Arg Thr Asp Pro Pro Lys Thr His Met Thr His His Pro
                205                210                215

atc tct gac cat gag gcc acc ctg agg tgc tgg gcc ctg gcc ttc tac      783
Ile Ser Asp His Glu Ala Thr Leu Arg Cys Trp Ala Leu Gly Phe Tyr
                220                225                230

cct gcg gag atc aca ctg acc tgg cag cgg gat ggg gag gac cag acc      831
Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln Thr
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Gln Asp Thr Glu Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr Phe	
250 255 260 265	
cag aag tgg gcg gct gtg gtg gtg cct tct gga gag gag cag aga tac	927
Gln Lys Trp Ala Ala Val Val Val Pro Ser Gly Glu Glu Gln Arg Tyr	
270 275 280	
acc tgc cat gtg cag cat gag ggt ctg ccc aag ccc ctc acc ctg aga	975
Thr Cys His Val Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu Arg	
285 290 295	
tgg gag ctg tct tcc cag ccc acc atc ccc atc gtg ggc atc att gct	1023
Trp Glu Leu Ser Ser Gln Pro Thr Ile Pro Ile Val Gly Ile Ile Ala	
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ggc ctg gtt ctc ctt gga gct gtg atc act gga gct gtg gtc gct gcc	1071
Gly Leu Val Leu Leu Gly Ala Val Ile Thr Gly Ala Val Val Ala Ala	
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gtg atg tgg agg agg aag agc tca gat aga aaa gga ggg agt tac act	1119
Val Met Trp Arg Arg Lys Ser Ser Asp Arg Lys Gly Gly Ser Tyr Thr	
330 335 340 345	
cag gct gca agc agt gac agt gcc cag ggc tct gat gtg tct ctc aca	1167
Gln Ala Ala Ser Ser Asp Ser Ala Gln Gly Ser Asp Val Ser Leu Thr	
350 355 360	
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Ala Cys Lys Val	
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ctgcccttcc ctttgtgact tgaagaaccc tgactttgtt tctgcaaagg cacctgcatg	1282
tgctgtgttt cgtgtaggca taatgtgagg aggtggggag agcaccacac ccccatgtcc	1342
accatgaccc tcttcccacg ctgacctgtg ctccctctcc aatcatcttt cctgttccag	1402
agaggtgggg ctgaggtgtc tccatctctg totcaacttc atggtgcact gagctgtaac	1462
ttcttcttc cctattaaaa ttagaacctg agtataaatt tactttctca aattcttgcc	1522
atgagaggtt gatgagttaa ttaaaggaga agattcctaa aatttgagag acaaaattaa	1582
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<210> SEQ ID NO 4

<211> LENGTH: 365

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 4

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Leu Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe
20 25 30

Phe Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ala
35 40 45

Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
50 55 60

Ala Ser Gln Lys Met Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly
65 70 75 80

Pro Glu Tyr Trp Asp Gln Glu Thr Arg Asn Met Lys Ala His Ser Gln
85 90 95

Thr Asp Arg Ala Asn Leu Gly Thr Leu Arg Gly Tyr Tyr Asn Gln Ser
100 105 110

Glu Asp Gly Ser His Thr Ile Gln Ile Met Tyr Gly Cys Asp Val Gly

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115	120	125
Pro Asp Gly Arg Phe Leu Arg Gly Tyr Arg Gln Asp Ala Tyr Asp Gly		
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Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala		
145	150	155
Asp Met Ala Ala Gln Ile Thr Lys Arg Lys Trp Glu Ala Val His Ala		
	165	170
Ala Glu Gln Arg Arg Val Tyr Leu Glu Gly Arg Cys Val Asp Gly Leu		
	180	185
Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Thr Asp Pro		
	195	200
Pro Lys Thr His Met Thr His His Pro Ile Ser Asp His Glu Ala Thr		
	210	215
Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr		
	225	230
Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu		
	245	250
Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val		
	260	265
Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu		
	275	280
Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Leu Ser Ser Gln Pro		
	290	295
Thr Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu Leu Gly Ala		
	305	310
Val Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Arg Lys Ser		
	325	330
Ser Asp Arg Lys Gly Gly Ser Tyr Thr Gln Ala Ala Ser Ser Asp Ser		
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<211> LENGTH: 1578

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (55)..(1143)

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Leu Val Met Ala Pro Arg Thr Val Leu Leu Leu Ser Ala Ala Leu	
5	10
gcc ctg acc gag acc tgg gcc ggc tcc cac tcc atg agg tat ttc tac	153
Ala Leu Thr Glu Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe Tyr	
20	25
acc tcc gtg tcc cgg ccc ggc cgc ggg gag ccc cgc ttc atc tca gtg	201
Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser Val	
35	40
ggc tac gtg gac gac acc cag ttc gtg agg ttc gac agc gac gcc gcg	249
Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala Ala	

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50	55	60	65	
agt ccg aga gag gag ccg cgg gcg ccg tgg ata gag cag gag ggg ccg				297
Ser Pro Arg Glu Glu Pro Arg Ala Pro Trp Ile Glu Gln Glu Gly Pro	70	75	80	
gag tat tgg gac cgg aac aca cag atc tac aag gcc cag gca cag act				345
Glu Tyr Trp Asp Arg Asn Thr Gln Ile Tyr Lys Ala Gln Ala Gln Thr	85	90	95	
gac cga gag agc ctg cgg aac ctg cgc ggc tac tac aac cag agc gag				393
Asp Arg Glu Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser Glu	100	105	110	
gcc ggg tct cac acc ctc cag agc atg tac ggc tgc gac gtg ggg ccg				441
Ala Gly Ser His Thr Leu Gln Ser Met Tyr Gly Cys Asp Val Gly Pro	115	120	125	
gac ggg cgc ctc ctc cgc ggg cat gac cag tac gcc tac gac ggc aag				489
Asp Gly Arg Leu Leu Arg Gly His Asp Gln Tyr Ala Tyr Asp Gly Lys	130	135	140	145
gat tac atc gcc ctg aac gag gac ctg cgc tcc tgg acc gcc gcg gac				537
Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp	150	155	160	
acg gcg gct cag atc acc cag cgc aag tgg gag gcg gcc cgt gag gcg				585
Thr Ala Ala Gln Ile Thr Gln Arg Lys Trp Glu Ala Ala Arg Glu Ala	165	170	175	
gag cag cgg aga gcc tac ctg gag ggc gag tgc gtg gag tgg ctc cgc				633
Glu Gln Arg Arg Ala Tyr Leu Glu Gly Glu Cys Val Glu Trp Leu Arg	180	185	190	
aga tac ctg gag aac ggg aag gac aag ctg gag cgc gct gac ccc cca				681
Arg Tyr Leu Glu Asn Gly Lys Asp Lys Leu Glu Arg Ala Asp Pro Pro	195	200	205	
aag aca cac gtg acc cac cac ccc atc tct gac cat gag gcc acc ctg				729
Lys Thr His Val Thr His His Pro Ile Ser Asp His Glu Ala Thr Leu	210	215	220	225
agg tgc tgg gcc ctg ggt ttc tac cct gcg gag atc aca ctg acc tgg				777
Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp	230	235	240	
cag cgg gat ggc gag gac caa act cag gac act gag ctt gtg gag acc				825
Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu Thr	245	250	255	
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Arg Pro Ala Gly Asp Arg Thr Phe Gln Lys Trp Ala Val Val Val	260	265	270	
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Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly	275	280	285	
ctg ccg aag ccc ctc acc ctg aga tgg gag ccg tct tcc cag tcc acc				969
Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Ser Thr	290	295	300	305
gtc ccc atc gtg ggc att gtt gct ggc ctg gct gtc cta gca gtt gtg				1017
Val Pro Ile Val Glu Ile Val Ala Gly Leu Ala Val Leu Ala Val Val	310	315	320	
gtc atc gga gct gtg gtc gct gct gtg atg tgt agg agg aag agt tca				1065
Val Ile Gly Ala Val Val Ala Ala Val Met Cys Arg Arg Lys Ser Ser	325	330	335	
ggt gga aaa gga ggg agc tac tct cag gct gcg tgc agc gac agt gcc				1113
Gly Gly Lys Gly Gly Ser Tyr Ser Gln Ala Ala Cys Ser Asp Ser Ala	340	345	350	
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Gln Gly Ser Asp Val Ser Leu Thr Ala				

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<211> LENGTH: 362

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

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Tyr	Thr	Ser	Val	Ser	Arg	Pro	Gly	Arg	Gly	Glu	Pro	Arg	Phe	Ile	Ser
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Val	Gly	Tyr	Val	Asp	Asp	Thr	Gln	Phe	Val	Arg	Phe	Asp	Ser	Asp	Ala
	50					55					60				
Ala	Ser	Pro	Arg	Glu	Glu	Pro	Arg	Ala	Pro	Trp	Ile	Glu	Gln	Glu	Gly
	65				70					75				80	
Pro	Glu	Tyr	Trp	Asp	Arg	Asn	Thr	Gln	Ile	Tyr	Lys	Ala	Gln	Ala	Gln
			85					90					95		
Thr	Asp	Arg	Glu	Ser	Leu	Arg	Asn	Leu	Arg	Gly	Tyr	Tyr	Asn	Gln	Ser
			100					105					110		
Glu	Ala	Gly	Ser	His	Thr	Leu	Gln	Ser	Met	Tyr	Gly	Cys	Asp	Val	Gly
			115				120					125			
Pro	Asp	Gly	Arg	Leu	Leu	Arg	Gly	His	Asp	Gln	Tyr	Ala	Tyr	Asp	Gly
	130					135					140				
Lys	Asp	Tyr	Ile	Ala	Leu	Asn	Glu	Asp	Leu	Arg	Ser	Trp	Thr	Ala	Ala
	145				150					155				160	
Asp	Thr	Ala	Ala	Gln	Ile	Thr	Gln	Arg	Lys	Trp	Glu	Ala	Ala	Arg	Glu
			165					170						175	
Ala	Glu	Gln	Arg	Arg	Ala	Tyr	Leu	Glu	Gly	Glu	Cys	Val	Glu	Trp	Leu
			180					185					190		
Arg	Arg	Tyr	Leu	Glu	Asn	Gly	Lys	Asp	Lys	Leu	Glu	Arg	Ala	Asp	Pro
		195					200					205			
Pro	Lys	Thr	His	Val	Thr	His	His	Pro	Ile	Ser	Asp	His	Glu	Ala	Thr
		210				215					220				
Leu	Arg	Cys	Trp	Ala	Leu	Gly	Phe	Tyr	Pro	Ala	Glu	Ile	Thr	Leu	Thr
	225				230					235				240	
Trp	Gln	Arg	Asp	Gly	Glu	Asp	Gln	Thr	Gln	Asp	Thr	Glu	Leu	Val	Glu
			245					250					255		
Thr	Arg	Pro	Ala	Gly	Asp	Arg	Thr	Phe	Gln	Lys	Trp	Ala	Ala	Val	Val
			260				265						270		
Val	Pro	Ser	Gly	Glu	Glu	Gln	Arg	Tyr	Thr	Cys	His	Val	Gln	His	Glu

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275	280	285	
Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser Ser Gln Ser			
290	295	300	
Thr Val Pro Ile Val Gly Ile Val Ala Gly Leu Ala Val Leu Ala Val			
305	310	315	320
Val Val Ile Gly Ala Val Val Ala Ala Val Met Cys Arg Arg Lys Ser			
	325	330	335
Ser Gly Gly Lys Gly Gly Ser Tyr Ser Gln Ala Ala Cys Ser Asp Ser			
	340	345	350
Ala Gln Gly Ser Asp Val Ser Leu Thr Ala			
355	360		
<210> SEQ ID NO 7			
<211> LENGTH: 1586			
<212> TYPE: DNA			
<213> ORGANISM: Homo sapiens			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (66)..(1166)			
<400> SEQUENCE: 7			
tccgcagtc cgggtctctaaa gtccccagtc acccaccggg actcacattc tccccagagg			60
ccgag atg cgg gtc atg gcg ccc cga gcc ctc ctc ctg ctg ctc tcg gga			110
Met Arg Val Met Ala Pro Arg Ala Leu Leu Leu Leu Ser Gly			
1 5 10 15			
ggc ctg gcc ctg acc gag acc tgg gcc tgc tcc cac tcc atg agg tat			158
Gly Leu Ala Leu Thr Glu Thr Trp Ala Cys Ser His Ser Met Arg Tyr			
20 25 30			
ttc gac acc gcc gtg tcc cgg ccc gcc cgc gga gag ccc cgc ttc atc			206
Phe Asp Thr Ala Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile			
35 40 45			
tca gtg gcc tac gtg gac gac acg cag ttc gtg cgg ttc gac agc gac			254
Ser Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp			
50 55 60			
gcc gcg agt ccg aga ggg gag ccg cgg gcg ccg tgg gtg gag cag gag			302
Ala Ala Ser Pro Arg Gly Glu Pro Arg Ala Pro Trp Val Glu Gln Glu			
65 70 75			
ggg ccg gag tat tgg gac cgg gag aca cag aag tac aag cgc cag gca			350
Gly Pro Glu Tyr Trp Asp Arg Glu Thr Gln Lys Tyr Lys Arg Gln Ala			
80 85 90 95			
cag gct gac cga gtg agc ctg cgg aac ctg cgc gcc tac tac aac cag			398
Gln Ala Asp Arg Val Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln			
100 105 110			
agc gag gac ggg tct cac acc ctc cag agg atg tct ggc tgc gac ctg			446
Ser Glu Asp Gly Ser His Thr Leu Gln Arg Met Ser Gly Cys Asp Leu			
115 120 125			
ggg ccc gac ggg cgc ctc ctc cgc ggg tat gac cag tcc gcc tac gac			494
Gly Pro Asp Gly Arg Leu Leu Arg Gly Tyr Asp Gln Ser Ala Tyr Asp			
130 135 140			
ggc aag gat tac atc gcc ctg aac gag gac ctg cgc tcc tgg acc gcc			542
Gly Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala			
145 150 155			
gcg gac acc gcg gct cag atc acc cag cgc aag ttg gag gcg gcc cgt			590
Ala Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Leu Glu Ala Ala Arg			
160 165 170 175			
gcg gcg gag cag ctg aga gcc tac ctg gag gcc acg tgc gtg gag tgg			638
Ala Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp			

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180	185	190	
ctc cgc aga tac ctg gag aac ggg aag gag acg ctg cag cgc gca gaa Leu Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Ala Glu 195 200 205			686
ccc cca aag aca cac gtg acc cac cac ccc ctc tct gac cat gag gcc Pro Pro Lys Thr His Val Thr His His Pro Leu Ser Asp His Glu Ala 210 215 220			734
acc ctg agg tgc tgg gcc ctg ggc ttc tac cct gcg gag atc aca ctg Thr Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu 225 230 235			782
acc tgg cag cgg gat ggg gag gac cag acc cag gac acc gag ctt gtg Thr Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val 240 245 250 255			830
gag acc agg cca gca gga gat gga acc ttc cag aag tgg gca gct gtg Glu Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val 260 265 270			878
gtg gtg cct tct gga caa gag cag aga tac acg tgc cat atg cag cac Val Val Pro Ser Gly Gln Glu Gln Arg Tyr Thr Cys His Met Gln His 275 280 285			926
gag ggg ctg caa gag ccc ctc acc ctg agc tgg gag cca tct tcc cag Glu Gly Leu Gln Glu Pro Leu Thr Leu Ser Trp Glu Pro Ser Ser Gln 290 295 300			974
ccc acc atc ccc atc atg ggc atc gtt gct ggc ctg gct gtc ctg gtt Pro Thr Ile Pro Ile Met Gly Ile Val Ala Gly Leu Ala Val Leu Val 305 310 315			1022
gtc cta gct gtc ctt gga gct gtg gtc acc gct atg atg tgt agg agg Val Leu Ala Val Leu Gly Ala Val Val Thr Ala Met Met Cys Arg Arg 320 325 330 335			1070
aag agc tca ggt gga aaa gga ggg agc tgc tct cag gct gcg tgc agc Lys Ser Ser Gly Lys Gly Gly Ser Cys Ser Gln Ala Ala Cys Ser 340 345 350			1118
aac agt gcc cag ggc tct gat gag tct ctc atc act tgt aaa gcc tga Asn Ser Ala Gln Gly Ser Asp Glu Ser Leu Ile Thr Cys Lys Ala 355 360 365			1166
gacagctgcc tgtgtgggac tgagatgcag gatttcttca cacctctcct ttgtgacttc			1226
aagagcctct ggcatctctt tctgcaaagg cacctgaatg tgtctgcgtt cctgttagca			1286
taatgtgagg aggtggagag acagcccacc cccgtgtcca cctgacccc tgtcccaca			1346
ctgacctgtg ttcctctccc gatcatcttt cctgttcag agaggtgggg ctggatgtct			1406
ccatctctgt ctcaaattca tgggtgcactg agctgcaact tcttacttcc ctaatgaagt			1466
taagaacctg aatataaatt tgtgttctca aatatttgct atgaagcggt gatggattaa			1526
ttaaataagt caattctag aagttgagag agcaaataaa gacctgagaa ccttcagaa			1586

<210> SEQ ID NO 8

<211> LENGTH: 366

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 8

Met Arg Val Met Ala Pro Arg Ala Leu Leu Leu Leu Leu Ser Gly Gly
1 5 10 15

Leu Ala Leu Thr Glu Thr Trp Ala Cys Ser His Ser Met Arg Tyr Phe
20 25 30

Asp Thr Ala Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser
35 40 45

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Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Ser Asp Ala
 50 55 60
 Ala Ser Pro Arg Gly Glu Pro Arg Ala Pro Trp Val Glu Gln Glu Gly
 65 70 75 80
 Pro Glu Tyr Trp Asp Arg Glu Thr Gln Lys Tyr Lys Arg Gln Ala Gln
 85 90 95
 Ala Asp Arg Val Ser Leu Arg Asn Leu Arg Gly Tyr Tyr Asn Gln Ser
 100 105 110
 Glu Asp Gly Ser His Thr Leu Gln Arg Met Ser Gly Cys Asp Leu Gly
 115 120 125
 Pro Asp Gly Arg Leu Leu Arg Gly Tyr Asp Gln Ser Ala Tyr Asp Gly
 130 135 140
 Lys Asp Tyr Ile Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
 145 150 155 160
 Asp Thr Ala Ala Gln Ile Thr Gln Arg Lys Leu Glu Ala Ala Arg Ala
 165 170 175
 Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu
 180 185 190
 Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Ala Glu Pro
 195 200 205
 Pro Lys Thr His Val Thr His His Pro Leu Ser Asp His Glu Ala Thr
 210 215 220
 Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr
 225 230 235 240
 Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu Leu Val Glu
 245 250 255
 Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val
 260 265 270
 Val Pro Ser Gly Gln Glu Gln Arg Tyr Thr Cys His Met Gln His Glu
 275 280 285
 Gly Leu Gln Glu Pro Leu Thr Leu Ser Trp Glu Pro Ser Ser Gln Pro
 290 295 300
 Thr Ile Pro Ile Met Gly Ile Val Ala Gly Leu Ala Val Leu Val Val
 305 310 315 320
 Leu Ala Val Leu Gly Ala Val Val Thr Ala Met Met Cys Arg Arg Lys
 325 330 335
 Ser Ser Gly Gly Lys Gly Gly Ser Cys Ser Gln Ala Ala Cys Ser Asn
 340 345 350
 Ser Ala Gln Gly Ser Asp Glu Ser Leu Ile Thr Cys Lys Ala
 355 360 365

<210> SEQ ID NO 9
 <211> LENGTH: 2679
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (127) .. (1203)

<400> SEQUENCE: 9

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 cagactccc gactataaag tccccatccg gactcaagaa gttctcagga ctcagaggct 120

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gggatc atg gta gat gga acc ctc ctt tta ctc ctc tcg gag gcc ctg	168
Met Val Asp Gly Thr Leu Leu Leu Leu Ser Glu Ala Leu	
1 5 10	
gcc ctt acc cag acc tgg gcg ggc tcc cac tcc ttg aag tat ttc cac	216
Ala Leu Thr Gln Thr Trp Ala Gly Ser His Ser Leu Lys Tyr Phe His	
15 20 25 30	
act tcc gtg tcc cgg ccc ggc cgc ggg gag ccc cgc ttc atc tct gtg	264
Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser Val	
35 40 45	
ggc tac gtg gac gac acc cag ttc gtg cgc ttc gac aac gac gcc gcg	312
Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp Asn Asp Ala Ala	
50 55 60	
agt ccg agg atg gtg ccg cgg gcg ccg tgg atg gag cag gag ggg tca	360
Ser Pro Arg Met Val Pro Arg Ala Pro Trp Met Glu Gln Glu Gly Ser	
65 70 75	
gag tat tgg gac cgg gag aca cgg agc gcc agg gac acc gca cag att	408
Glu Tyr Trp Asp Arg Glu Thr Arg Ser Ala Arg Asp Thr Ala Gln Ile	
80 85 90	
ttc cga gtg aat ctg cgg acg ctg cgc ggc tac tac aat cag agc gag	456
Phe Arg Val Asn Leu Arg Thr Leu Arg Gly Tyr Tyr Asn Gln Ser Glu	
95 100 105 110	
gcc ggg tct cac acc ctg cag tgg atg cat ggc tgc gag ctg ggg ccc	504
Ala Gly Ser His Thr Leu Gln Trp Met His Gly Cys Glu Leu Gly Pro	
115 120 125	
gac ggg cgc ttc ctc cgc ggg tat gaa cag ttc gcc tac gac ggc aag	552
Asp Gly Arg Phe Leu Arg Gly Tyr Glu Gln Phe Ala Tyr Asp Gly Lys	
130 135 140	
gat tat ctc acc ctg aat gag gac ctg cgc tcc tgg acc gcg gtg gac	600
Asp Tyr Leu Thr Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Val Asp	
145 150 155	
acg gcg gct cag atc tcc gag caa aag tca aat gat gcc tct gag gcg	648
Thr Ala Ala Gln Ile Ser Glu Gln Lys Ser Asn Asp Ala Ser Glu Ala	
160 165 170	
gag cac cag aga gcc tac ctg gaa gac aca tgc gtg gag tgg ctc cac	696
Glu His Gln Arg Ala Tyr Leu Glu Asp Thr Cys Val Glu Trp Leu His	
175 180 185 190	
aaa tac ctg gag aag ggg aag gag acg ctg ctt cac ctg gag ccc cca	744
Lys Tyr Leu Glu Lys Gly Lys Glu Thr Leu Leu His Leu Glu Pro Pro	
195 200 205	
aag aca cac gtg act cac cac ccc atc tct gac cat gag gcc acc ctg	792
Lys Thr His Val Thr His His Pro Ile Ser Asp His Glu Ala Thr Leu	
210 215 220	
agg tgc tgg gcc ctg ggc ttc tac cct gcg gag atc aca ctg acc tgg	840
Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp	
225 230 235	
cag cag gat ggg gag ggc cat acc cag gac acg gag ctc gtg gag acc	888
Gln Gln Asp Gly Glu Gly His Thr Gln Asp Thr Glu Leu Val Glu Thr	
240 245 250	
agg cct gca ggg gat gga acc ttc cag aag tgg gca gct gtg gtg gtg	936
Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val	
255 260 265 270	
cct tct gga gag gag cag aga tac acg tgc cat gtg cag cat gag ggg	984
Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly	
275 280 285	
cta ccc gag ccc gtc acc ctg aga tgg aag ccg gct tcc cag ccc acc	1032
Leu Pro Glu Pro Val Thr Leu Arg Trp Lys Pro Ala Ser Gln Pro Thr	
290 295 300	

atc Ile	ccc Pro	atc Ile	gtg Val	ggc Gly	atc Ile	att Ile	gct Ala	ggc Gly	ctg Leu	gtt Val	ctc Leu	ctt Leu	gga Gly	tct Ser	gtg Val	1080
305																
gtc Val	tct Ser	gga Gly	gct Ala	gtg Val	gtt Val	gct Ala	gct Ala	gtg Val	ata Ile	tgg Trp	agg Arg	aag Lys	aag Lys	agc Ser	tca Ser	1128
320																
325																
ggt Gly	gga Gly	aaa Lys	gga Gly	ggg Gly	agc Ser	tac Tyr	tct Ser	aag Lys	gct Ala	gag Glu	tgg Trp	agc Ser	gac Asp	agt Ser	gcc Ala	1176
335																
340																
345																
350																
cag Gln	ggg Gly	tct Ser	gag Glu	tct Ser	cac His	agc Ser	ttg Leu	taa	agcctgagac	agctgccttg						1223
355																
																1283
																1343
																1403
																1463
																1523
																1583
																1643
																1703
																1763
																1823
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																2003
																2063
																2123
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																2243
																2303
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<210> SEQ ID NO 10
<211> LENGTH: 358
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
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<400> SEQUENCE: 10

Met Val Asp Gly Thr Leu Leu Leu Leu Leu Ser Glu Ala Leu Ala Leu
1 5 10 15

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Thr	Gln	Thr	Trp	Ala	Gly	Ser	His	Ser	Leu	Lys	Tyr	Phe	His	Thr	Ser
			20					25					30		
Val	Ser	Arg	Pro	Gly	Arg	Gly	Glu	Pro	Arg	Phe	Ile	Ser	Val	Gly	Tyr
	35						40					45			
Val	Asp	Asp	Thr	Gln	Phe	Val	Arg	Phe	Asp	Asn	Asp	Ala	Ala	Ser	Pro
	50					55				60					
Arg	Met	Val	Pro	Arg	Ala	Pro	Trp	Met	Glu	Gln	Glu	Gly	Ser	Glu	Tyr
	65				70					75				80	
Trp	Asp	Arg	Glu	Thr	Arg	Ser	Ala	Arg	Asp	Thr	Ala	Gln	Ile	Phe	Arg
				85					90					95	
Val	Asn	Leu	Arg	Thr	Leu	Arg	Gly	Tyr	Tyr	Asn	Gln	Ser	Glu	Ala	Gly
			100					105					110		
Ser	His	Thr	Leu	Gln	Trp	Met	His	Gly	Cys	Glu	Leu	Gly	Pro	Asp	Gly
		115					120					125			
Arg	Phe	Leu	Arg	Gly	Tyr	Glu	Gln	Phe	Ala	Tyr	Asp	Gly	Lys	Asp	Tyr
	130					135					140				
Leu	Thr	Leu	Asn	Glu	Asp	Leu	Arg	Ser	Trp	Thr	Ala	Val	Asp	Thr	Ala
	145				150					155					160
Ala	Gln	Ile	Ser	Glu	Gln	Lys	Ser	Asn	Asp	Ala	Ser	Glu	Ala	Glu	His
				165					170					175	
Gln	Arg	Ala	Tyr	Leu	Glu	Asp	Thr	Cys	Val	Glu	Trp	Leu	His	Lys	Tyr
		180					185						190		
Leu	Glu	Lys	Gly	Lys	Glu	Thr	Leu	Leu	His	Leu	Glu	Pro	Pro	Lys	Thr
	195						200					205			
His	Val	Thr	His	His	Pro	Ile	Ser	Asp	His	Glu	Ala	Thr	Leu	Arg	Cys
	210					215				220					
Trp	Ala	Leu	Gly	Phe	Tyr	Pro	Ala	Glu	Ile	Thr	Leu	Thr	Trp	Gln	Gln
	225				230					235				240	
Asp	Gly	Glu	Gly	His	Thr	Gln	Asp	Thr	Glu	Leu	Val	Glu	Thr	Arg	Pro
				245					250					255	
Ala	Gly	Asp	Gly	Thr	Phe	Gln	Lys	Trp	Ala	Ala	Val	Val	Val	Pro	Ser
		260						265					270		
Gly	Glu	Glu	Gln	Arg	Tyr	Thr	Cys	His	Val	Gln	His	Glu	Gly	Leu	Pro
	275						280					285			
Glu	Pro	Val	Thr	Leu	Arg	Trp	Lys	Pro	Ala	Ser	Gln	Pro	Thr	Ile	Pro
	290					295					300				
Ile	Val	Gly	Ile	Ile	Ala	Gly	Leu	Val	Leu	Leu	Gly	Ser	Val	Val	Ser
	305				310					315					320
Gly	Ala	Val	Val	Ala	Ala	Val	Ile	Trp	Arg	Lys	Lys	Ser	Ser	Gly	Gly
				325					330					335	
Lys	Gly	Gly	Ser	Tyr	Ser	Lys	Ala	Glu	Trp	Ser	Asp	Ser	Ala	Gln	Gly
			340					345					350		
Ser	Glu	Ser	His	Ser	Leu										
			355												

<210> SEQ ID NO 11
 <211> LENGTH: 1301
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (125)..(1165)

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<400> SEQUENCE: 11

tttctcactc ccattgggcg tcgcgtttct agagaagcca atcagtgctg ccgcagttcc	60
caggttctaa agtcccaagc accccgcggg actcatatct ttccagacg cggaggttgg	120
ggtc atg gcg ccc cga agc ctc ctc ctg ctg ctc tca ggg gcc ctg gcc	169
Met Ala Pro Arg Ser Leu Leu Leu Leu Ser Gly Ala Leu Ala	
1 5 10 15	
ctg acc gat act tgg gcg ggc tcc cac tcc ttg agg tat ttc agc acc	217
Leu Thr Asp Thr Trp Ala Gly Ser His Ser Leu Arg Tyr Phe Ser Thr	
20 25 30	
gct gtg tcg cgg ccc ggc cgc ggg gag ccc cgc tac atc gcc gtg gag	265
Ala Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Tyr Ile Ala Val Glu	
35 40 45	
tac gta gac gac acg caa ttc ctg cgg ttc gac agc gac gcc gcg att	313
Tyr Val Asp Asp Thr Gln Phe Leu Arg Phe Asp Ser Asp Ala Ala Ile	
50 55 60	
ccg agg atg gag ccg cgg gag ccg tgg gtg gag caa gag ggg ccg cag	361
Pro Arg Met Glu Pro Arg Glu Pro Trp Val Glu Gln Glu Gly Pro Gln	
65 70 75	
tat tgg gag tgg acc aca ggg tac gcc aag gcc aac gca cag act gac	409
Tyr Trp Glu Trp Thr Thr Gly Tyr Ala Lys Ala Asn Ala Gln Thr Asp	
80 85 90 95	
cga gtg gcc ctg agg aac ctg ctc cgc cgc tac aac cag agc gag gct	457
Arg Val Ala Leu Arg Asn Leu Leu Arg Arg Tyr Asn Gln Ser Glu Ala	
100 105 110	
ggg tct cac acc ctc cag gga atg aat ggc tgc gac atg ggg ccc gac	505
Gly Ser His Thr Leu Gln Gly Met Asn Gly Cys Asp Met Gly Pro Asp	
115 120 125	
gga cgc ctc ctc cgc ggg tat cac cag cac gcg tac gac ggc aag gat	553
Gly Arg Leu Leu Arg Gly Tyr His Gln His Ala Tyr Asp Gly Lys Asp	
130 135 140	
tac atc tcc ctg aac gag gac ctg cgc tcc tgg acc gcg gcg gac acc	601
Tyr Ile Ser Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr	
145 150 155	
gtg gct cag atc acc cag cgc ttc tat gag gca gag gaa tat gca gag	649
Val Ala Gln Ile Thr Gln Arg Phe Tyr Glu Ala Glu Glu Tyr Ala Glu	
160 165 170 175	
gag ttc agg acc tac ctg gag ggc gag tgc ctg gag ttg ctc cgc aga	697
Glu Phe Arg Thr Tyr Leu Glu Gly Glu Cys Leu Glu Leu Leu Arg Arg	
180 185 190	
tac ttg gag aat ggg aag gag acg cta cag cgc gca gat cct cca aag	745
Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys	
195 200 205	
gca cac gtt gcc cac cac ccc atc tct gac cat gag gcc acc ctg agg	793
Ala His Val Ala His His Pro Ile Ser Asp His Glu Ala Thr Leu Arg	
210 215 220	
tgc tgg gcc ctg ggc ttc tac cct gcg gag atc acg ctg acc tgg cag	841
Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln	
225 230 235	
cgg gat ggg gag gaa cag acc cag gac aca gag ctt gtg gag acc agg	889
Arg Asp Gly Glu Glu Thr Gln Asp Thr Glu Leu Val Glu Thr Arg	
240 245 250 255	
cct gca ggg gat gga acc ttc cag aag tgg gcc gct gtg gtg gtg cct	937
Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val Val Pro	
260 265 270	
cct gga gag gaa cag aga tac aca tgc cat gtg cag cac gag ggg ctg	985
Pro Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu Gly Leu	

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275	280	285	
ccc cag ccc ctc atc ctg aga tgg gag cag tct ccc cag ccc acc atc			1033
Pro Gln Pro Leu Ile Leu Arg Trp Glu Gln Ser Pro Gln Pro Thr Ile			
290	295	300	
ccc atc gtg ggc atc gtt gct ggc ctt gtt gtc ctt gga gct gtg gtc			1081
Pro Ile Val Gly Ile Val Ala Gly Leu Val Val Leu Gly Ala Val Val			
305	310	315	
act gga gct gtg gtc gct gct gtg atg tgg agg aag aag agc tca gat			1129
Thr Gly Ala Val Val Ala Ala Val Met Trp Arg Lys Lys Ser Ser Asp			
320	325	330	335
aga aac aga ggg agc tac tct cag gct gca gtg tga gacagcttcc			1175
Arg Asn Arg Gly Ser Tyr Ser Gln Ala Ala Val			
340	345		
ttgtgtggga ctgagaagca agatatcaat gtagcagaat tgcacttggtg cctcacgaac			1235
atacataaat tttaaaaata aagaataaaa atatattcttt ttatagataa aaaaaaaaaa			1295
aaaaaa			1301
<210> SEQ ID NO 12			
<211> LENGTH: 346			
<212> TYPE: PRT			
<213> ORGANISM: Homo sapiens			
<400> SEQUENCE: 12			
Met Ala Pro Arg Ser Leu Leu Leu Leu Leu Ser Gly Ala Leu Ala Leu			
1	5	10	15
Thr Asp Thr Trp Ala Gly Ser His Ser Leu Arg Tyr Phe Ser Thr Ala			
20	25	30	
Val Ser Arg Pro Gly Arg Gly Glu Pro Arg Tyr Ile Ala Val Glu Tyr			
35	40	45	
Val Asp Asp Thr Gln Phe Leu Arg Phe Asp Ser Asp Ala Ala Ile Pro			
50	55	60	
Arg Met Glu Pro Arg Glu Pro Trp Val Glu Gln Glu Gly Pro Gln Tyr			
65	70	75	80
Trp Glu Trp Thr Thr Gly Tyr Ala Lys Ala Asn Ala Gln Thr Asp Arg			
85	90	95	
Val Ala Leu Arg Asn Leu Leu Arg Arg Tyr Asn Gln Ser Glu Ala Gly			
100	105	110	
Ser His Thr Leu Gln Gly Met Asn Gly Cys Asp Met Gly Pro Asp Gly			
115	120	125	
Arg Leu Leu Arg Gly Tyr His Gln His Ala Tyr Asp Gly Lys Asp Tyr			
130	135	140	
Ile Ser Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala Asp Thr Val			
145	150	155	160
Ala Gln Ile Thr Gln Arg Phe Tyr Glu Ala Glu Glu Tyr Ala Glu Glu			
165	170	175	
Phe Arg Thr Tyr Leu Glu Gly Glu Cys Leu Glu Leu Leu Arg Arg Tyr			
180	185	190	
Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg Ala Asp Pro Pro Lys Ala			
195	200	205	
His Val Ala His His Pro Ile Ser Asp His Glu Ala Thr Leu Arg Cys			
210	215	220	
Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Thr Leu Thr Trp Gln Arg			
225	230	235	240

<400> SEQUENCE: 13

agtgtgtgtac	tttgtcttga	ggagatgtcc	tggaactaca	cggaaactta	gggctacgga	60										
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gtcctgggttc	taaagtccctc	gctcaccacc	cgggactcat	tctccccaga	cgccaagg	178										
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Pro	Glu	Tyr	Trp	Glu	Glu	Glu	Thr	Arg	Asn	Thr	Lys	Ala	His	Ala	Gln	
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Ser	Asp	Gly	Arg	Leu	Leu	Arg	Gly	Tyr	Glu	Gln	Tyr	Ala	Tyr	Asp	Gly	
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Asp Thr Ala Ala Gln Ile Ser Lys Arg Lys Cys Glu Ala Ala Asn Val		165	170	175	
gct gaa caa agg aga gcc tac ctg gag ggc acg tgc gtg gag tgg ctc					754
Ala Glu Gln Arg Arg Ala Tyr Leu Glu Gly Thr Cys Val Glu Trp Leu		180	185	190	
cac aga tac ctg gag aac ggg aag gag atg ctg cag cgc gcg gac ccc					802
His Arg Tyr Leu Glu Asn Gly Lys Glu Met Leu Gln Arg Ala Asp Pro		195	200	205	
ccc aag aca cac gtg acc cac cac cct gtc ttt gac tat gag gcc acc					850
Pro Lys Thr His Val Thr His His Pro Val Phe Asp Tyr Glu Ala Thr		210	215	220	
ctg agg tgc tgg gcc ctg ggc ttc tac cct gcg gag atc ata ctg acc					898
Leu Arg Cys Trp Ala Leu Gly Phe Tyr Pro Ala Glu Ile Ile Leu Thr		225	230	235	240
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Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Val Glu Leu Val Glu		245	250	255	
acc agg cct gca ggg gat gga acc ttc cag aag tgg gca gct gtg gtg					994
Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala Ala Val Val		260	265	270	
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Val Pro Ser Gly Glu Glu Gln Arg Tyr Thr Cys His Val Gln His Glu		275	280	285	
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Gly Leu Pro Glu Pro Leu Met Leu Arg Trp Lys Gln Ser Ser Leu Pro		290	295	300	
acc atc ccc atc atg ggt atc gtt gct ggc ctg gtt gtc ctt gca gct					1138
Thr Ile Pro Ile Met Gly Ile Val Ala Gly Leu Val Val Leu Ala Ala		305	310	315	320
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Val Val Thr Gly Ala Ala Val Ala Ala Val Leu Trp Arg Lys Lys Ser		325	330	335	
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Ser Asp					
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<210> SEQ ID NO 14

<211> LENGTH: 338

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 14

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Leu Thr Leu Thr Glu Thr Trp Ala Gly Ser His Ser Met Arg Tyr Phe	20	25	30
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 Pro Glu Tyr Trp Glu Glu Glu Thr Arg Asn Thr Lys Ala His Ala Gln
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 Thr Asp Arg Met Asn Leu Gln Thr Leu Arg Gly Tyr Tyr Asn Gln Ser
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 Lys Asp Tyr Leu Ala Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Ala
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 Pro Lys Thr His Val Thr His His Pro Val Phe Asp Tyr Glu Ala Thr
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<210> SEQ ID NO 15
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 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Vector sequence for human B2M-HLA-A0201 fusion protein

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<211> LENGTH: 480
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: HLA-bBA0201 (human B2M-HLA-A0201 fusion
peptide)

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His Pro Ala Glu Asn Gly Lys Ser Asn Phe Leu Asn Cys Tyr Val Ser
35          40          45
Gly Phe His Pro Ser Asp Ile Glu Val Asp Leu Leu Lys Asn Gly Glu
50          55          60
Arg Ile Glu Lys Val Glu His Ser Asp Leu Ser Phe Ser Lys Asp Trp
65          70          75          80
Ser Phe Tyr Leu Leu Tyr Tyr Thr Glu Phe Thr Pro Thr Glu Lys Asp
85          90          95
Glu Tyr Ala Cys Arg Val Asn His Val Thr Leu Ser Gln Pro Lys Ile
100         105         110
Val Lys Trp Asp Arg Asp Met Gly Gly Gly Gly Ser Gly Gly Gly Gly
115         120         125
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Ser His Ser Met
130         135         140
Arg Tyr Phe Phe Thr Ser Val Ser Arg Pro Gly Arg Gly Glu Pro Arg
145         150         155         160
Phe Ile Ala Val Gly Tyr Val Asp Asp Thr Gln Phe Val Arg Phe Asp
165         170         175
Ser Asp Ala Ala Ser Gln Arg Met Glu Pro Arg Ala Pro Trp Ile Glu
180         185         190
Gln Glu Gly Pro Glu Tyr Trp Asp Gly Glu Thr Arg Lys Val Lys Ala
195         200         205
His Ser Gln Thr His Arg Val Asp Leu Gly Thr Leu Arg Gly Tyr Tyr
210         215         220
Asn Gln Ser Glu Ala Gly Ser His Thr Val Gln Arg Met Tyr Gly Cys
225         230         235         240
Asp Val Gly Ser Asp Trp Arg Phe Leu Arg Gly Tyr His Gln Tyr Ala
245         250         255
Tyr Asp Gly Lys Asp Tyr Ile Ala Leu Lys Glu Asp Leu Arg Ser Trp
260         265         270
Thr Ala Ala Asp Met Ala Ala Gln Thr Thr Lys His Lys Trp Glu Ala
275         280         285
Ala His Val Ala Glu Gln Leu Arg Ala Tyr Leu Glu Gly Thr Cys Val
290         295         300
Glu Trp Leu Arg Arg Tyr Leu Glu Asn Gly Lys Glu Thr Leu Gln Arg
305         310         315         320
Thr Asp Ala Pro Lys Thr His Met Thr His His Ala Val Ser Asp His
325         330         335
Glu Ala Thr Leu Arg Cys Trp Ala Leu Ser Phe Tyr Pro Ala Glu Ile
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Thr Leu Thr Trp Gln Arg Asp Gly Glu Asp Gln Thr Gln Asp Thr Glu

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Leu Val Glu Thr Arg Pro Ala Gly Asp Gly Thr Phe Gln Lys Trp Ala		
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Gln His Glu Gly Leu Pro Lys Pro Leu Thr Leu Arg Trp Glu Pro Ser		
405	410	415
Ser Gln Pro Thr Ile Pro Ile Val Gly Ile Ile Ala Gly Leu Val Leu		
420	425	430
Phe Gly Ala Val Ile Thr Gly Ala Val Val Ala Ala Val Met Trp Arg		
435	440	445
Arg Lys Ser Ser Asp Arg Lys Gly Gly Ser Tyr Ser Gln Ala Ala Ser		
450	455	460
Ser Asp Ser Ala Gln Gly Ser Asp Val Ser Leu Thr Ala Cys Lys Val		
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<210> SEQ ID NO 17

<211> LENGTH: 9224

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Vector sequence for HLA-gBE

<400> SEQUENCE: 17

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tcaattacgg ggctcattagt tcatagccca tatatggagt tccgcgttac ataacttacg    180
gtaaattggc cgcttggtg accgcccac gacccccgc cattgacgtc aataatgacg      240
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cgctaaactg cccacttggc agtacatcaa gtgtatcata tgccaagtac gccccctatt    360
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<210> SEQ ID NO 18

<211> LENGTH: 476

<212> TYPE: PRT

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: HLA-gBE

<400> SEQUENCE: 18

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

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 180 185 190
 Gln Glu Gly Ser Glu Tyr Trp Asp Arg Glu Thr Arg Ser Ala Arg Asp
 195 200 205
 Thr Ala Gln Ile Phe Arg Val Asn Leu Arg Thr Leu Arg Gly Tyr Tyr
 210 215 220
 Asn Gln Ser Glu Ala Gly Ser His Thr Leu Gln Trp Met His Gly Cys
 225 230 235 240
 Glu Leu Gly Pro Asp Gly Arg Phe Leu Arg Gly Tyr Glu Gln Phe Ala
 245 250 255
 Tyr Asp Gly Lys Asp Tyr Leu Thr Leu Asn Glu Asp Leu Arg Ser Trp
 260 265 270
 Thr Ala Val Asp Thr Ala Ala Gln Ile Ser Glu Gln Lys Ser Asn Asp
 275 280 285
 Ala Ser Glu Ala Glu His Gln Arg Ala Tyr Leu Glu Asp Thr Cys Val
 290 295 300
 Glu Trp Leu His Lys Tyr Leu Glu Lys Gly Lys Glu Thr Leu Leu His
 305 310 315 320
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 325 330 335
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 340 345 350
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 385 390 395 400
 Gln His Glu Gly Leu Pro Glu Pro Val Thr Leu Arg Trp Lys Pro Ala
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 Leu Gly Ser Val Val Ser Gly Ala Val Val Ala Ala Val Ile Trp Arg
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<210> SEQ ID NO 19

<211> LENGTH: 9287

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Vector sequence for HLA-bGBE

<400> SEQUENCE: 19

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<210> SEQ ID NO 20
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: HLA-bGBE

<400> SEQUENCE: 20

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Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Gln Arg Thr
35     40     45

Pro Lys Ile Gln Val Tyr Ser Arg His Pro Ala Glu Asn Gly Lys Ser
50     55     60

Asn Phe Leu Asn Cys Tyr Val Ser Gly Phe His Pro Ser Asp Ile Glu
65     70     75     80

Val Asp Leu Leu Lys Asn Gly Glu Arg Ile Glu Lys Val Glu His Ser
85     90     95

Asp Leu Ser Phe Ser Lys Asp Trp Ser Phe Tyr Leu Leu Tyr Tyr Thr
100    105    110

Glu Phe Thr Pro Thr Glu Lys Asp Glu Tyr Ala Cys Arg Val Asn His
115    120    125

Val Thr Leu Ser Gln Pro Lys Ile Val Lys Trp Asp Arg Asp Met Gly
130    135    140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145    150    155    160

Gly Gly Ser Gly Ser His Ser Leu Lys Tyr Phe His Thr Ser Val Ser
165    170    175

Arg Pro Gly Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr Val Asp
180    185    190

Asp Thr Gln Phe Val Arg Phe Asp Asn Asp Ala Ala Ser Pro Arg Met
195    200    205

Val Pro Arg Ala Pro Trp Met Glu Gln Glu Gly Ser Glu Tyr Trp Asp
210    215    220

Arg Glu Thr Arg Ser Ala Arg Asp Thr Ala Gln Ile Phe Arg Val Asn
225    230    235    240

Leu Arg Thr Leu Arg Gly Tyr Tyr Asn Gln Ser Glu Ala Gly Ser His
245    250    255

Thr Leu Gln Trp Met His Gly Cys Glu Leu Gly Pro Asp Gly Arg Phe
260    265    270

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275    280    285

Leu Asn Glu Asp Leu Arg Ser Trp Thr Ala Val Asp Thr Ala Ala Gln
290    295    300

Ile Ser Glu Gln Lys Ser Asn Asp Ala Ser Glu Ala Glu His Gln Arg
305    310    315    320

Ala Tyr Leu Glu Asp Thr Cys Val Glu Trp Leu His Lys Tyr Leu Glu
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Lys Gly Lys Glu Thr Leu Leu His Leu Glu Pro Pro Lys Thr His Val
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<210> SEQ ID NO 21

<211> LENGTH: 7159

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Vector sequence for pA2-B2METKNpA

<400> SEQUENCE: 21

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caaaatccct taacgtgagt tttcgttcca ctgagcgtoa gaccccgtag aaaagatcaa	6540
aggatcttct tgagatcctt tttttctgcg cgtaatctgc tgcctgcaa caaaaaac	6600
accgctacca gcggtggtt gtttccgga tcaagagcta ccaactcttt ttcgaaggt	6660
aactggcttc agcagagcgc agataccaaa tactgtcctt ctagtgtagc cgtagttagg	6720
ccaccacttc aagaactctg tagcaccgcc tacatacctc gctctgctaa tctgttacc	6780
agtggctgct gccagtggc ataagtcgtg tcttaccggg ttggactcaa gacgatagtt	6840
accggataag gcgcagcggc cgggctgaac ggggggttcg tgcacacagc ccagcttggg	6900
gcgaacgacc tacaccgaac tgagatacct acagcgtgag ctatgagaaa gcgccacgct	6960
tcccgaagg agaaaggcgc acaggtatcc ggtaagcggc agggtcggaa caggagagcg	7020
cacgagggag cttccagggg gaaacgcctg gtatctttat agtcctgtcg ggtttcgcca	7080
cctctgactt gagcgtcgat ttttgatgag ctgcgcaggg gggcggagcc tatggaaaaa	7140
cgccagcaac gcggcctttt tacggttcct ggccttttgc tggccttttg ctcacatgt	7199

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<210> SEQ ID NO 23
 <211> LENGTH: 29
 <212> TYPE: PRT
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: HLA-G peptide

<400> SEQUENCE: 23

Met Ala Pro Arg Thr Leu Phe Leu Gly Gly Gly Gly Ser Gly Gly Gly
 1 5 10 15

Gly Ser Gly Gly Gly Gly Ser Ile Gln Arg Thr Pro Lys
 20 25

<210> SEQ ID NO 24
 <211> LENGTH: 1369
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (506) .. (1219)

<400> SEQUENCE: 24

ccggacgccc caccggctcct gttccgggtg cagagggccc gccctccccg ctccctcagtc 60
 ttgtcggaca agaaaggggc tgtgtgagac gcagggaagg aggcacaccc ggggggtggcg 120
 cagtgaggag ggggcgcgac ggccaggagg ctggtggagc gacaccaggg caggagaggg 180
 ggaagaactc tctcccttcc tgaaccccct tttccttgag agacgagttg ggggagtcct 240
 ccacgcatta cccactcggg ccgcaaaaac tcccttcttt agccctctgc ccccgccctt 300
 gcttataagc ctttgagacc gcagaaggga ccttggtgtg gaacgggacg gccaagagga 360
 agccagatcg ctgagggtcc ggtctccagt ttgcctcctg ctatatccat tggaagagaa 420
 aagtttgtga cttgggcccc caagttttga gagaactggg ctttcggcgc ggggggacag 480
 aggaggctcg tggggagcct tcccc atg gag ctt acc cag cct gca gaa gac 532
 Met Glu Leu Thr Gln Pro Ala Glu Asp
 1 5
 ctc atc cag acc cag cag acc cct gcc tca gaa ctt ggg gac cct gaa 580
 Leu Ile Gln Thr Gln Gln Thr Pro Ala Ser Glu Leu Gly Asp Pro Glu
 10 15 20 25
 gac ccc gga gag gag gct gca gat gcc tca gac act gtg gtc ctc agt 628
 Asp Pro Gly Glu Glu Ala Ala Asp Gly Ser Asp Thr Val Val Leu Ser
 30 35 40
 ctc ttt ccc tgc acc cct gag cct gtg aat cct gaa ccg gat gcc agt 676
 Leu Phe Pro Cys Thr Pro Glu Pro Val Asn Pro Glu Pro Asp Ala Ser
 45 50 55
 gtt tcc tct cca cag ggc agc tcc ctg aag cac tcc acc act ctc acc 724
 Val Ser Ser Pro Gln Gly Ser Ser Leu Lys His Ser Thr Thr Leu Thr
 60 65 70
 aac cgg cag cga ggg aac gag gtg tca gct ctg ccg gcc acc cta gac 772
 Asn Arg Gln Arg Gly Asn Glu Val Ser Ala Leu Pro Ala Thr Leu Asp
 75 80 85
 tgt gac aac ctc gtc aac aag cca gac gag cgc ggc ttc acc ccc ctc 820
 Cys Asp Asn Leu Val Asn Lys Pro Asp Glu Arg Gly Phe Thr Pro Leu
 90 95 100 105
 atc tgg gcc tcc gcc ttt gga gag att gag acc gtt cgc ttc ctg ctg 868
 Ile Trp Ala Ser Ala Phe Gly Glu Ile Glu Thr Val Arg Phe Leu Leu
 110 115 120
 gag tgg ggt gcc gac ccc cac atc ctg gca aaa gag cga gag agc gcc 916
 Glu Trp Gly Ala Asp Pro His Ile Leu Ala Lys Glu Arg Glu Ser Ala

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125	130	135	
ctg tcg ctg gcc agc aca ggc ggc tac aca gac att gtg ggg ctg ctg			964
Leu Ser Leu Ala Ser Thr Gly Gly Tyr Thr Asp Ile Val Gly Leu Leu			
140	145	150	
ctg gag cgt gac gtg gac atc aac atc tat gat tgg aat gga ggg acg			1012
Leu Glu Arg Asp Val Asp Ile Asn Ile Tyr Asp Trp Asn Gly Gly Thr			
155	160	165	
cca ctg ctg tac gct gtg cgc ggg aac cac gtg aaa tgc gtt gag gcc			1060
Pro Leu Leu Tyr Ala Val Arg Gly Asn His Val Lys Cys Val Glu Ala			
170	175	180	185
ttg ctg gcc cga ggc gct gac ctc acc acc gaa gcc gac tct ggc tac			1108
Leu Leu Ala Arg Gly Ala Asp Leu Thr Thr Glu Ala Asp Ser Gly Tyr			
190	195	200	
acc ccg atg gac ctt gcc gtg gcc ctg gga tac cgg aaa gtg caa cag			1156
Thr Pro Met Asp Leu Ala Val Ala Leu Gly Tyr Arg Lys Val Gln Gln			
205	210	215	
gtg atc gag aac cac atc ctc aag ctc ttc cag agc aac ctg gtg ccc			1204
Val Ile Glu Asn His Ile Leu Lys Leu Phe Gln Ser Asn Leu Val Pro			
220	225	230	
gct gac cct gag tga aggccgcctg ccgggggactc agacactcag ggaacaaaat			1259
Ala Asp Pro Glu			
235			
ggtcagccag agctggggaa acccagaact gacttcaaag gcagcttctg gacaggtggt			1319
gggagggggac ccttcccaag aggaaccaat aaaccttctg tgcagaatga			1369
<210> SEQ ID NO 25			
<211> LENGTH: 237			
<212> TYPE: PRT			
<213> ORGANISM: Homo sapiens			
<400> SEQUENCE: 25			
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1	5	10	15
Pro Ala Ser Glu Leu Gly Asp Pro Glu Asp Pro Gly Glu Glu Ala Ala			
20	25	30	
Asp Gly Ser Asp Thr Val Val Leu Ser Leu Phe Pro Cys Thr Pro Glu			
35	40	45	
Pro Val Asn Pro Glu Pro Asp Ala Ser Val Ser Ser Pro Gln Gly Ser			
50	55	60	
Ser Leu Lys His Ser Thr Thr Leu Thr Asn Arg Gln Arg Gly Asn Glu			
65	70	75	80
Val Ser Ala Leu Pro Ala Thr Leu Asp Cys Asp Asn Leu Val Asn Lys			
85	90	95	
Pro Asp Glu Arg Gly Phe Thr Pro Leu Ile Trp Ala Ser Ala Phe Gly			
100	105	110	
Glu Ile Glu Thr Val Arg Phe Leu Leu Glu Trp Gly Ala Asp Pro His			
115	120	125	
Ile Leu Ala Lys Glu Arg Glu Ser Ala Leu Ser Leu Ala Ser Thr Gly			
130	135	140	
Gly Tyr Thr Asp Ile Val Gly Leu Leu Leu Glu Arg Asp Val Asp Ile			
145	150	155	160
Asn Ile Tyr Asp Trp Asn Gly Gly Thr Pro Leu Leu Tyr Ala Val Arg			
165	170	175	
Gly Asn His Val Lys Cys Val Glu Ala Leu Leu Ala Arg Gly Ala Asp			

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180					185					190					
Leu	Thr	Thr	Glu	Ala	Asp	Ser	Gly	Tyr	Thr	Pro	Met	Asp	Leu	Ala	Val
		195					200					205			
Ala	Leu	Gly	Tyr	Arg	Lys	Val	Gln	Gln	Val	Ile	Glu	Asn	His	Ile	Leu
	210					215					220				
Lys	Leu	Phe	Gln	Ser	Asn	Leu	Val	Pro	Ala	Asp	Pro	Glu			
225						230					235				

<210> SEQ ID NO 26
 <211> LENGTH: 1438
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (506) .. (1288)

<400> SEQUENCE: 26

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cagtgaaggag ggggcgcgac gcccaggagg ctggtggagc gacaccaggg caggagaggg    180
ggaagaactc tctcccttct tgaacccctt ttctcttgag agacgagttg ggggagtcct    240
ccacgcatta cccactcggg ccgcaaaaac tcccttcttt agccctctgc ccccgccctt    300
gcttataaag ctttgagacc gcagaaggga ccttgttgtg gaacgggacg gccaaagagga    360
agccagatcg ctgagggtcc ggtctccagt ttgcctctcg ctatatccat tggaagagaa    420
aagtttgtga cttgggcccc caagttttga gagaactggg ctttcggcgc ggggggacag    480
aggaggctcg tggggagctt tcccc atg gag ctt acc cag cct gca gaa gac      532
                        Met Glu Leu Thr Gln Pro Ala Glu Asp
                        1                               5

ctc atc cag acc cag cag acc cct gcc tca gaa ctt ggg gac cct gaa      580
Leu Ile Gln Thr Gln Gln Thr Pro Ala Ser Glu Leu Gly Asp Pro Glu
10                               15                               20                               25

gac ccc gga gag gag gct gca gat ggc tca gac act gtg gtc ctc agt      628
Asp Pro Gly Glu Glu Ala Ala Asp Gly Ser Asp Thr Val Val Leu Ser
30                               35                               40

ctc ttt ccc tgc acc cct gag cct gtg aat cct gaa ccg gat gcc agt      676
Leu Phe Pro Cys Thr Pro Glu Pro Val Asn Pro Glu Pro Asp Ala Ser
45                               50                               55

gtt tcc tct cca cag gca ggc agc tcc ctg aag cac tcc acc act ctc      724
Val Ser Ser Pro Gln Ala Gly Ser Ser Leu Lys His Ser Thr Thr Leu
60                               65                               70

acc aac cgg cag cga ggg aac gag gtg tca gct ctg ccg gcc acc cta      772
Thr Asn Arg Gln Arg Gly Asn Glu Val Ser Ala Leu Pro Ala Thr Leu
75                               80                               85

gac tcc ctg tcc atc cac cag ctc gca gca cag ggg gag ctg gac cag      820
Asp Ser Leu Ser Ile His Gln Leu Ala Ala Gln Gly Glu Leu Asp Gln
90                               95                               100                               105

ctg aag gag cat ttg cgg aaa ggt gac aac ctc gtc aac aag cca gac      868
Leu Lys Glu His Leu Arg Lys Gly Asp Asn Leu Val Asn Lys Pro Asp
110                               115                               120

gag cgc ggc ttc acc ccc ctc atc tgg gcc tcc gcc ttt gga gag att      916
Glu Arg Gly Phe Thr Pro Leu Ile Trp Ala Ser Ala Phe Gly Glu Ile
125                               130                               135

gag acc gtt cgc ttc ctg ctg gag tgg ggt gcc gac ccc cac atc ctg      964
Glu Thr Val Arg Phe Leu Leu Glu Trp Gly Ala Asp Pro His Ile Leu

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140	145	150	
gca aaa gag cga gag agc gcc ctg tcg ctg gcc agc aca ggc ggc tac			1012
Ala Lys Glu Arg Glu Ser Ala Leu Ser Leu Ala Ser Thr Gly Gly Tyr			
155	160	165	
aca gac att gtg ggg ctg ctg ctg gag cgt gac gtg gac atc aac atc			1060
Thr Asp Ile Val Gly Leu Leu Leu Glu Arg Asp Val Asp Ile Asn Ile			
170	175	180	185
tat gat tgg aat gga ggg acg cca ctg ctg tac gct gtg cgc ggg aac			1108
Tyr Asp Trp Asn Gly Gly Thr Pro Leu Leu Tyr Ala Val Arg Gly Asn			
190	195	200	
cac gtg aaa tgc gtt gag gcc ttg ctg gcc cga ggc gct gac ctc acc			1156
His Val Lys Cys Val Glu Ala Leu Leu Ala Arg Gly Ala Asp Leu Thr			
205	210	215	
acc gaa gcc gac tct ggc tac acc ccg atg gac ctt gcc gtg gcc ctg			1204
Thr Glu Ala Asp Ser Gly Tyr Thr Pro Met Asp Leu Ala Val Ala Leu			
220	225	230	
gga tac cgg aaa gtg caa cag gtg atc gag aac cac atc ctc aag ctc			1252
Gly Tyr Arg Lys Val Gln Gln Val Ile Glu Asn His Ile Leu Lys Leu			
235	240	245	
ttc cag agc aac ctg gtg ccc gct gac cct gag tga aggccgcctg			1298
Phe Gln Ser Asn Leu Val Pro Ala Asp Pro Glu			
250	255	260	
ccgggggactc agacactcag ggaacaaaat ggtcagccag agctggggaa acccagaact			1358
gacttcaaag gcagcttctg gacaggtggt gggaggggac ccttcccaag aggaaccaat			1418
aaaccttctg tgcagaatga			1438
<210> SEQ ID NO 27			
<211> LENGTH: 260			
<212> TYPE: PRT			
<213> ORGANISM: Homo sapiens			
<400> SEQUENCE: 27			
Met Glu Leu Thr Gln Pro Ala Glu Asp Leu Ile Gln Thr Gln Gln Thr			
1	5	10	15
Pro Ala Ser Glu Leu Gly Asp Pro Glu Asp Pro Gly Glu Glu Ala Ala			
20	25	30	
Asp Gly Ser Asp Thr Val Val Leu Ser Leu Phe Pro Cys Thr Pro Glu			
35	40	45	
Pro Val Asn Pro Glu Pro Asp Ala Ser Val Ser Ser Pro Gln Ala Gly			
50	55	60	
Ser Ser Leu Lys His Ser Thr Thr Leu Thr Asn Arg Gln Arg Gly Asn			
65	70	75	80
Glu Val Ser Ala Leu Pro Ala Thr Leu Asp Ser Leu Ser Ile His Gln			
85	90	95	
Leu Ala Ala Gln Gly Glu Leu Asp Gln Leu Lys Glu His Leu Arg Lys			
100	105	110	
Gly Asp Asn Leu Val Asn Lys Pro Asp Glu Arg Gly Phe Thr Pro Leu			
115	120	125	
Ile Trp Ala Ser Ala Phe Gly Glu Ile Glu Thr Val Arg Phe Leu Leu			
130	135	140	
Glu Trp Gly Ala Asp Pro His Ile Leu Ala Lys Glu Arg Glu Ser Ala			
145	150	155	160
Leu Ser Leu Ala Ser Thr Gly Gly Tyr Thr Asp Ile Val Gly Leu Leu			
165	170	175	

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Leu Glu Arg Asp Val Asp Ile Asn Ile Tyr Asp Trp Asn Gly Gly Thr
 180 185 190
 Pro Leu Leu Tyr Ala Val Arg Gly Asn His Val Lys Cys Val Glu Ala
 195 200 205
 Leu Leu Ala Arg Gly Ala Asp Leu Thr Thr Glu Ala Asp Ser Gly Tyr
 210 215 220
 Thr Pro Met Asp Leu Ala Val Ala Leu Gly Tyr Arg Lys Val Gln Gln
 225 230 235 240
 Val Ile Glu Asn His Ile Leu Lys Leu Phe Gln Ser Asn Leu Val Pro
 245 250 255
 Ala Asp Pro Glu
 260

<210> SEQ ID NO 28
 <211> LENGTH: 3618
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (222) .. (2072)

<400> SEQUENCE: 28

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 gctggagtga aggtggctac gagttttcca gatttaggag acttcagaaa ggtggggcag 120
 atagaatgga gatggcaaa atctcttttg gcataatagg gcctggcgaa gtaatggaat 180
 aatttctaattttcggagaa ggcaagtgcc ctcatgccgg g atg gca gaa gat gag 236
 Met Ala Glu Asp Glu
 1 5
 cct gat gct aag agc ccc aag act ggg gga agg gcc ccc cca ggt ggt 284
 Pro Asp Ala Lys Ser Pro Lys Thr Gly Gly Arg Ala Pro Pro Gly Gly
 10 15 20
 gct gag gct ggg gaa cct acc acc ctt ctt cag agg ctc cga ggt acc 332
 Ala Glu Ala Gly Glu Pro Thr Thr Leu Leu Gln Arg Leu Arg Gly Thr
 25 30 35
 att tcc aag gcc gtg cag aac aaa gta gag ggg atc ctg caa gat gta 380
 Ile Ser Lys Ala Val Gln Asn Lys Val Glu Gly Ile Leu Gln Asp Val
 40 45 50
 cag aaa ttt tct gac aat gac aag ctg tat ctc tac ctt cag ctc ccc 428
 Gln Lys Phe Ser Asp Asn Asp Lys Leu Tyr Leu Tyr Leu Gln Leu Pro
 55 60 65
 tca gga ccc acc act gga gac aaa agc tca gag cca agt aca ctg agc 476
 Ser Gly Pro Thr Thr Gly Asp Lys Ser Ser Glu Pro Ser Thr Leu Ser
 70 75 80 85
 aat gag gag tac atg tat gcc tat agg tgg atc cgc aac cac ctg gaa 524
 Asn Glu Glu Tyr Met Tyr Ala Tyr Arg Trp Ile Arg Asn His Leu Glu
 90 95 100
 gag cac act gac acc tgt ctg cca aag caa agt gtt tat gat gcc tat 572
 Glu His Thr Asp Thr Cys Leu Pro Lys Gln Ser Val Tyr Asp Ala Tyr
 105 110 115
 cgg aag tac tgt gag agt ctt gcc tgt tgc cgc cca ctc agc aca gcc 620
 Arg Lys Tyr Cys Glu Ser Leu Ala Cys Cys Arg Pro Leu Ser Thr Ala
 120 125 130
 aac ttt ggc aag atc atc aga gag atc ttc cct gac atc aaa gct cga 668
 Asn Phe Gly Lys Ile Ile Arg Glu Ile Phe Pro Asp Ile Lys Ala Arg
 135 140 145

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agg ctt ggt ggc cgg ggc cag tcc aaa tat tgc tac agt ggc ata agg	716
Arg Leu Gly Gly Arg Gly Gln Ser Lys Tyr Cys Tyr Ser Gly Ile Arg	
150 155 160 165	
agg aag acc ttg gtg tct atg cca ccc ctg cct gga ctt gac cta aag	764
Arg Lys Thr Leu Val Ser Met Pro Pro Leu Pro Gly Leu Asp Leu Lys	
170 175 180	
ggg tct gag agt cca gaa atg ggc cca gaa gta acc cca gca cct cga	812
Gly Ser Glu Ser Pro Glu Met Gly Pro Glu Val Thr Pro Ala Pro Arg	
185 190 195	
gat gaa ctg gtg gag gca gcg tgt gcc ctg acc tgt gac tgg gca gag	860
Asp Glu Leu Val Glu Ala Ala Cys Ala Leu Thr Cys Asp Trp Ala Glu	
200 205 210	
cgg atc ctg aaa cgg tcc ttc agt tcc atc gtt gag gtc gcc cgc ttc	908
Arg Ile Leu Lys Arg Ser Phe Ser Ser Ile Val Glu Val Ala Arg Phe	
215 220 225	
ctg cta cag cag cat ctc atc tct gcc cga tct gca cat gcc cat gtg	956
Leu Leu Gln Gln His Leu Ile Ser Ala Arg Ser Ala His Ala His Val	
230 235 240 245	
ctt aag gcc atg ggg ctt gct gaa gag gac gaa cat gca cct cgg gaa	1004
Leu Lys Ala Met Gly Leu Ala Glu Glu Asp Glu His Ala Pro Arg Glu	
250 255 260	
cgg tca tct aaa cca aag aat ggt tta gag aac cca gag ggt gga gcc	1052
Arg Ser Ser Lys Pro Lys Asn Gly Leu Glu Asn Pro Glu Gly Gly Ala	
265 270 275	
cac aag aag cca gag aga ctg gcc cag cct cct aag gat ctg gaa gcc	1100
His Lys Lys Pro Glu Arg Leu Ala Gln Pro Pro Lys Asp Leu Glu Ala	
280 285 290	
cga act ggg gcc ggt cct ctc gca cgt gga gag cgg aag aag agt gta	1148
Arg Thr Gly Ala Gly Pro Leu Ala Arg Gly Glu Arg Lys Lys Ser Val	
295 300 305	
gtt gag agc tcg gcc cca gga gcc aat aac ctg cag gtt aat gcc cta	1196
Val Glu Ser Ser Ala Pro Gly Ala Asn Asn Leu Gln Val Asn Ala Leu	
310 315 320 325	
gtg gct cgg ctg cct ctg ctc ctt ccc cgg gcc cct cgc tca cta att	1244
Val Ala Arg Leu Pro Leu Leu Leu Pro Arg Ala Pro Arg Ser Leu Ile	
330 335 340	
ccg cca atc cca gtc tct cca cct att ctg gcc ccc agg ctt tct tca	1292
Pro Pro Ile Pro Val Ser Pro Pro Ile Leu Ala Pro Arg Leu Ser Ser	
345 350 355	
ggg gcc ctg aaa gtg gct aca ctg cct ctg tct agt agg gcc ggg gca	1340
Gly Ala Leu Lys Val Ala Thr Leu Pro Leu Ser Ser Arg Ala Gly Ala	
360 365 370	
ccc cca gca gct gtg ccc atc att aac atg atc tta cca act gtt cct	1388
Pro Pro Ala Ala Val Pro Ile Ile Asn Met Ile Leu Pro Thr Val Pro	
375 380 385	
gct ttg cct gga cct gga cct ggg cct ggg cga gct cca cct ggg gga	1436
Ala Leu Pro Gly Pro Gly Pro Gly Pro Gly Arg Ala Pro Pro Gly Gly	
390 395 400 405	
ctc act cag ccc cgg ggc aca gag aac aga gag gta ggc ata ggt ggt	1484
Leu Thr Gln Pro Arg Gly Thr Glu Asn Arg Glu Val Gly Ile Gly Gly	
410 415 420	
gac caa gga cca cat gac aag ggt gtc aag agg aca gct gaa gta cct	1532
Asp Gln Gly Pro His Asp Lys Gly Val Lys Arg Thr Ala Glu Val Pro	
425 430 435	
gtg agt gag gcc agt ggg cag gct cca cca gct aaa gca gca aag cag	1580
Val Ser Glu Ala Ser Gly Gln Ala Pro Pro Ala Lys Ala Ala Lys Gln	
440 445 450	

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gat ata gag gat aca gca agt gat gcc aaa agg aaa cgg ggg cgc cct	1628
Asp Ile Glu Asp Thr Ala Ser Asp Ala Lys Arg Lys Arg Gly Arg Pro	
455 460 465	
cga aaa aag tca ggt gga agt ggg gaa agg aat tct acc cct ctc aag	1676
Arg Lys Lys Ser Gly Gly Ser Gly Glu Arg Asn Ser Thr Pro Leu Lys	
470 475 480 485	
tca gca gct gcc atg gaa tct gcc cag tcc tca agg tta cca tgg gag	1724
Ser Ala Ala Ala Met Glu Ser Ala Gln Ser Ser Arg Leu Pro Trp Glu	
490 495 500	
aca tgg ggc tca gga ggg gaa ggc aac tca gct gga ggg gca gag agg	1772
Thr Trp Gly Ser Gly Gly Glu Gly Asn Ser Ala Gly Gly Ala Glu Arg	
505 510 515	
cca ggg cca atg gga gag gct gaa aag ggg gca gta ctt gcc cag ggt	1820
Pro Gly Pro Met Gly Glu Ala Glu Lys Gly Ala Val Leu Ala Gln Gly	
520 525 530	
cag gga gat ggt act gtt tcc aaa gga gga agg ggc ccc ggt tcc cag	1868
Gln Gly Asp Gly Thr Val Ser Lys Gly Gly Arg Gly Pro Gly Ser Gln	
535 540 545	
cat acc aaa gaa gca gaa gat aaa att ccc ttg gtc ccc tca aaa gtg	1916
His Thr Lys Glu Ala Glu Asp Lys Ile Pro Leu Val Pro Ser Lys Val	
550 555 560 565	
agt gtc atc aag ggc agc aga agc caa aag gag gct ttt cct ttg gca	1964
Ser Val Ile Lys Gly Ser Arg Ser Gln Lys Glu Ala Phe Pro Leu Ala	
570 575 580	
aag gga gag gta gac act gca cca cag ggt aat aaa gac tta aag gag	2012
Lys Gly Glu Val Asp Thr Ala Pro Gln Gly Asn Lys Asp Leu Lys Glu	
585 590 595	
cat gtg ctt caa agt tcc tta tcc cag gag cat aaa gac cca aaa gca	2060
His Val Leu Gln Ser Ser Leu Ser Gln Glu His Lys Asp Pro Lys Ala	
600 605 610	
aca ccc cca tga tacaggtctg tggggaagag tgtttatatc cctacgttaa	2112
Thr Pro Pro	
615	
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gaagtccatt ctccctctgta cagacagctg agtcaccag tctacttagt acctggttgc	2232
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aaataaaaag gatttattgg ttcattgtaac tagaaagtcc ataggtagtg ctggctccag	2472
gtgaagactt gacccagtag ttcagtatgt ctctaaatac cggactgact tttttctcac	2532
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aatcactgtg gccaggagga tgatacatgc taatttgctt attctatata atggacaaca	2772
cctttgggga aaaggggtggg ggtcagcctc cccaaaatca catggattcc ccaagtggaa	2832
actaggagca gggagtgtct tgggtggccg ctaacaccag gctactctta ttttagcttg	2892
ctaagttgag atcagctaga cctgctttct tttctcctca gtcttgcaat tccctcaata	2952
caagctgtag cctctttcct cgtttctagt ctcaagaagga aggagaggga agccattctc	3012
ctctagggac tcttcagtct catttagatg atagtcctct tttttctacc tccatattag	3072

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agatggagct ccttcctttt cctgtttctt aatttttgtc ttctcattcc tgettccctc 3132
tcaccttatt gccagttcca ccaactagag tgaaagactt cctagccatt tcattaaatc 3192
tattctgtat ccaccaggtg gcagcatctt gtcatacgtg tcaggactta ggactgcggg 3252
gtttaggtta gatgtcacgg aaaaagctag ttctgtggtc aggcggcacc aatgagaaaag 3312
gaatgcagac cctccagatg tatccttggg aaaagcagta aaccaactaa tatttattga 3372
agacctactt tgtcctctac atagggtagc ttctgtcagg gaatcttggg tcttcccaag 3432
aaacactgat tttctttcag ggagacttca tgtgttcatt tatttccacc acagcagatt 3492
ttaagaaatt ataatatgta atatttgata tctataaaga gtatatctaa cgtgaataaa 3552
ttatgaagca tactaatgag tacctatgac ccataacaca tatacatata aacattttaa 3612
atacca 3618

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<210> SEQ ID NO 29

<211> LENGTH: 616

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 29

```

Met Ala Glu Asp Glu Pro Asp Ala Lys Ser Pro Lys Thr Gly Gly Arg
1      5      10      15
Ala Pro Pro Gly Gly Ala Glu Ala Gly Glu Pro Thr Thr Leu Leu Gln
20      25      30
Arg Leu Arg Gly Thr Ile Ser Lys Ala Val Gln Asn Lys Val Glu Gly
35      40      45
Ile Leu Gln Asp Val Gln Lys Phe Ser Asp Asn Asp Lys Leu Tyr Leu
50      55      60
Tyr Leu Gln Leu Pro Ser Gly Pro Thr Thr Gly Asp Lys Ser Ser Glu
65      70      75      80
Pro Ser Thr Leu Ser Asn Glu Glu Tyr Met Tyr Ala Tyr Arg Trp Ile
85      90      95
Arg Asn His Leu Glu Glu His Thr Asp Thr Cys Leu Pro Lys Gln Ser
100     105     110
Val Tyr Asp Ala Tyr Arg Lys Tyr Cys Glu Ser Leu Ala Cys Cys Arg
115     120     125
Pro Leu Ser Thr Ala Asn Phe Gly Lys Ile Ile Arg Glu Ile Phe Pro
130     135     140
Asp Ile Lys Ala Arg Arg Leu Gly Gly Arg Gly Gln Ser Lys Tyr Cys
145     150     155     160
Tyr Ser Gly Ile Arg Arg Lys Thr Leu Val Ser Met Pro Pro Leu Pro
165     170     175
Gly Leu Asp Leu Lys Gly Ser Glu Ser Pro Glu Met Gly Pro Glu Val
180     185     190
Thr Pro Ala Pro Arg Asp Glu Leu Val Glu Ala Ala Cys Ala Leu Thr
195     200     205
Cys Asp Trp Ala Glu Arg Ile Leu Lys Arg Ser Phe Ser Ser Ile Val
210     215     220
Glu Val Ala Arg Phe Leu Leu Gln Gln His Leu Ile Ser Ala Arg Ser
225     230     235     240
Ala His Ala His Val Leu Lys Ala Met Gly Leu Ala Glu Glu Asp Glu
245     250     255

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His	Ala	Pro	Arg	Glu	Arg	Ser	Ser	Lys	Pro	Lys	Asn	Gly	Leu	Glu	Asn	
			260					265					270			
Pro	Glu	Gly	Gly	Ala	His	Lys	Lys	Pro	Glu	Arg	Leu	Ala	Gln	Pro	Pro	
		275					280					285				
Lys	Asp	Leu	Glu	Ala	Arg	Thr	Gly	Ala	Gly	Pro	Leu	Ala	Arg	Gly	Glu	
	290					295					300					
Arg	Lys	Lys	Ser	Val	Val	Glu	Ser	Ser	Ala	Pro	Gly	Ala	Asn	Asn	Leu	
305					310					315					320	
Gln	Val	Asn	Ala	Leu	Val	Ala	Arg	Leu	Pro	Leu	Leu	Leu	Pro	Arg	Ala	
			325						330					335		
Pro	Arg	Ser	Leu	Ile	Pro	Pro	Ile	Pro	Val	Ser	Pro	Pro	Ile	Leu	Ala	
			340					345						350		
Pro	Arg	Leu	Ser	Ser	Gly	Ala	Leu	Lys	Val	Ala	Thr	Leu	Pro	Leu	Ser	
		355					360					365				
Ser	Arg	Ala	Gly	Ala	Pro	Pro	Ala	Ala	Val	Pro	Ile	Ile	Asn	Met	Ile	
	370					375					380					
Leu	Pro	Thr	Val	Pro	Ala	Leu	Pro	Gly	Pro	Gly	Pro	Gly	Pro	Gly	Arg	
385					390					395					400	
Ala	Pro	Pro	Gly	Gly	Leu	Thr	Gln	Pro	Arg	Gly	Thr	Glu	Asn	Arg	Glu	
			405						410					415		
Val	Gly	Ile	Gly	Gly	Asp	Gln	Gly	Pro	His	Asp	Lys	Gly	Val	Lys	Arg	
		420						425					430			
Thr	Ala	Glu	Val	Pro	Val	Ser	Glu	Ala	Ser	Gly	Gln	Ala	Pro	Pro	Ala	
		435					440					445				
Lys	Ala	Ala	Lys	Gln	Asp	Ile	Glu	Asp	Thr	Ala	Ser	Asp	Ala	Lys	Arg	
	450					455					460					
Lys	Arg	Gly	Arg	Pro	Arg	Lys	Lys	Ser	Gly	Gly	Ser	Gly	Glu	Arg	Asn	
465					470					475					480	
Ser	Thr	Pro	Leu	Lys	Ser	Ala	Ala	Ala	Met	Glu	Ser	Ala	Gln	Ser	Ser	
			485						490					495		
Arg	Leu	Pro	Trp	Glu	Thr	Trp	Gly	Ser	Gly	Gly	Glu	Gly	Asn	Ser	Ala	
		500						505						510		
Gly	Gly	Ala	Glu	Arg	Pro	Gly	Pro	Met	Gly	Glu	Ala	Glu	Lys	Gly	Ala	
		515					520					525				
Val	Leu	Ala	Gln	Gly	Gln	Gly	Asp	Gly	Thr	Val	Ser	Lys	Gly	Gly	Arg	
	530					535					540					
Gly	Pro	Gly	Ser	Gln	His	Thr	Lys	Glu	Ala	Glu	Asp	Lys	Ile	Pro	Leu	
545					550					555					560	
Val	Pro	Ser	Lys	Val	Ser	Val	Ile	Lys	Gly	Ser	Arg	Ser	Gln	Lys	Glu	
			565						570					575		
Ala	Phe	Pro	Leu	Ala	Lys	Gly	Glu	Val	Asp	Thr	Ala	Pro	Gln	Gly	Asn	
		580						585					590			
Lys	Asp	Leu	Lys	Glu	His	Val	Leu	Gln	Ser	Ser	Leu	Ser	Gln	Glu	His	
	595						600					605				
Lys	Asp	Pro	Lys	Ala	Thr	Pro	Pro									
	610					615										

<210> SEQ ID NO 30

<211> LENGTH: 3611

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

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<222> LOCATION: (215) .. (2065)

<400> SEQUENCE: 30

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attcagaaaa aggaaaaataa agcaacgcac gagccggctg ggccaggacc ttggggctgg      60
gctggagtga aggtggctac gagttttcca gatttaggag acttcagaaa ggtggggcag      120
atagaatgga gatggcaaag atctctttgg gcatatatgg gcctggcgaa gtaatggaat      180
aattttcta tttcggagaa gccctcatgc cggg atg gca gaa gat gag cct gat      235
                               Met Ala Glu Asp Glu Pro Asp
                               1           5

gct aag agc ccc aag act ggg gga agg gcc ccc cca ggt ggt gct gag      283
Ala Lys Ser Pro Lys Thr Gly Gly Arg Ala Pro Pro Gly Gly Ala Glu
      10           15           20

gct ggg gaa cct acc acc ctt ctt cag agg ctc cga ggt acc att tcc      331
Ala Gly Glu Pro Thr Thr Leu Leu Gln Arg Leu Arg Gly Thr Ile Ser
      25           30           35

aag gcc gtg cag aac aaa gta gag ggg atc ctg caa gat gta cag aaa      379
Lys Ala Val Gln Asn Lys Val Glu Gly Ile Leu Gln Asp Val Gln Lys
      40           45           50           55

ttt tct gac aat gac aag ctg tat ctc tac ctt cag ctc ccc tca gga      427
Phe Ser Asp Asn Asp Lys Leu Tyr Leu Tyr Leu Gln Leu Pro Ser Gly
      60           65           70

ccc acc act gga gac aaa agc tca gag cca agt aca ctg agc aat gag      475
Pro Thr Thr Gly Asp Lys Ser Ser Glu Pro Ser Thr Leu Ser Asn Glu
      75           80           85

gag tac atg tat gcc tat agg tgg atc cgc aac cac ctg gaa gag cac      523
Glu Tyr Met Tyr Ala Tyr Arg Trp Ile Arg Asn His Leu Glu Glu His
      90           95           100

act gac acc tgt ctg cca aag caa agt gtt tat gat gcc tat cgg aag      571
Thr Asp Thr Cys Leu Pro Lys Gln Ser Val Tyr Asp Ala Tyr Arg Lys
      105           110           115

tac tgt gag agt ctt gcc tgt tgc cgc cca ctc agc aca gcc aac ttt      619
Tyr Cys Glu Ser Leu Ala Cys Cys Arg Pro Leu Ser Thr Ala Asn Phe
      120           125           130           135

ggc aag atc atc aga gag atc ttc cct gac atc aaa gct cga agg ctt      667
Gly Lys Ile Ile Arg Glu Ile Phe Pro Asp Ile Lys Ala Arg Arg Leu
      140           145           150

ggt ggc cgg ggc cag tcc aaa tat tgc tac agt ggc ata agg agg aag      715
Gly Gly Arg Gly Gln Ser Lys Tyr Cys Tyr Ser Gly Ile Arg Arg Lys
      155           160           165

acc ttg gtg tct atg cca ccc ctg cct gga ctt gac cta aag ggt tct      763
Thr Leu Val Ser Met Pro Pro Leu Pro Gly Leu Asp Leu Lys Gly Ser
      170           175           180

gag agt cca gaa atg ggc cca gaa gta acc cca gca cct cga gat gaa      811
Glu Ser Pro Glu Met Gly Pro Glu Val Thr Pro Ala Pro Arg Asp Glu
      185           190           195

ctg gtg gag gca gcg tgt gcc ctg acc tgt gac tgg gca gag cgg atc      859
Leu Val Glu Ala Ala Cys Ala Leu Thr Cys Asp Trp Ala Glu Arg Ile
      200           205           210           215

ctg aaa cgg tcc ttc agt tcc atc gtt gag gtc gcc cgc ttc ctg cta      907
Leu Lys Arg Ser Phe Ser Ser Ile Val Glu Val Ala Arg Phe Leu Leu
      220           225           230

cag cag cat ctc atc tct gcc cga tct gca cat gcc cat gtg ctt aag      955
Gln Gln His Leu Ile Ser Ala Arg Ser Ala His Ala His Val Leu Lys
      235           240           245

gcc atg ggg ctt gct gaa gag gac gaa cat gca cct cgg gaa cgg tca      1003
Ala Met Gly Leu Ala Glu Glu Asp Glu His Ala Pro Arg Glu Arg Ser

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250	255	260	
tct aaa cca aag aat ggt tta gag aac cca gag ggt gga gcc cac aag			1051
Ser Lys Pro Lys Asn Gly Leu Glu Asn Pro Glu Gly Gly Ala His Lys			
265	270	275	
aag cca gag aga ctg gcc cag cct cct aag gat ctg gaa gcc cga act			1099
Lys Pro Glu Arg Leu Ala Gln Pro Pro Lys Asp Leu Glu Ala Arg Thr			
280	285	290	295
ggg gcc ggt cct ctc gca cgt gga gag cgg aag aag agt gta gtt gag			1147
Gly Ala Gly Pro Leu Ala Arg Gly Glu Arg Lys Lys Ser Val Val Glu			
300	305	310	
agc tcg gcc cca gga gcc aat aac ctg cag gtt aat gcc cta gtg gct			1195
Ser Ser Ala Pro Gly Ala Asn Asn Leu Gln Val Asn Ala Leu Val Ala			
315	320	325	
cgg ctg cct ctg ctc ctt ccc cgg gcc cct cgc tca cta att ccg cca			1243
Arg Leu Pro Leu Leu Leu Pro Arg Ala Pro Arg Ser Leu Ile Pro Pro			
330	335	340	
atc cca gtc tct cca cct att ctg gcc ccc agg ctt tct tca ggt gcc			1291
Ile Pro Val Ser Pro Pro Ile Leu Ala Pro Arg Leu Ser Ser Gly Ala			
345	350	355	
ctg aaa gtg gct aca ctg cct ctg tct agt agg gcc ggg gca ccc cca			1339
Leu Lys Val Ala Thr Leu Pro Leu Ser Ser Arg Ala Gly Ala Pro Pro			
360	365	370	375
gca gct gtg ccc atc att aac atg atc tta cca act gtt cct gct ttg			1387
Ala Ala Val Pro Ile Ile Asn Met Ile Leu Pro Thr Val Pro Ala Leu			
380	385	390	
cct gga cct gga cct ggg cct ggg cga gct cca cct ggg gga ctc act			1435
Pro Gly Pro Gly Pro Gly Pro Gly Arg Ala Pro Pro Gly Gly Leu Thr			
395	400	405	
cag ccc cgg ggc aca gag aac aga gag gta ggc ata ggt ggt gac caa			1483
Gln Pro Arg Gly Thr Glu Asn Arg Glu Val Gly Ile Gly Gly Asp Gln			
410	415	420	
gga cca cat gac aag ggt gtc aag agg aca gct gaa gta cct gtg agt			1531
Gly Pro His Asp Lys Gly Val Lys Arg Thr Ala Glu Val Pro Val Ser			
425	430	435	
gag gcc agt ggg cag gct cca cca gct aaa gca gca aag cag gat ata			1579
Glu Ala Ser Gly Gln Ala Pro Pro Ala Lys Ala Ala Lys Gln Asp Ile			
440	445	450	455
gag gat aca gca agt gat gcc aaa agg aaa cgg ggg cgc cct cga aaa			1627
Glu Asp Thr Ala Ser Asp Ala Lys Arg Lys Arg Gly Arg Pro Arg Lys			
460	465	470	
aag tca ggt gga agt ggg gaa agg aat tct acc cct ctc aag tca gca			1675
Lys Ser Gly Gly Ser Gly Glu Arg Asn Ser Thr Pro Leu Lys Ser Ala			
475	480	485	
gct gcc atg gaa tct gcc cag tcc tca agg tta cca tgg gag aca tgg			1723
Ala Ala Met Glu Ser Ala Gln Ser Ser Arg Leu Pro Trp Glu Thr Trp			
490	495	500	
ggc tca gga ggg gaa ggc aac tca gct gga ggg gca gag agg cca ggg			1771
Gly Ser Gly Gly Glu Gly Asn Ser Ala Gly Gly Ala Glu Arg Pro Gly			
505	510	515	
cca atg gga gag gct gaa aag ggg gca gta ctt gcc cag ggt cag gga			1819
Pro Met Gly Glu Ala Glu Lys Gly Ala Val Leu Ala Gln Gly Gln Gly			
520	525	530	535
gat ggt act gtt tcc aaa gga gga agg ggc ccc ggt tcc cag cat acc			1867
Asp Gly Thr Val Ser Lys Gly Gly Arg Gly Pro Gly Ser Gln His Thr			
540	545	550	
aaa gaa gca gaa gat aaa att ccc ttg gtc ccc tca aaa gtg agt gtc			1915
Lys Glu Ala Glu Asp Lys Ile Pro Leu Val Pro Ser Lys Val Ser Val			

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555	560	565	
atc aag ggc agc aga agc caa aag gag gct ttt cct ttg gca aag gga			1963
Ile Lys Gly Ser Arg Ser Gln Lys Glu Ala Phe Pro Leu Ala Lys Gly			
570	575	580	
gag gta gac act gca cca cag ggt aat aaa gac tta aag gag cat gtg			2011
Glu Val Asp Thr Ala Pro Gln Gly Asn Lys Asp Leu Lys Glu His Val			
585	590	595	
ctt caa agt tcc tta tcc cag gag cat aaa gac cca aaa gca aca ccc			2059
Leu Gln Ser Ser Leu Ser Gln Glu His Lys Asp Pro Lys Ala Thr Pro			
600	605	610	615
cca tga tacaggctctg tggggaagag tggttatatc cctacgttaa ctttgccctag			2115
Pro			
tagaggccct tctttgcact tgcttctcat ttggtattc ttttcctaag gaagtccatt			2175
ctcctctgta cagacagctg agtcaccag tctacttagt acctggttgc tgccctcgac			2235
cttttcagct tgataccctg ggcttttagtg taaccaataa atctgtagtg accttacctg			2295
tattccctgt gctatcctgt gggaaggtag gaatgggcta agtatgatga atatataggt			2355
tagggatctt ttggttttaa atcacagaaa acctaatca aactggctta aaataaaaag			2415
gatttattgg ttcattgtaac tagaaagtcc ataggtagtg ctggctccag gtgaagactt			2475
gaccagtag ttcagtatgt ctctaaatc cggactgact tttttctcac tgttgcactt			2535
tctgtaggac catttaagtc tggggccactt aatggctgcc agcattccta agattacact			2595
tttccccatt tatgtccaat cagaaaaaga aggcattctt gtaccagaaa tctcagcaaa			2655
agccctaata ttcacactga ttaggcctgg gtcacatgac caccctgacc aatcactgtg			2715
gccaggagga tgatacatgc taatttgctt attctatatc atggacaaca cctttgggga			2775
aaagggtggg ggtcagcctc cccaaaatca catggattcc ccaagtggaa actaggagca			2835
gggagttgct tgggtggcgc ctaacaccag gctactctta ttttagcttg ctaagttgag			2895
atcagctaga cctgctttct tttctctca gtcttgcat tccctcaata caagctgtag			2955
cctctttcct cgtttctagt ctcaagaaga aggagaggga agccattctc ctctaggagc			3015
tcttcagtct cattttagtg atagtccctt tttttctacc tccatattag agatggagct			3075
ccttctttt cctgtttctt aatttttgtc ttctcattcc tgcttccctc tcacctatt			3135
gccagttcca ccaactagag tgaaagactt cctagccatt tcattaaatc tattctgtat			3195
ccaccaggtg gcagcatctt gtcatacgtg tcaggactta ggactgcggg gtttaggtta			3255
gatgtcacgg aaaaagctag ttctgtggtc aggcggcacc aatgagaaag gaatgcagac			3315
cctccagatg tacccttggg aaaagcagta aaccaactaa tatttattga agacctactt			3375
tgctctctac atagggtagc ttctgtcagg gaatcttggg tcttccaag aaacactgat			3435
tttctttcag ggagacttca tgtgttcatt tatttccacc acagcagatt ttaagaaatt			3495
ataatatgta atatttgata tctataaaga gtatatctaa cgtgaataaa ttatgaagca			3555
tactaatgag tacctatgac ccataacaca tatacatata aacattttta atacca			3611

<210> SEQ ID NO 31

<211> LENGTH: 616

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 31

Met Ala Glu Asp Glu Pro Asp Ala Lys Ser Pro Lys Thr Gly Gly Arg

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1	5	10	15
Ala Pro Pro Gly Gly Ala Glu Ala Gly Glu Pro Thr Thr Leu Leu Gln	20	25	30
Arg Leu Arg Gly Thr Ile Ser Lys Ala Val Gln Asn Lys Val Glu Gly	35	40	45
Ile Leu Gln Asp Val Gln Lys Phe Ser Asp Asn Asp Lys Leu Tyr Leu	50	55	60
Tyr Leu Gln Leu Pro Ser Gly Pro Thr Thr Gly Asp Lys Ser Ser Glu	65	70	75
Pro Ser Thr Leu Ser Asn Glu Glu Tyr Met Tyr Ala Tyr Arg Trp Ile	85	90	95
Arg Asn His Leu Glu Glu His Thr Asp Thr Cys Leu Pro Lys Gln Ser	100	105	110
Val Tyr Asp Ala Tyr Arg Lys Tyr Cys Glu Ser Leu Ala Cys Cys Arg	115	120	125
Pro Leu Ser Thr Ala Asn Phe Gly Lys Ile Ile Arg Glu Ile Phe Pro	130	135	140
Asp Ile Lys Ala Arg Arg Leu Gly Gly Arg Gly Gln Ser Lys Tyr Cys	145	150	155
Tyr Ser Gly Ile Arg Arg Lys Thr Leu Val Ser Met Pro Pro Leu Pro	165	170	175
Gly Leu Asp Leu Lys Gly Ser Glu Ser Pro Glu Met Gly Pro Glu Val	180	185	190
Thr Pro Ala Pro Arg Asp Glu Leu Val Glu Ala Ala Cys Ala Leu Thr	195	200	205
Cys Asp Trp Ala Glu Arg Ile Leu Lys Arg Ser Phe Ser Ser Ile Val	210	215	220
Glu Val Ala Arg Phe Leu Leu Gln Gln His Leu Ile Ser Ala Arg Ser	225	230	235
Ala His Ala His Val Leu Lys Ala Met Gly Leu Ala Glu Glu Asp Glu	245	250	255
His Ala Pro Arg Glu Arg Ser Ser Lys Pro Lys Asn Gly Leu Glu Asn	260	265	270
Pro Glu Gly Gly Ala His Lys Lys Pro Glu Arg Leu Ala Gln Pro Pro	275	280	285
Lys Asp Leu Glu Ala Arg Thr Gly Ala Gly Pro Leu Ala Arg Gly Glu	290	295	300
Arg Lys Lys Ser Val Val Glu Ser Ser Ala Pro Gly Ala Asn Asn Leu	305	310	315
Gln Val Asn Ala Leu Val Ala Arg Leu Pro Leu Leu Leu Pro Arg Ala	325	330	335
Pro Arg Ser Leu Ile Pro Pro Ile Pro Val Ser Pro Pro Ile Leu Ala	340	345	350
Pro Arg Leu Ser Ser Gly Ala Leu Lys Val Ala Thr Leu Pro Leu Ser	355	360	365
Ser Arg Ala Gly Ala Pro Pro Ala Ala Val Pro Ile Ile Asn Met Ile	370	375	380
Leu Pro Thr Val Pro Ala Leu Pro Gly Pro Gly Pro Gly Pro Gly Arg	385	390	395
Ala Pro Pro Gly Gly Leu Thr Gln Pro Arg Gly Thr Glu Asn Arg Glu	405	410	415

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Val Gly Ile Gly Gly Asp Gln Gly Pro His Asp Lys Gly Val Lys Arg
420 425 430

Thr Ala Glu Val Pro Val Ser Glu Ala Ser Gly Gln Ala Pro Pro Ala
435 440 445

Lys Ala Ala Lys Gln Asp Ile Glu Asp Thr Ala Ser Asp Ala Lys Arg
450 455 460

Lys Arg Gly Arg Pro Arg Lys Lys Ser Gly Gly Ser Gly Glu Arg Asn
465 470 475 480

Ser Thr Pro Leu Lys Ser Ala Ala Ala Met Glu Ser Ala Gln Ser Ser
485 490 495

Arg Leu Pro Trp Glu Thr Trp Gly Ser Gly Gly Glu Gly Asn Ser Ala
500 505 510

Gly Gly Ala Glu Arg Pro Gly Pro Met Gly Glu Ala Glu Lys Gly Ala
515 520 525

Val Leu Ala Gln Gly Gln Gly Asp Gly Thr Val Ser Lys Gly Gly Arg
530 535 540

Gly Pro Gly Ser Gln His Thr Lys Glu Ala Glu Asp Lys Ile Pro Leu
545 550 555 560

Val Pro Ser Lys Val Ser Val Ile Lys Gly Ser Arg Ser Gln Lys Glu
565 570 575

Ala Phe Pro Leu Ala Lys Gly Glu Val Asp Thr Ala Pro Gln Gly Asn
580 585 590

Lys Asp Leu Lys Glu His Val Leu Gln Ser Ser Leu Ser Gln Glu His
595 600 605

Lys Asp Pro Lys Ala Thr Pro Pro
610 615

<210> SEQ ID NO 32

<211> LENGTH: 2825

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (157) .. (975)

<400> SEQUENCE: 32

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cgcgaggct gcggtcgcg aggcgcagtc ggggcgcctt cccggtatag gcgcctttta      60
ccccagcgtg tcctgagctt ttggttcgcg aagtgcgctt aggccaaagca ggtgctaaaa      120
gccccggggtc gtggaccccg gccagggtctt agcagc atg gag gcg cag ggt gta      174
                               Met Glu Ala Gln Gly Val
                               1          5
gcg gag ggc gcg ggg ccg ggc gcc gcc agc ggc gtg ccc cac ccc gcg      222
Ala Glu Gly Ala Gly Pro Gly Ala Ala Ser Gly Val Pro His Pro Ala
          10          15          20
gcc cta gcc ccg gct gcg gct ccc acc ttg gcg cca gcc tcg gtg gcg      270
Ala Leu Ala Pro Ala Ala Ala Pro Thr Leu Ala Pro Ala Ser Val Ala
          25          30          35
gcc gcg gcc tct caa ttc acc ctg cta gtg atg caa ccc tgt gct ggg      318
Ala Ala Ala Ser Gln Phe Thr Leu Leu Val Met Gln Pro Cys Ala Gly
          40          45          50
cag gac gag gct gcg gcc ccc ggg ggc agc gtt ggg gcg ggc aag ccc      366
Gln Asp Glu Ala Ala Ala Pro Gly Gly Ser Val Gly Ala Gly Lys Pro
          55          60          65          70
gtt agg tac ctg tgc gaa ggg gcc ggg gat ggc gaa gag gag gct ggg      414

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Val	Arg	Tyr	Leu	Cys 75	Glu	Gly	Ala	Gly	Asp 80	Gly	Glu	Glu	Glu	Ala 85	Gly		
gag Glu	gac Asp	gag Glu	gcg Ala	gac Asp	ctg Leu	tta Leu	gac Asp	act Thr	tcg Ser	gac Asp	cct Pro	ccg Pro	ggg Gly	gga Gly	ggc Gly	462	
gag Glu	agc Ser	gcg Ala	gct Ala	agt Ser	ttg Leu	gag Glu	gat Asp	cta Leu	gag Glu	gac Asp	gag Glu	gag Glu	act Thr	cac His	tcg Ser	510	
ggg Gly	ggc Gly	gag Glu	ggc Gly	agc Ser	agc Ser	ggg Gly	ggc Gly	gcc Ala	cgg Arg	agg Arg	cgg Arg	ggc Gly	agc Ser	ggg Gly	ggg Gly	558	
ggc Gly	agc Ser	atg Met	agc Ser	aag Lys	acc Thr	tgc Cys	acc Thr	tac Tyr	gaa Glu	ggc Gly	tgc Cys	agc Ser	gag Glu	acc Thr	acg Thr	606	
agc Ser	cag Gln	gtg Val	gcc Ala	aag Lys	cag Gln	cgc Arg	aaa Lys	ccg Pro	tgg Trp	atg Met	tgc Cys	aag Lys	aaa Lys	cac His	cgc Arg	654	
aac Asn	aag Lys	atg Met	tac Tyr	aag Lys	gac Asp	aag Lys	tat Tyr	aaa Lys	aag Lys	aag Lys	aag Lys	agc Ser	gac Asp	cag Gln	gcc Ala	702	
ctg Leu	aac Asn	tgc Cys	ggg Gly	ggg Gly	act Thr	gcc Ala	tcg Ser	act Thr	ggc Gly	agc Ser	gcg Ala	gga Gly	aac Asn	gtc Val	aaa Lys	750	
ctc Leu	gag Glu	gaa Glu	agt Ser	gca Ala	gat Asp	aac Asn	ata Ile	ctc Leu	tcc Ser	att Ile	gtt Val	aaa Lys	caa Gln	aga Arg	aca Thr	798	
gga Gly	tct Ser	ttt Phe	ggg Gly	gat Asp	cgt Arg	cct Pro	gca Ala	aga Arg	cct Pro	act Thr	ctt Leu	tta Leu	gaa Glu	caa Gln	gtg Val	846	
tta Leu	aat Asn	caa Gln	aaa Lys	aga Arg	ctg Leu	tcg Ser	tta Leu	cta Leu	aga Arg	agt Ser	cca Pro	gaa Glu	gta Val	gtg Val	caa Gln	894	
ttt Phe	tta Leu	cag Gln	aaa Lys	cag Gln	caa Gln	cag Gln	cta Leu	tta Leu	aat Asn	cag Gln	caa Gln	gtt Val	ttg Leu	gag Glu	caa Gln	942	
aga Arg	caa Gln	cag Gln	cag Gln	ttt Phe	cca Pro	gga Gly	aca Thr	tca Ser	atg Met	tga	gggaacttac				caagaacatc		995
tacatgggttt tttatotttat tgtaatatagat gagcatattt ttttaccaga cataaatggg																	1055
gtaataatct atgcctgtag aacataaaca ttttcctgta aatgtatgtg tgcatttggg																	1115
gataagtaag tattgcactt tgtgcatcta atctttcaga ttactgtgag tttgaagaag																	1175
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gatattaatc ttgactcatc tagctcagtg gttctcatca agggtcattt tgattgtcat																	1355
agtgcacctg aaaaccactg gctttttagt agtggccagg aatgctaaat gttctgcagt																	1415
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gaaatgttga tggetatttt gtgggtgctaa catgtagtgt gggcacctat aattggggtc																	1535
tcttaataac ctttctttgc agttaagact gaagctgtca aagaggttaag cacattttat																	1595
atagacgtaa ggaaagtgat tattgtttaa tatctgtgaa ttaggatgt gcattctctt																	1655
tcagagggtg gttagtaaaaa cctgacggat taactaagca cactgggatg tgtctcctac																	1715
agttggcttc tctctttgat gttacctgtt agtgctgato tcttaaagca gacatttctt																	1775

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gtttgttgaa tttgtgaaca gtatagatct cagcccacca atgccaagac aaaattatTT 1835
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tttctcctag gaaaacttta aaacttttaa aaggcaaacc taccaatagg aataacaaat 2075
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<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 33

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

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165										170										175									
Lys	Lys	Ser	Asp	Gln	Ala	Leu	Asn	Cys	Gly	Gly	Thr	Ala	Ser	Thr	Gly														
			180					185						190															
Ser	Ala	Gly	Asn	Val	Lys	Leu	Glu	Glu	Ser	Ala	Asp	Asn	Ile	Leu	Ser														
		195				200						205																	
Ile	Val	Lys	Gln	Arg	Thr	Gly	Ser	Phe	Gly	Asp	Arg	Pro	Ala	Arg	Pro														
	210					215					220																		
Thr	Leu	Leu	Glu	Gln	Val	Leu	Asn	Gln	Lys	Arg	Leu	Ser	Leu	Leu	Arg														
225					230					235					240														
Ser	Pro	Glu	Val	Val	Gln	Phe	Leu	Gln	Lys	Gln	Gln	Gln	Leu	Leu	Asn														
			245					250					255																
Gln	Gln	Val	Leu	Glu	Gln	Arg	Gln	Gln	Gln	Phe	Pro	Gly	Thr	Ser	Met														
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ggattcctac aca atg cgt tgc ctg gct cca cgc cct gct ggg tcc tac																									169				
Met Arg Cys Leu Ala Pro Arg Pro Ala Gly Ser Tyr																													
1										5										10									
ctg tca gag ccc caa ggc agc tca cag tgt gcc acc atg gag ttg ggg																									217				
Leu Ser Glu Pro Gln Gly Ser Ser Gln Cys Ala Thr Met Glu Leu Gly																													
15										20										25									
ccc cta gaa ggt ggc tac ctg gag ctt ctt aac agc gat gct gac ccc																									265				
Pro Leu Glu Gly Gly Tyr Leu Glu Leu Leu Asn Ser Asp Ala Asp Pro																													
30										35										40									
ctg tgc ctg tac cac ttc tat gac cag atg gac ctg gct gga gaa gaa																									313				
Leu Cys Leu Tyr His Phe Tyr Asp Gln Met Asp Leu Ala Gly Glu Glu																													
45										50										55									
gag att gag ctg tac tca gaa ccc gac aca gac acc atc aac tgc gac																									361				
Glu Ile Glu Leu Tyr Ser Glu Pro Asp Thr Asp Thr Ile Asn Cys Asp																													
65										70										75									
cag ttc agc agg ctg ttg tgt gac atg gaa ggt gat gaa gag acc agg																									409				
Gln Phe Ser Arg Leu Leu Cys Asp Met Glu Gly Asp Glu Glu Thr Arg																													
80										85										90									
gag gct tat gcc aat atc gcg gaa ctg gac cag tat gtc ttc cag gac																									457				
Glu Ala Tyr Ala Asn Ile Ala Glu Leu Asp Gln Tyr Val Phe Gln Asp																													
95										100										105									
tcc cag ctg gag ggc ctg agc aag gac att ttc aag cac ata gga cca																									505				
Ser Gln Leu Glu Gly Leu Ser Lys Asp Ile Phe Lys His Ile Gly Pro																													
110										115										120									
gat gaa gtg atc ggt gag agt atg gag atg cca gca gaa gtt ggg cag																									553				
Asp Glu Val Ile Gly Glu Ser Met Glu Met Pro Ala Glu Val Gly Gln																													
125										130										135									
aaa agt cag aaa aga ccc ttc cca gag gag ctt ccg gca gac ctg aag																									601				
Lys Ser Gln Lys Arg Pro Phe Pro Glu Glu Leu Pro Ala Asp Leu Lys																													
145										150										155									
cac tgg aag cca gct gag ccc ccc act gtg gtg act ggc agt ctg cta																									649				

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His	Trp	Lys	Pro	Ala	Glu	Pro	Pro	Thr	Val	Val	Thr	Gly	Ser	Leu	Leu	
			160					165					170			
gtg	gga	cca	gtg	agc	gac	tgc	tcc	acc	ctg	ccc	tgc	ctg	cca	ctg	cct	697
Val	Gly	Pro	Val	Ser	Asp	Cys	Ser	Thr	Leu	Pro	Cys	Leu	Pro	Leu	Pro	
		175					180					185				
gcg	ctg	ttc	aac	cag	gag	cca	gcc	tcc	ggc	cag	atg	cgc	ctg	gag	aaa	745
Ala	Leu	Phe	Asn	Gln	Glu	Pro	Ala	Ser	Gly	Gln	Met	Arg	Leu	Glu	Lys	
		190					195				200					
acc	gac	cag	att	ccc	atg	cct	ttc	tcc	agt	tcc	tgc	ttg	agc	tgc	ctg	793
Thr	Asp	Gln	Ile	Pro	Met	Pro	Phe	Ser	Ser	Ser	Ser	Leu	Ser	Cys	Leu	
		205			210						215				220	
aat	ctc	cct	gag	gga	ccc	atc	cag	ttt	gtc	ccc	acc	atc	tcc	act	ctg	841
Asn	Leu	Pro	Glu	Gly	Pro	Ile	Gln	Phe	Val	Pro	Thr	Ile	Ser	Thr	Leu	
			225						230					235		
ccc	cat	ggg	ctc	tgg	caa	atc	tct	gag	gct	gga	aca	ggg	gtc	tcc	agt	889
Pro	His	Gly	Leu	Trp	Gln	Ile	Ser	Glu	Ala	Gly	Thr	Gly	Val	Ser	Ser	
		240						245					250			
ata	ttc	atc	tac	cat	ggg	gag	gtg	ccc	cag	gcc	agc	caa	gta	ccc	cct	937
Ile	Phe	Ile	Tyr	His	Gly	Glu	Val	Pro	Gln	Ala	Ser	Gln	Val	Pro	Pro	
		255					260					265				
ccc	agt	gga	ttc	act	gtc	cac	ggc	ctc	cca	aca	tct	cca	gac	cgg	cca	985
Pro	Ser	Gly	Phe	Thr	Val	His	Gly	Leu	Pro	Thr	Ser	Pro	Asp	Arg	Pro	
		270					275					280				
ggc	tcc	acc	agc	ccc	ttc	gct	cca	tca	gcc	act	gac	ctg	ccc	agc	atg	1033
Gly	Ser	Thr	Ser	Pro	Phe	Ala	Pro	Ser	Ala	Thr	Asp	Leu	Pro	Ser	Met	
		285			290					295					300	
cct	gaa	cct	gcc	ctg	acc	tcc	cga	gca	aac	atg	aca	gag	cac	aag	acg	1081
Pro	Glu	Pro	Ala	Leu	Thr	Ser	Arg	Ala	Asn	Met	Thr	Glu	His	Lys	Thr	
			305						310					315		
tcc	ccc	acc	caa	tgc	ccg	gca	gct	gga	gag	gtc	tcc	aac	aag	ctt	cca	1129
Ser	Pro	Thr	Gln	Cys	Pro	Ala	Ala	Gly	Glu	Val	Ser	Asn	Lys	Leu	Pro	
			320					325					330			
aaa	tgg	cct	gag	ccg	gtg	gag	cag	ttc	tac	cgc	tca	ctg	cag	gac	acg	1177
Lys	Trp	Pro	Glu	Pro	Val	Glu	Gln	Phe	Tyr	Arg	Ser	Leu	Gln	Asp	Thr	
		335					340					345				
tat	ggt	gcc	gag	ccc	gca	ggc	ccg	gat	ggc	atc	cta	gtg	gag	gtg	gat	1225
Tyr	Gly	Ala	Glu	Pro	Ala	Gly	Pro	Asp	Gly	Ile	Leu	Val	Glu	Val	Asp	
		350				355					360					
ctg	gtg	cag	gcc	agg	ctg	gag	agg	agc	agc	agc	aag	agc	ctg	gag	cgg	1273
Leu	Val	Gln	Ala	Arg	Leu	Glu	Arg	Ser	Ser	Ser	Lys	Ser	Leu	Glu	Arg	
		365			370					375					380	
gaa	ctg	gcc	acc	ccg	gac	tgg	gca	gaa	ccg	cag	ctg	gcc	caa	gga	ggc	1321
Glu	Leu	Ala	Thr	Pro	Asp	Trp	Ala	Glu	Arg	Gln	Leu	Ala	Gln	Gly	Gly	
			385						390					395		
ctg	gct	gag	gtg	ctg	ttg	gct	gcc	aag	gag	cac	cgg	cgg	ccg	cgt	gag	1369
Leu	Ala	Glu	Val	Leu	Leu	Ala	Ala	Lys	Glu	His	Arg	Arg	Pro	Arg	Glu	
		400						405					410			
aca	cga	gtg	att	gct	gtg	ctg	ggc	aaa	gct	ggg	cag	ggc	aag	agc	tat	1417
Thr	Arg	Val	Ile	Ala	Val	Leu	Gly	Lys	Ala	Gly	Gln	Gly	Lys	Ser	Tyr	
		415					420					425				
tgg	gct	ggg	gca	gtg	agc	ccg	gcc	tgg	gct	tgt	ggc	cgg	ctt	ccc	cag	1465
Trp	Ala	Gly	Ala	Val	Ser	Arg	Ala	Trp	Ala	Cys	Gly	Arg	Leu	Pro	Gln	
		430					435				440					
tac	gac	ttt	gtc	ttc	tct	gtc	ccc	tgc	cat	tgc	ttg	aac	cgt	ccg	ggg	1513
Tyr	Asp	Phe	Val	Phe	Ser	Val	Pro	Cys	His	Cys	Leu	Asn	Arg	Pro	Gly	
		445				450				455					460	
gat	gcc	tat	ggc	ctg	cag	gat	ctg	ctc	ttc	tcc	ctg	ggc	cca	cag	cca	1561

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Asp	Ala	Tyr	Gly	Leu	Gln	Asp	Leu	Leu	Phe	Ser	Leu	Gly	Pro	Gln	Pro	
			465						470					475		
ctc	gtg	gcg	gcc	gat	gag	gtt	ttc	agc	cac	atc	ttg	aag	aga	cct	gac	1609
Leu	Val	Ala	Ala	Asp	Glu	Val	Phe	Ser	His	Ile	Leu	Lys	Arg	Pro	Asp	
			480					485					490			
cgc	gtt	ctg	ctc	atc	cta	gac	ggc	ttc	gag	gag	ctg	gaa	gcg	caa	gat	1657
Arg	Val	Leu	Leu	Ile	Leu	Asp	Gly	Phe	Glu	Glu	Leu	Glu	Ala	Gln	Asp	
		495					500					505				
ggc	ttc	ctg	cac	agc	acg	tgc	gga	ccg	gca	ccg	gcg	gag	ccc	tgc	tcc	1705
Gly	Phe	Leu	His	Ser	Thr	Cys	Gly	Pro	Ala	Pro	Ala	Glu	Pro	Cys	Ser	
		510				515					520					
ctc	cgg	ggg	ctg	ctg	gcc	ggc	ctt	ttc	cag	aag	aag	ctg	ctc	cga	ggt	1753
Leu	Arg	Gly	Leu	Leu	Ala	Gly	Leu	Phe	Gln	Lys	Lys	Leu	Leu	Arg	Gly	
	525				530				535					540		
tgc	acc	ctc	ctc	ctc	aca	gcc	cgg	ccc	cgg	ggc	cgc	ctg	gtc	cag	agc	1801
Cys	Thr	Leu	Leu	Leu	Thr	Ala	Arg	Pro	Arg	Gly	Arg	Leu	Val	Gln	Ser	
			545					550						555		
ctg	agc	aag	gcc	gac	gcc	cta	ttt	gag	ctg	tcc	ggc	ttc	tcc	atg	gag	1849
Leu	Ser	Lys	Ala	Asp	Ala	Leu	Phe	Glu	Leu	Ser	Gly	Phe	Ser	Met	Glu	
		560					565					570				
cag	gcc	cag	gca	tac	gtg	atg	cgc	tac	ttt	gag	agc	tca	ggg	atg	aca	1897
Gln	Ala	Gln	Ala	Tyr	Val	Met	Arg	Tyr	Phe	Glu	Ser	Ser	Gly	Met	Thr	
		575					580					585				
gag	cac	caa	gac	aga	gcc	ctg	acg	ctc	ctc	cgg	gac	cgg	cca	ctt	ctt	1945
Glu	His	Gln	Asp	Arg	Ala	Leu	Thr	Leu	Leu	Arg	Asp	Arg	Pro	Leu	Leu	
	590				595					600						
ctc	agt	cac	agc	cac	agc	cct	act	ttg	tgc	cgg	gca	gtg	tgc	cag	ctc	1993
Leu	Ser	His	Ser	His	Ser	Pro	Thr	Leu	Cys	Arg	Ala	Val	Cys	Gln	Leu	
	605			610					615					620		
tca	gag	gcc	ctg	ctg	gag	ctt	ggg	gag	gac	gcc	aag	ctg	ccc	tcc	acg	2041
Ser	Glu	Ala	Leu	Leu	Glu	Leu	Gly	Glu	Asp	Ala	Lys	Leu	Pro	Ser	Thr	
			625					630					635			
ctc	acg	gga	ctc	tat	gtc	ggc	ctg	ctg	ggc	cgt	gca	gcc	ctc	gac	agc	2089
Leu	Thr	Gly	Leu	Tyr	Val	Gly	Leu	Leu	Gly	Arg	Ala	Ala	Leu	Asp	Ser	
		640					645						650			
ccc	ccc	ggg	gcc	ctg	gca	gag	ctg	gcc	aag	ctg	gcc	tgg	gag	ctg	ggc	2137
Pro	Pro	Gly	Ala	Leu	Ala	Glu	Leu	Ala	Lys	Leu	Ala	Trp	Glu	Leu	Gly	
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cgc	aga	cat	caa	agt	acc	cta	cag	gag	gac	cag	ttc	cca	tcc	gca	gac	2185
Arg	Arg	His	Gln	Ser	Thr	Leu	Gln	Glu	Asp	Gln	Phe	Pro	Ser	Ala	Asp	
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gtg	agg	acc	tgg	gcg	atg	gcc	aaa	ggc	tta	gtc	caa	cac	cca	ccg	cgg	2233
Val	Arg	Thr	Trp	Ala	Met	Ala	Lys	Gly	Leu	Val	Gln	His	Pro	Pro	Arg	
	685			690					695					700		
gcc	gca	gag	tcc	gag	ctg	gcc	ttc	ccc	agc	ttc	ctc	ctg	caa	tgc	ttc	2281
Ala	Ala	Glu	Ser	Glu	Leu	Ala	Phe	Pro	Ser	Phe	Leu	Leu	Gln	Cys	Phe	
			705					710					715			
ctg	ggg	gcc	ctg	tgg	ctg	gct	ctg	agt	ggc	gaa	atc	aag	gac	aag	gag	2329
Leu	Gly	Ala	Leu	Trp	Leu	Ala	Leu	Ser	Gly	Glu	Ile	Lys	Asp	Lys	Glu	
		720					725					730				
ctc	ccg	cag	tac	cta	gca	ttg	acc	cca	agg	aag	aag	agg	ccc	tat	gac	2377
Leu	Pro	Gln	Tyr	Leu	Ala	Leu	Thr	Pro	Arg	Lys	Lys	Arg	Pro	Tyr	Asp	
		735				740						745				
aac	tgg	ctg	gag	ggc	gtg	cca	cgc	ttt	ctg	gct	ggg	ctg	atc	ttc	cag	2425
Asn	Trp	Leu	Glu	Gly	Val	Pro	Arg	Phe	Leu	Ala	Gly	Leu	Ile	Phe	Gln	
	750				755				760							
cct	ccc	gcc	cgc	tgc	ctg	gga	gcc	cta	ctc	ggg	cca	tcg	gcg	gct	gcc	2473

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Pro 765	Pro 765	Ala 765	Arg 765	Cys 765	Leu 770	Gly 770	Ala 770	Leu 770	Leu 770	Gly 775	Pro 775	Ser 775	Ala 775	Ala 780	Ala 780	
tcg	gtg	gac	agg	aag	cag	aag	gtg	ctt	gcg	agg	tac	ctg	aag	cgg	ctg	2521
Ser	Val	Asp	Arg	Lys	Gln	Lys	Val	Leu	Ala	Arg	Tyr	Leu	Lys	Arg	Leu	
				785						790				795		
cag	ccg	ggg	aca	ctg	cgg	gcg	cgg	cag	ctg	ctg	gag	ctg	ctg	cac	tgc	2569
Gln	Pro	Gly	Thr	Leu	Arg	Ala	Arg	Gln	Leu	Leu	Glu	Leu	Leu	His	Cys	
			800					805						810		
gcc	cac	gag	gcc	gag	gag	gct	gga	att	tgg	cag	cac	gtg	gta	cag	gag	2617
Ala	His	Glu	Ala	Glu	Glu	Ala	Gly	Ile	Trp	Gln	His	Val	Val	Gln	Glu	
		815					820					825				
ctc	ccc	ggc	cgc	ctc	tct	ttt	ctg	ggc	acc	cgc	ctc	acg	cct	cct	gat	2665
Leu	Pro	Gly	Arg	Leu	Ser	Phe	Leu	Gly	Thr	Arg	Leu	Thr	Pro	Pro	Asp	
	830						835				840					
gca	cat	gta	ctg	ggc	aag	gcc	ttg	gag	gcg	gcg	ggc	caa	gac	ttc	tcc	2713
Ala	His	Val	Leu	Gly	Lys	Ala	Leu	Glu	Ala	Ala	Gly	Gln	Asp	Phe	Ser	
	845				850				855						860	
ctg	gac	ctc	cgc	agc	act	ggc	att	tgc	ccc	tct	gga	ttg	ggg	agc	ctc	2761
Leu	Asp	Leu	Arg	Ser	Thr	Gly	Ile	Cys	Pro	Ser	Gly	Leu	Gly	Ser	Leu	
				865					870					875		
gtg	gga	ctc	agc	tgt	gtc	acc	cgt	ttc	agg	gct	gcc	ttg	agc	gac	acg	2809
Val	Gly	Leu	Ser	Cys	Val	Thr	Arg	Phe	Arg	Ala	Ala	Leu	Ser	Asp	Thr	
			880					885					890			
gtg	gcg	ctg	tgg	gag	tcc	ctg	cag	cag	cat	ggg	gag	acc	aag	cta	ctt	2857
Val	Ala	Leu	Trp	Glu	Ser	Leu	Gln	Gln	His	Gly	Glu	Thr	Lys	Leu	Leu	
		895					900					905				
cag	gca	gca	gag	gag	aag	ttc	acc	atc	gag	cct	ttc	aaa	gcc	aag	tcc	2905
Gln	Ala	Ala	Glu	Glu	Lys	Phe	Thr	Ile	Glu	Pro	Phe	Lys	Ala	Lys	Ser	
	910						915				920					
ctg	aag	gat	gtg	gaa	gac	ctg	gga	aag	ctt	gtg	cag	act	cag	agg	acg	2953
Leu	Lys	Asp	Val	Glu	Asp	Leu	Gly	Lys	Leu	Val	Gln	Thr	Gln	Arg	Thr	
	925				930					935				940		
aga	agt	tcc	tcg	gaa	gac	aca	gct	ggg	gag	ctc	cct	gct	gtt	cgg	gac	3001
Arg	Ser	Ser	Ser	Glu	Asp	Thr	Ala	Gly	Glu	Leu	Pro	Ala	Val	Arg	Asp	
				945					950					955		
cta	aag	aaa	ctg	gag	ttt	gcg	ctg	ggc	cct	gtc	tca	ggc	ccc	cag	gct	3049
Leu	Lys	Lys	Leu	Glu	Phe	Ala	Leu	Gly	Pro	Val	Ser	Gly	Pro	Gln	Ala	
			960					965					970			
ttc	ccc	aaa	ctg	gtg	cgg	atc	ctc	acg	gcc	ttt	tcc	tcc	ctg	cag	cat	3097
Phe	Pro	Lys	Leu	Val	Arg	Ile	Leu	Thr	Ala	Phe	Ser	Ser	Leu	Gln	His	
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ctg	gac	ctg	gat	gcg	ctg	agt	gag	aac	aag	atc	ggg	gac	gag	ggg	gtc	3145
Leu	Asp	Leu	Asp	Ala	Leu	Ser	Glu	Asn	Lys	Ile	Gly	Asp	Glu	Gly	Val	
	990					995					1000					
tcg	cag	ctc	tca	gcc	acc	ttc	ccc	cag	ctg	aag	tcc	ttg	gaa	acc		3190
Ser	Gln	Leu	Ser	Ala	Thr	Phe	Pro	Gln	Leu	Lys	Ser	Leu	Glu	Thr		
	1005				1010					1015						
ctc	aat	ctg	tcc	cag	aac	aac	atc	act	gac	ctg	ggg	gcc	tac	aaa		3235
Leu	Asn	Leu	Ser	Gln	Asn	Asn	Ile	Thr	Asp	Leu	Gly	Ala	Tyr	Lys		
	1020				1025					1030						
ctc	gcc	gag	gcc	ctg	cct	tcg	ctc	gct	gca	tcc	ctg	ctc	agg	cta		3280
Leu	Ala	Glu	Ala	Leu	Pro	Ser	Leu	Ala	Ala	Ser	Leu	Leu	Arg	Leu		
	1035				1040					1045						
agc	ttg	tac	aat	aac	tgc	atc	tgc	gac	gtg	gga	gcc	gag	agc	ttg		3325
Ser	Leu	Tyr	Asn	Asn	Cys	Ile	Cys	Asp	Val	Gly	Ala	Glu	Ser	Leu		
	1050				1055					1060						
gct	cgt	gtg	ctt	ccg	gac	atg	gtg	tcc	ctc	cgg	gtg	atg	gac	gtc		3370

-continued

Ala	Arg	Val	Leu	Pro	Asp	Met	Val	Ser	Leu	Arg	Val	Met	Asp	Val	
1065					1070					1075					
cag	tac	aac	aag	ttc	acg	gct	gcc	ggg	gcc	cag	cag	ctc	gct	gcc	3415
Gln	Tyr	Asn	Lys	Phe	Thr	Ala	Ala	Gly	Ala	Gln	Gln	Leu	Ala	Ala	
1080					1085					1090					
agc	ctt	egg	agg	tgt	cct	cat	gtg	gag	acg	ctg	gcg	atg	tgg	acg	3460
Ser	Leu	Arg	Arg	Cys	Pro	His	Val	Glu	Thr	Leu	Ala	Met	Trp	Thr	
1095					1100					1105					
ccc	acc	atc	cca	ttc	agt	gtc	cag	gaa	cac	ctg	caa	caa	cag	gat	3505
Pro	Thr	Ile	Pro	Phe	Ser	Val	Gln	Glu	His	Leu	Gln	Gln	Gln	Asp	
1110					1115					1120					
tca	egg	atc	agc	ctg	aga	tga	tcccagctgt	gctctggaca	ggcatgttct						3556
Ser	Arg	Ile	Ser	Leu	Arg										
1125					1130										
ctgaggacac	taaccacgct	ggaccttgaa	ctgggtactt	gtggacacag	ctcttctcca										3616
ggctgtatcc	catgagcctc	agcctcctgg	cacccggccc	ctgctggttc	agggttgccc										3676
cctgcccggc	tgcggaatga	accacatctt	gctctgctga	cagacacagg	cccggctcca										3736
ggctccttta	gcgccagtt	gggtggatgc	ctggtggcag	ctgcgggtcca	cccaggagcc										3796
ccgaggcctt	ctctgaagga	cattgcccgc	agccacggcc	aggccagagg	gagtgcagaa										3856
ggcagcccca	ttctgctctc	ccaggcccct	gccaccctgg	ggagaaagta	cttctttttt										3916
tttattttta	gacagagtct	cactgtttgc	caggctggcg	tgacgtgggt	cgatctgggt										3976
tcactgcaac	ctccgcctct	tgggttcaag	cgattcttct	gcttcagcct	cccagtagtc										4036
tgggactaca	ggcaccaccc	atcatgtctg	gctaattttt	catttttagt	agagacaggg										4096
ttttgccatg	ttggccaggc	tgggtctaaa	ctcttgacct	caggtgatcc	acccacctca										4156
gcctcccaaa	gtgctgggat	tacaagcgtg	agccactgca	ccgggccaca	gagaaagtac										4216
ttctccaccc	tgctctccga	ccagacacct	tgacagggca	caccgggcac	tcagaagaca										4276
ctgatgggca	acccccagcc	tgctaattcc	ccagattgca	acaggctggg	cttcagtggc										4336
agctgctttt	gtctatggga	ctcaatgcac	tgacattggt	ggccaaagcc	aaagctaggc										4396
ctggccagat	gcaccagccc	ttagcaggga	aacagctaata	gggacactaa	tggggcggtg										4456
agaggggaac	agactggaag	cacagcttca	tttcctgtgt	cttttttcac	tacattataa										4516
atgtctcttt	aatgtcacag	gcaggctccag	ggtttgagtt	cataccctgt	taccattttg										4576
gggtacccac	tgctctggtt	atctaatatg	taacaagcca	ccccaaatca	tagtggttta										4636
aaacaacact	cacatttta														4654

<210> SEQ ID NO 35

<211> LENGTH: 1130

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 35

Met	Arg	Cys	Leu	Ala	Pro	Arg	Pro	Ala	Gly	Ser	Tyr	Leu	Ser	Glu	Pro
1			5					10						15	

Gln	Gly	Ser	Ser	Gln	Cys	Ala	Thr	Met	Glu	Leu	Gly	Pro	Leu	Glu	Gly
	20						25					30			

Gly	Tyr	Leu	Glu	Leu	Leu	Asn	Ser	Asp	Ala	Asp	Pro	Leu	Cys	Leu	Tyr
	35						40				45				

His	Phe	Tyr	Asp	Gln	Met	Asp	Leu	Ala	Gly	Glu	Glu	Glu	Ile	Glu	Leu
	50					55				60					

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Tyr	Ser	Glu	Pro	Asp	Thr	Asp	Thr	Ile	Asn	Cys	Asp	Gln	Phe	Ser	Arg	65	70	75	80
Leu	Leu	Cys	Asp	Met	Glu	Gly	Asp	Glu	Glu	Thr	Arg	Glu	Ala	Tyr	Ala	85	90	95	
Asn	Ile	Ala	Glu	Leu	Asp	Gln	Tyr	Val	Phe	Gln	Asp	Ser	Gln	Leu	Glu	100	105	110	
Gly	Leu	Ser	Lys	Asp	Ile	Phe	Lys	His	Ile	Gly	Pro	Asp	Glu	Val	Ile	115	120	125	
Gly	Glu	Ser	Met	Glu	Met	Pro	Ala	Glu	Val	Gly	Gln	Lys	Ser	Gln	Lys	130	135	140	
Arg	Pro	Phe	Pro	Glu	Glu	Leu	Pro	Ala	Asp	Leu	Lys	His	Trp	Lys	Pro	145	150	155	160
Ala	Glu	Pro	Pro	Thr	Val	Val	Thr	Gly	Ser	Leu	Leu	Val	Gly	Pro	Val	165	170	175	
Ser	Asp	Cys	Ser	Thr	Leu	Pro	Cys	Leu	Pro	Leu	Pro	Ala	Leu	Phe	Asn	180	185	190	
Gln	Glu	Pro	Ala	Ser	Gly	Gln	Met	Arg	Leu	Glu	Lys	Thr	Asp	Gln	Ile	195	200	205	
Pro	Met	Pro	Phe	Ser	Ser	Ser	Ser	Leu	Ser	Cys	Leu	Asn	Leu	Pro	Glu	210	215	220	
Gly	Pro	Ile	Gln	Phe	Val	Pro	Thr	Ile	Ser	Thr	Leu	Pro	His	Gly	Leu	225	230	235	240
Trp	Gln	Ile	Ser	Glu	Ala	Gly	Thr	Gly	Val	Ser	Ser	Ile	Phe	Ile	Tyr	245	250	255	
His	Gly	Glu	Val	Pro	Gln	Ala	Ser	Gln	Val	Pro	Pro	Pro	Ser	Gly	Phe	260	265	270	
Thr	Val	His	Gly	Leu	Pro	Thr	Ser	Pro	Asp	Arg	Pro	Gly	Ser	Thr	Ser	275	280	285	
Pro	Phe	Ala	Pro	Ser	Ala	Thr	Asp	Leu	Pro	Ser	Met	Pro	Glu	Pro	Ala	290	295	300	
Leu	Thr	Ser	Arg	Ala	Asn	Met	Thr	Glu	His	Lys	Thr	Ser	Pro	Thr	Gln	305	310	315	320
Cys	Pro	Ala	Ala	Gly	Glu	Val	Ser	Asn	Lys	Leu	Pro	Lys	Trp	Pro	Glu	325	330	335	
Pro	Val	Glu	Gln	Phe	Tyr	Arg	Ser	Leu	Gln	Asp	Thr	Tyr	Gly	Ala	Glu	340	345	350	
Pro	Ala	Gly	Pro	Asp	Gly	Ile	Leu	Val	Glu	Val	Asp	Leu	Val	Gln	Ala	355	360	365	
Arg	Leu	Glu	Arg	Ser	Ser	Ser	Lys	Ser	Leu	Glu	Arg	Glu	Leu	Ala	Thr	370	375	380	
Pro	Asp	Trp	Ala	Glu	Arg	Gln	Leu	Ala	Gln	Gly	Gly	Leu	Ala	Glu	Val	385	390	395	400
Leu	Leu	Ala	Ala	Lys	Glu	His	Arg	Arg	Pro	Arg	Glu	Thr	Arg	Val	Ile	405	410	415	
Ala	Val	Leu	Gly	Lys	Ala	Gly	Gln	Gly	Lys	Ser	Tyr	Trp	Ala	Gly	Ala	420	425	430	
Val	Ser	Arg	Ala	Trp	Ala	Cys	Gly	Arg	Leu	Pro	Gln	Tyr	Asp	Phe	Val	435	440	445	
Phe	Ser	Val	Pro	Cys	His	Cys	Leu	Asn	Arg	Pro	Gly	Asp	Ala	Tyr	Gly	450	455	460	

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Leu	Gln	Asp	Leu	Leu	Phe	Ser	Leu	Gly	Pro	Gln	Pro	Leu	Val	Ala	Ala	
465					470					475					480	
Asp	Glu	Val	Phe	Ser	His	Ile	Leu	Lys	Arg	Pro	Asp	Arg	Val	Leu	Leu	
			485						490					495		
Ile	Leu	Asp	Gly	Phe	Glu	Glu	Leu	Glu	Ala	Gln	Asp	Gly	Phe	Leu	His	
			500					505					510			
Ser	Thr	Cys	Gly	Pro	Ala	Pro	Ala	Glu	Pro	Cys	Ser	Leu	Arg	Gly	Leu	
		515					520					525				
Leu	Ala	Gly	Leu	Phe	Gln	Lys	Lys	Leu	Leu	Arg	Gly	Cys	Thr	Leu	Leu	
		530				535					540					
Leu	Thr	Ala	Arg	Pro	Arg	Gly	Arg	Leu	Val	Gln	Ser	Leu	Ser	Lys	Ala	
545					550					555					560	
Asp	Ala	Leu	Phe	Glu	Leu	Ser	Gly	Phe	Ser	Met	Glu	Gln	Ala	Gln	Ala	
			565						570					575		
Tyr	Val	Met	Arg	Tyr	Phe	Glu	Ser	Ser	Gly	Met	Thr	Glu	His	Gln	Asp	
			580					585						590		
Arg	Ala	Leu	Thr	Leu	Leu	Arg	Asp	Arg	Pro	Leu	Leu	Leu	Ser	His	Ser	
		595					600					605				
His	Ser	Pro	Thr	Leu	Cys	Arg	Ala	Val	Cys	Gln	Leu	Ser	Glu	Ala	Leu	
		610				615					620					
Leu	Glu	Leu	Gly	Glu	Asp	Ala	Lys	Leu	Pro	Ser	Thr	Leu	Thr	Gly	Leu	
625					630					635					640	
Tyr	Val	Gly	Leu	Leu	Gly	Arg	Ala	Ala	Leu	Asp	Ser	Pro	Pro	Gly	Ala	
			645						650					655		
Leu	Ala	Glu	Leu	Ala	Lys	Leu	Ala	Trp	Glu	Leu	Gly	Arg	Arg	His	Gln	
			660					665					670			
Ser	Thr	Leu	Gln	Glu	Asp	Gln	Phe	Pro	Ser	Ala	Asp	Val	Arg	Thr	Trp	
		675				680						685				
Ala	Met	Ala	Lys	Gly	Leu	Val	Gln	His	Pro	Pro	Arg	Ala	Ala	Glu	Ser	
		690				695					700					
Glu	Leu	Ala	Phe	Pro	Ser	Phe	Leu	Leu	Gln	Cys	Phe	Leu	Gly	Ala	Leu	
705					710					715					720	
Trp	Leu	Ala	Leu	Ser	Gly	Glu	Ile	Lys	Asp	Lys	Glu	Leu	Pro	Gln	Tyr	
			725						730					735		
Leu	Ala	Leu	Thr	Pro	Arg	Lys	Lys	Arg	Pro	Tyr	Asp	Asn	Trp	Leu	Glu	
			740					745					750			
Gly	Val	Pro	Arg	Phe	Leu	Ala	Gly	Leu	Ile	Phe	Gln	Pro	Pro	Ala	Arg	
		755					760					765				
Cys	Leu	Gly	Ala	Leu	Leu	Gly	Pro	Ser	Ala	Ala	Ala	Ser	Val	Asp	Arg	
		770				775						780				
Lys	Gln	Lys	Val	Leu	Ala	Arg	Tyr	Leu	Lys	Arg	Leu	Gln	Pro	Gly	Thr	
785					790					795					800	
Leu	Arg	Ala	Arg	Gln	Leu	Leu	Glu	Leu	Leu	His	Cys	Ala	His	Glu	Ala	
			805						810					815		
Glu	Glu	Ala	Gly	Ile	Trp	Gln	His	Val	Val	Gln	Glu	Leu	Pro	Gly	Arg	
			820					825					830			
Leu	Ser	Phe	Leu	Gly	Thr	Arg	Leu	Thr	Pro	Pro	Asp	Ala	His	Val	Leu	
		835					840					845				
Gly	Lys	Ala	Leu	Glu	Ala	Ala	Gly	Gln	Asp	Phe	Ser	Leu	Asp	Leu	Arg	
		850				855					860					
Ser	Thr	Gly	Ile	Cys	Pro	Ser	Gly	Leu	Gly	Ser	Leu	Val	Gly	Leu	Ser	

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865	870	875	880
Cys Val Thr Arg Phe Arg Ala Ala Leu Ser Asp Thr Val Ala Leu Trp	885	890	895
Glu Ser Leu Gln Gln His Gly Glu Thr Lys Leu Leu Gln Ala Ala Glu	900	905	910
Glu Lys Phe Thr Ile Glu Pro Phe Lys Ala Lys Ser Leu Lys Asp Val	915	920	925
Glu Asp Leu Gly Lys Leu Val Gln Thr Gln Arg Thr Arg Ser Ser Ser	930	935	940
Glu Asp Thr Ala Gly Glu Leu Pro Ala Val Arg Asp Leu Lys Lys Leu	945	950	955
Glu Phe Ala Leu Gly Pro Val Ser Gly Pro Gln Ala Phe Pro Lys Leu	965	970	975
Val Arg Ile Leu Thr Ala Phe Ser Ser Leu Gln His Leu Asp Leu Asp	980	985	990
Ala Leu Ser Glu Asn Lys Ile Gly Asp Glu Gly Val Ser Gln Leu Ser	995	1000	1005
Ala Thr Phe Pro Gln Leu Lys Ser Leu Glu Thr Leu Asn Leu Ser	1010	1015	1020
Gln Asn Asn Ile Thr Asp Leu Gly Ala Tyr Lys Leu Ala Glu Ala	1025	1030	1035
Leu Pro Ser Leu Ala Ala Ser Leu Leu Arg Leu Ser Leu Tyr Asn	1040	1045	1050
Asn Cys Ile Cys Asp Val Gly Ala Glu Ser Leu Ala Arg Val Leu	1055	1060	1065
Pro Asp Met Val Ser Leu Arg Val Met Asp Val Gln Tyr Asn Lys	1070	1075	1080
Phe Thr Ala Ala Gly Ala Gln Gln Leu Ala Ala Ser Leu Arg Arg	1085	1090	1095
Cys Pro His Val Glu Thr Leu Ala Met Trp Thr Pro Thr Ile Pro	1100	1105	1110
Phe Ser Val Gln Glu His Leu Gln Gln Gln Asp Ser Arg Ile Ser	1115	1120	1125
Leu Arg	1130		

<210> SEQ ID NO 36
 <211> LENGTH: 1697
 <212> TYPE: DNA
 <213> ORGANISM: Homo sapiens
 <220> FEATURE:
 <221> NAME/KEY: CDS
 <222> LOCATION: (108)..(890)

<400> SEQUENCE: 36

atttccagtg ctagagggccc acagtttcag tctcatctgc ctccactcgg cctcagttcc	60
tcatactgt tctgtgtctc acagtcacatca attatagacc ccacaac atg cgc cct	116
	Met Arg Pro
	1
gaa gac aga atg ttc cat atc aga gct gtg atc ttg aga gcc ctc tcc	164
Glu Asp Arg Met Phe His Ile Arg Ala Val Ile Leu Arg Ala Leu Ser	
5 10 15	
ttg gct ttc ctg ctg agt ctc cga gga gct ggg gcc atc aag gcg gac	212
Leu Ala Phe Leu Leu Ser Leu Arg Gly Ala Gly Ala Ile Lys Ala Asp	

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20	25	30	35	
cat gtg tca act tat gcc gcg ttt gta cag acg cat aga cca aca ggg				260
His Val Ser Thr Tyr Ala Ala Phe Val Gln Thr His Arg Pro Thr Gly	40	45	50	
gag ttt atg ttt gaa ttt gat gaa gat gag atg ttc tat gtg gat ctg				308
Glu Phe Met Phe Glu Phe Asp Glu Asp Glu Met Phe Tyr Val Asp Leu	55	60	65	
gac aag aag gag acc gtc tgg cat ctg gag gag ttt ggc caa gcc ttt				356
Asp Lys Lys Glu Thr Val Trp His Leu Glu Glu Phe Gly Gln Ala Phe	70	75	80	
tcc ttt gag gct cag ggc ggg ctg gct aac att gct ata ttg aac aac				404
Ser Phe Glu Ala Gln Gly Gly Leu Ala Asn Ile Ala Ile Leu Asn Asn	85	90	95	
aac ttg aat acc ttg atc cag cgt tcc aac cac act cag gcc acc aac				452
Asn Leu Asn Thr Leu Ile Gln Arg Ser Asn His Thr Gln Ala Thr Asn	100	105	110	115
gat ccc cct gag gtg acc gtg ttt ccc aag gag cct gtg gag ctg ggc				500
Asp Pro Pro Glu Val Thr Val Phe Pro Lys Glu Pro Val Glu Leu Gly	120	125	130	
cag ccc aac acc ctc atc tgc cac att gac aag ttc ttc cca cca gtg				548
Gln Pro Asn Thr Leu Ile Cys His Ile Asp Lys Phe Phe Pro Pro Val	135	140	145	
ctc aac gtc acg tgg ctg tgc aac ggg gag ctg gtc act gag ggt gtc				596
Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Leu Val Thr Glu Gly Val	150	155	160	
gct gag agc ctc ttc ctg ccc aga aca gat tac agc ttc cac aag ttc				644
Ala Glu Ser Leu Phe Leu Pro Arg Thr Asp Tyr Ser Phe His Lys Phe	165	170	175	
cat tac ctg acc ttt gtg ccc tca gca gag gac ttc tat gac tgc agg				692
His Tyr Leu Thr Phe Val Pro Ser Ala Glu Asp Phe Tyr Asp Cys Arg	180	185	190	195
gtg gag cac tgg ggc ttg gac cag ccg ctc ctc aag cac tgg gag gcc				740
Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His Trp Glu Ala	200	205	210	
caa gag cca atc cag atg cct gag aca acg gag act gtg ctc tgt gcc				788
Gln Glu Pro Ile Gln Met Pro Glu Thr Thr Glu Thr Val Leu Cys Ala	215	220	225	
ctg ggc ctg gtg ctg ggc cta gtc ggc atc atc gtg ggc acc gtc ctc				836
Leu Gly Leu Val Leu Gly Leu Val Gly Ile Ile Val Gly Thr Val Leu	230	235	240	
atc ata aag tct ctg cgt tct ggc cat gac ccc cgg gcc cag ggg acc				884
Ile Ile Lys Ser Leu Arg Ser Gly His Asp Pro Arg Ala Gln Gly Thr	245	250	255	
ctg tga aatactgtaa aggtgacaaa atatctgaac agaagaggac ttaggagaga				940
Leu				260
tctgaactcc agctgcccta caaactccat ctcagctttt cttctcactt catgtgaaaa				1000
ctactccagt ggctgactga attgtgacc cttcaagctc tgtccttate cattacctca				1060
aagcagtcatt tccttagtaa agtttccaac aaatagaaat taatgacact ttggtagcac				1120
taatatggag attatccttt cattgagcct ttctcctct gttctccttt gaagaacccc				1180
tcactgtcac cttcccagaga ataccctaag accaataaat acttcagtat ttcagagcgg				1240
ggagactctg agtcattctt actggaagtc taggaccagg tcacatgtga atactatttc				1300
ttgaagggtg ggtttcaacc tctgttgccg atgtgggttac taaaggttct gatccactt				1360

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gaacggaaag gtctgaggat attgattcag tcctggggtt tcccctaact acaggatagg 1420
gtggggtaga gaaaggatat ttgggggaaa ttttacttgg atgaagattt tcttgatgt 1480
agtttgaaga ctgcagtgtt tgaagtctct gaggaagag atttggctctg tctggatcaa 1540
gatttcaggc agattaggat tccattcaca gcccctgagc ttccttccca aggetgtatt 1600
gtaattatag caatatttca tggaggattt ttctacatga taaactaaga gccaaagaaat 1660
aaaattttta aaatgcccta aaaaaaaaaa aaaaaaaa 1697

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<210> SEQ ID NO 37
<211> LENGTH: 260
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 37

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Met Arg Pro Glu Asp Arg Met Phe His Ile Arg Ala Val Ile Leu Arg
1           5           10           15
Ala Leu Ser Leu Ala Phe Leu Leu Ser Leu Arg Gly Ala Gly Ala Ile
20          25          30
Lys Ala Asp His Val Ser Thr Tyr Ala Ala Phe Val Gln Thr His Arg
35          40          45
Pro Thr Gly Glu Phe Met Phe Glu Phe Asp Glu Asp Glu Met Phe Tyr
50          55          60
Val Asp Leu Asp Lys Lys Glu Thr Val Trp His Leu Glu Glu Phe Gly
65          70          75          80
Gln Ala Phe Ser Phe Glu Ala Gln Gly Gly Leu Ala Asn Ile Ala Ile
85          90          95
Leu Asn Asn Asn Leu Asn Thr Leu Ile Gln Arg Ser Asn His Thr Gln
100         105         110
Ala Thr Asn Asp Pro Pro Glu Val Thr Val Phe Pro Lys Glu Pro Val
115         120         125
Glu Leu Gly Gln Pro Asn Thr Leu Ile Cys His Ile Asp Lys Phe Phe
130         135         140
Pro Pro Val Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Leu Val Thr
145         150         155         160
Glu Gly Val Ala Glu Ser Leu Phe Leu Pro Arg Thr Asp Tyr Ser Phe
165         170         175
His Lys Phe His Tyr Leu Thr Phe Val Pro Ser Ala Glu Asp Phe Tyr
180         185         190
Asp Cys Arg Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His
195         200         205
Trp Glu Ala Gln Glu Pro Ile Gln Met Pro Glu Thr Thr Glu Thr Val
210         215         220
Leu Cys Ala Leu Gly Leu Val Leu Gly Leu Val Gly Ile Ile Val Gly
225         230         235         240
Thr Val Leu Ile Ile Lys Ser Leu Arg Ser Gly His Asp Pro Arg Ala
245         250         255
Gln Gly Thr Leu
260

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<210> SEQ ID NO 38
<211> LENGTH: 777
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens

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<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (1) .. (777)

<400> SEQUENCE: 38

atg atg gtt ctg cag gtt tct gcg gcc ccc cgg aca gtg gct ctg acg	48
Met Met Val Leu Gln Val Ser Ala Ala Pro Arg Thr Val Ala Leu Thr	
1 5 10 15	
gcg tta ctg atg gtg ctg ctc aca tct gtg gtc cag ggc agg gcc act	96
Ala Leu Leu Met Val Leu Leu Thr Ser Val Val Gln Gly Arg Ala Thr	
20 25 30	
cca gag aat tac gtg tac cag gga cgg cag gaa tgc tac gcg ttt aat	144
Pro Glu Asn Tyr Val Tyr Gln Gly Arg Gln Glu Cys Tyr Ala Phe Asn	
35 40 45	
ggg aca cag cgc ttc ctg gag aga tac atc tac aac cgg gag gag tac	192
Gly Thr Gln Arg Phe Leu Glu Arg Tyr Ile Tyr Asn Arg Glu Glu Tyr	
50 55 60	
gcg cgc ttc gac agc gac gtg ggg gag ttc cgg gcg gtg acg gag ctg	240
Ala Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val Thr Glu Leu	
65 70 75 80	
ggg cgg cct gct gcg gag tac tgg aac agc cag aag gac atc ctg gag	288
Gly Arg Pro Ala Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu	
85 90 95	
gag aag cgg gca gtg ccg gac agg gta tgc aga cac aac tac gag ctg	336
Glu Lys Arg Ala Val Pro Asp Arg Val Cys Arg His Asn Tyr Glu Leu	
100 105 110	
gac gag gcc gtg acc ctg cag cgc cga gtc cag cct aag gtg aac gtt	384
Asp Glu Ala Val Thr Leu Gln Arg Arg Val Gln Pro Lys Val Asn Val	
115 120 125	
tcc ccc tcc aag aag ggg ccc ctg cag cac cac aac ctg ctt gtc tgc	432
Ser Pro Ser Lys Lys Gly Pro Leu Gln His His Asn Leu Leu Val Cys	
130 135 140	
cac gtg aca gat ttc tac cca ggc agc att caa gtc cga tgg ttc ctg	480
His Val Thr Asp Phe Tyr Pro Gly Ser Ile Gln Val Arg Trp Phe Leu	
145 150 155 160	
aat gga cag gag gaa aca gct ggg gtc gtg tcc acc aac ctg atc cgt	528
Asn Gly Gln Glu Glu Thr Ala Gly Val Val Ser Thr Asn Leu Ile Arg	
165 170 175	
aat gga gac tgg acc ttc cag atc ctg gtg atg ctg gaa atg acc ccc	576
Asn Gly Asp Trp Thr Phe Gln Ile Leu Val Met Leu Glu Met Thr Pro	
180 185 190	
cag cag gga gac gtc tac atc tgc caa gtg gag cac acc agc ctg gac	624
Gln Gln Gly Asp Val Tyr Ile Cys Gln Val Glu His Thr Ser Leu Asp	
195 200 205	
agt cct gtc acc gtg gag tgg aag gca cag tct gat tct gcc cag agt	672
Ser Pro Val Thr Val Glu Trp Lys Ala Gln Ser Asp Ser Ala Gln Ser	
210 215 220	
aag aca ttg acg gga gct ggg ggc ttc gtg ctg ggg ctc atc atc tgt	720
Lys Thr Leu Thr Gly Ala Gly Gly Phe Val Leu Gly Leu Ile Ile Cys	
225 230 235 240	
gga gtg ggc atc ttc atg cac agg agg agc aag aaa gtt caa cga gga	768
Gly Val Gly Ile Phe Met His Arg Arg Ser Lys Lys Val Gln Arg Gly	
245 250 255	
tct gca taa	777
Ser Ala	

<210> SEQ ID NO 39

<211> LENGTH: 258

-continued

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 39

```

Met Met Val Leu Gln Val Ser Ala Ala Pro Arg Thr Val Ala Leu Thr
1      5      10      15
Ala Leu Leu Met Val Leu Leu Thr Ser Val Val Gln Gly Arg Ala Thr
20      25      30
Pro Glu Asn Tyr Val Tyr Gln Gly Arg Gln Glu Cys Tyr Ala Phe Asn
35      40      45
Gly Thr Gln Arg Phe Leu Glu Arg Tyr Ile Tyr Asn Arg Glu Glu Tyr
50      55      60
Ala Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val Thr Glu Leu
65      70      75      80
Gly Arg Pro Ala Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu
85      90      95
Glu Lys Arg Ala Val Pro Asp Arg Val Cys Arg His Asn Tyr Glu Leu
100     105     110
Asp Glu Ala Val Thr Leu Gln Arg Arg Val Gln Pro Lys Val Asn Val
115     120     125
Ser Pro Ser Lys Lys Gly Pro Leu Gln His His Asn Leu Leu Val Cys
130     135     140
His Val Thr Asp Phe Tyr Pro Gly Ser Ile Gln Val Arg Trp Phe Leu
145     150     155     160
Asn Gly Gln Glu Glu Thr Ala Gly Val Val Ser Thr Asn Leu Ile Arg
165     170     175
Asn Gly Asp Trp Thr Phe Gln Ile Leu Val Met Leu Glu Met Thr Pro
180     185     190
Gln Gln Gly Asp Val Tyr Ile Cys Gln Val Glu His Thr Ser Leu Asp
195     200     205
Ser Pro Val Thr Val Glu Trp Lys Ala Gln Ser Asp Ser Ala Gln Ser
210     215     220
Lys Thr Leu Thr Gly Ala Gly Gly Phe Val Leu Gly Leu Ile Ile Cys
225     230     235     240
Gly Val Gly Ile Phe Met His Arg Arg Ser Lys Lys Val Gln Arg Gly
245     250     255

Ser Ala

```

<210> SEQ ID NO 40

<211> LENGTH: 768

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (1)..(768)

<400> SEQUENCE: 40

```

atg atc cta aac aaa gct ctg ctg ctg ggg gcc ctc gct ctg acc acc      48
Met Ile Leu Asn Lys Ala Leu Leu Leu Gly Ala Leu Ala Leu Thr Thr
1      5      10      15
gtg atg agc ccc tgt gga ggt gaa gac att gtg gct gac cac gtt gcc      96
Val Met Ser Pro Cys Gly Gly Glu Asp Ile Val Ala Asp His Val Ala
20      25      30
tct tgt ggt gta aac ttg tac cag ttt tac ggt ccc tct ggc cag tac     144
Ser Cys Gly Val Asn Leu Tyr Gln Phe Tyr Gly Pro Ser Gly Gln Tyr

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-continued

35	40	45	
acc cat gaa ttt gat gga gat gag gag ttc tac gtg gac ctg gag agg			192
Thr His Glu Phe Asp Gly Asp Glu Glu Phe Tyr Val Asp Leu Glu Arg			
50	55	60	
aag gag act gcc tgg cgg tgg cct gag ttc agc aaa ttt gga ggt ttt			240
Lys Glu Thr Ala Trp Arg Trp Pro Glu Phe Ser Lys Phe Gly Gly Phe			
65	70	75	80
gac ccg cag ggt gca ctg aga aac atg gct gtg gca aaa cac aac ttg			288
Asp Pro Gln Gly Ala Leu Arg Asn Met Ala Val Ala Lys His Asn Leu			
85	90	95	
aac atc atg att aaa cgc tac aac tct acc gct gct acc aat gag gtt			336
Asn Ile Met Ile Lys Arg Tyr Asn Ser Thr Ala Ala Thr Asn Glu Val			
100	105	110	
cct gag gtc aca gtg ttt tcc aag tct ccc gtg aca ctg ggt cag ccc			384
Pro Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro			
115	120	125	
aac acc ctc att tgt ctt gtg gac aac atc ttt cct cct gtg gtc aac			432
Asn Thr Leu Ile Cys Leu Val Asp Asn Ile Phe Pro Pro Val Val Asn			
130	135	140	
atc aca tgg ctg agc aat ggg cag tca gtc aca gaa ggt gtt tct gag			480
Ile Thr Trp Leu Ser Asn Gly Gln Ser Val Thr Glu Gly Val Ser Glu			
145	150	155	160
acc agc ttc ctc tcc aag agt gat cat tcc ttc ttc aag atc agt tac			528
Thr Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr			
165	170	175	
ctc acc ttc ctc cct tct gct gat gag att tat gac tgc aag gtg gag			576
Leu Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu			
180	185	190	
cac tgg ggc ctg gac cag cct ctt ctg aaa cac tgg gag cct gag att			624
His Trp Gly Leu Asp Gln Pro Leu Leu Lys His Trp Glu Pro Glu Ile			
195	200	205	
cca gcc cct atg tca gag ctc aca gag act gtg gtc tgc gcc ctg ggg			672
Pro Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly			
210	215	220	
ttg tct gtg ggc ctc gtg ggc att gtg gtg ggc act gtc ttc atc atc			720
Leu Ser Val Gly Leu Val Gly Ile Val Val Gly Thr Val Phe Ile Ile			
225	230	235	240
caa ggc ctg cgt tca gtt ggt gct tcc aga cac caa ggg cca ttg tga			768
Gln Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu			
245	250	255	
<210> SEQ ID NO 41			
<211> LENGTH: 255			
<212> TYPE: PRT			
<213> ORGANISM: Homo sapiens			
<400> SEQUENCE: 41			
Met Ile Leu Asn Lys Ala Leu Leu Leu Gly Ala Leu Ala Leu Thr Thr			
1	5	10	15
Val Met Ser Pro Cys Gly Gly Glu Asp Ile Val Ala Asp His Val Ala			
20	25	30	
Ser Cys Gly Val Asn Leu Tyr Gln Phe Tyr Gly Pro Ser Gly Gln Tyr			
35	40	45	
Thr His Glu Phe Asp Gly Asp Glu Glu Phe Tyr Val Asp Leu Glu Arg			
50	55	60	
Lys Glu Thr Ala Trp Arg Trp Pro Glu Phe Ser Lys Phe Gly Gly Phe			
65	70	75	80

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```

Asp Pro Gln Gly Ala Leu Arg Asn Met Ala Val Ala Lys His Asn Leu
      85                      90                      95
Asn Ile Met Ile Lys Arg Tyr Asn Ser Thr Ala Ala Thr Asn Glu Val
      100                      105                      110
Pro Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro
      115                      120                      125
Asn Thr Leu Ile Cys Leu Val Asp Asn Ile Phe Pro Pro Val Val Asn
      130                      135                      140
Ile Thr Trp Leu Ser Asn Gly Gln Ser Val Thr Glu Gly Val Ser Glu
      145                      150                      155                      160
Thr Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr
      165                      170                      175
Leu Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu
      180                      185                      190
His Trp Gly Leu Asp Gln Pro Leu Leu Lys His Trp Glu Pro Glu Ile
      195                      200                      205
Pro Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly
      210                      215                      220
Leu Ser Val Gly Leu Val Gly Ile Val Val Gly Thr Val Phe Ile Ile
      225                      230                      235                      240
Gln Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
      245                      250                      255

```

<210> SEQ ID NO 42

<211> LENGTH: 786

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (1)..(786)

<400> SEQUENCE: 42

```

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

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ccc aca gtg acc atc tcc cca tcc agg aca gag gcc ctc aac cac cac      432
Pro Thr Val Thr Ile Ser Pro Ser Arg Thr Glu Ala Leu Asn His His
   130                               135                               140

aac ctg ctg gtc tgc tcg gtg aca gat ttc tat cca gcc cag atc aaa      480
Asn Leu Leu Val Cys Ser Val Thr Asp Phe Tyr Pro Ala Gln Ile Lys
   145                               150                               155                               160

gtc cgg tgg ttt cgg aat gac cag gag gag aca gct ggc gtt gtg tcc      528
Val Arg Trp Phe Arg Asn Asp Gln Glu Glu Thr Ala Gly Val Val Ser
                165                               170                               175

acc ccc ctt att agg aat ggt gac tgg acc ttc cag atc ctg gtg atg      576
Thr Pro Leu Ile Arg Asn Gly Asp Trp Thr Phe Gln Ile Leu Val Met
                180                               185                               190

ctg gaa atg act ccc cag cgt gga gac gtc tac acc tgc cac gtg gag      624
Leu Glu Met Thr Pro Gln Arg Gly Asp Val Tyr Thr Cys His Val Glu
   195                               200                               205

cac ccc agc ctc cag agc ccc atc acc gtg gag tgg cgg gct caa tct      672
His Pro Ser Leu Gln Ser Pro Ile Thr Val Glu Trp Arg Ala Gln Ser
   210                               215                               220

gaa tct gcc cag agc aag atg ctg agt ggc att gga ggc ttc gtg ctg      720
Glu Ser Ala Gln Ser Lys Met Leu Ser Gly Ile Gly Gly Phe Val Leu
   225                               230                               235                               240

ggg ctg atc ttc ctc ggg ctg ggc ctt atc atc cat cac agg agt cag      768
Gly Leu Ile Phe Leu Gly Leu Gly Leu Ile Ile His His Arg Ser Gln
   245                               250                               255

aaa ggg ctc ctg cac tga      786
Lys Gly Leu Leu His
   260

```

<210> SEQ ID NO 43

<211> LENGTH: 261

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 43

```

Met Ser Trp Lys Lys Ala Leu Arg Ile Pro Gly Gly Leu Arg Ala Ala
 1      5      10      15

Thr Val Thr Leu Met Leu Ser Met Leu Ser Thr Pro Val Ala Glu Gly
 20      25      30

Arg Asp Ser Pro Glu Asp Phe Val Tyr Gln Phe Lys Gly Met Cys Tyr
 35      40      45

Phe Thr Asn Gly Thr Glu Arg Val Arg Leu Val Ser Arg Ser Ile Tyr
 50      55      60

Asn Arg Glu Glu Ile Val Arg Phe Asp Ser Asp Val Gly Glu Phe Arg
 65      70      75      80

Ala Val Thr Leu Leu Gly Leu Pro Ala Ala Glu Tyr Trp Asn Ser Gln
 85      90      95

Lys Asp Ile Leu Glu Arg Lys Arg Ala Ala Val Asp Arg Val Cys Arg
100     105     110

His Asn Tyr Gln Leu Glu Leu Arg Thr Thr Leu Gln Arg Arg Val Glu
115     120     125

Pro Thr Val Thr Ile Ser Pro Ser Arg Thr Glu Ala Leu Asn His His
130     135     140

Asn Leu Leu Val Cys Ser Val Thr Asp Phe Tyr Pro Ala Gln Ile Lys
145     150     155     160

Val Arg Trp Phe Arg Asn Asp Gln Glu Glu Thr Ala Gly Val Val Ser

```

																165				170				175							
Thr	Pro	Leu	Ile	Arg	Asn	Gly	Asp	Trp	Thr	Phe	Gln	Ile	Leu	Val	Met																
			180													185					190										
Leu	Glu	Met	Thr	Pro	Gln	Arg	Gly	Asp	Val	Tyr	Thr	Cys	His	Val	Glu																
			195													200					205										
His	Pro	Ser	Leu	Gln	Ser	Pro	Ile	Thr	Val	Glu	Trp	Arg	Ala	Gln	Ser																
			210													215					220										
Glu	Ser	Ala	Gln	Ser	Lys	Met	Leu	Ser	Gly	Ile	Gly	Gly	Phe	Val	Leu																
			225													230					235										
Gly	Leu	Ile	Phe	Leu	Gly	Leu	Gly	Leu	Ile	Ile	His	His	Arg	Ser	Gln																
			245													250					255										
Lys	Gly	Leu	Leu	His																											
			260																												
<210> SEQ ID NO 44																															
<211> LENGTH: 1312																															
<212> TYPE: DNA																															
<213> ORGANISM: Homo sapiens																															
<220> FEATURE:																															
<221> NAME/KEY: CDS																															
<222> LOCATION: (110)..(874)																															
<400> SEQUENCE: 44																															
ttttaatgggt cagactctat tacaccccaac attctctttt cttttattct tgtctgttct																60															
gcctcactcc cgagctctac tgactcccaa cagagcgccc aagaagaaa atg gcc ata																118															
																Met Ala Ile															
																1															
agt gga gtc cct gtg cta gga ttt ttc atc ata gct gtg ctg atg agc																166															
Ser Gly Val			Pro Val			Leu Gly			Phe Phe			Ile Ile			Ala Val			Leu Met			Ser										
5						10						15																			
gct cag gaa tca tgg gct atc aaa gaa gaa cat gtg atc atc cag gcc																214															
Ala Gln			Glu Ser			Trp Ala			Ile Lys			Glu Glu			His Val			Ile Ile			Gln Ala										
20						25						30						35													
gag ttc tat ctg aat cct gac caa tca ggc gag ttt atg ttt gac ttt																262															
Glu Phe			Tyr Leu			Asn Pro			Asp Gln			Ser Gly			Glu Phe			Met Phe			Asp Phe										
			40						45						50																
gat ggt gat gag att ttc cat gtg gat atg gca aag aag gag acg gtc																310															
Asp Gly			Asp Glu			Ile Phe			His Val			Asp Met			Ala Lys			Glu Thr			Val										
			55						60						65																
tgg cgg ctt gaa gaa ttt gga cga ttt gcc agc ttt gag gct caa ggt																358															
Trp Arg			Leu Glu			Glu Phe			Gly Arg			Phe Ala			Ser Phe			Glu Ala			Gln Gly										
70						75						80																			
gca ttg gcc aac ata gct gtg gac aaa gcc aac ctg gaa atc atg aca																406															
Ala Leu			Ala Asn			Ile Ala			Val Asp			Lys Ala			Asn Leu			Glu Ile			Met Thr										
85						90						95																			
aag cgc tcc aac tat act ccg atc acc aat gta cct cca gag gta act																454															
Lys Arg			Ser Asn			Tyr Thr			Pro Ile			Thr Asn			Val Pro			Pro Glu			Val Thr										
100						105						110						115													
gtg ctc aca aac agc cct gtg gaa ctg aga gag ccc aac gtc ctc atc																502															
Val Leu			Thr Asn			Ser Pro			Val Glu			Leu Arg			Glu Pro			Asn Val			Leu Ile										
			120						125						130																
tgt ttc ata gac aag ttc acc cca cca gtg gtc aat gtc acg tgg ctt																550															
Cys Phe			Ile Asp			Lys Phe			Thr Pro			Pro Val			Val Val			Asn Val			Thr Trp										
			135						140						145																
cga aat gga aaa cct gtc acc aca gga gtg tca gag aca gtc ttc ctg																598															
Arg Asn			Gly Lys			Pro Val			Thr Thr			Gly Val			Ser Glu			Thr Val			Phe Leu										
150						155						160																			

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ccc agg gaa gac cac ctt ttc cgc aag ttc cac tat ctc ccc ttc ctg      646
Pro Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu Pro Phe Leu
    165                      170                      175

ccc tca act gag gac gtt tac gac tgc agg gtg gag cac tgg ggc ttg      694
Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His Trp Gly Leu
    180                      185                      190                      195

gat gag cct ctt ctc aag cac tgg gag ttt gat gct cca agc cct ctc      742
Asp Glu Pro Leu Leu Lys His Trp Glu Phe Asp Ala Pro Ser Pro Leu
                      200                      205                      210

cca gag act aca gag aac gtg gtg tgt gcc ctg ggc ctg act gtg ggt      790
Pro Glu Thr Thr Glu Asn Val Val Cys Ala Leu Gly Leu Thr Val Gly
                      215                      220                      225

ctg gtg ggc atc att att ggg acc atc ttc atc atc aag gga ttg cgc      838
Leu Val Gly Ile Ile Ile Gly Thr Ile Phe Ile Ile Lys Gly Leu Arg
    230                      235                      240

aaa agc aat gca gca gaa cgc agg ggg cct ctg taa ggcacatgga      884
Lys Ser Asn Ala Ala Glu Arg Arg Gly Pro Leu
    245                      250

gggtgatggtg tttcttagag agaagatcac tgaagaaact tctgctttaa tggctttaca      944

aagctggcaa tattacaatc cttgacctca gtgaaagcag tcctcttcag cattttccag 1004

ccctatagcc accccaagtg tggatatgcc tcttcgattg ctccgtactc taacatctag 1064

ctggettccc tgtctattgc cttttcctgt atctattttc ctctatttcc tatcatttta 1124

ttatcaccat gcaatgcctc tggaataaaa catacaggag tctgtctctg ctatggaatg 1184

ccccatgggg catctcttgt gtacttattg tttaaggttt cctcaaactg tgatttttct 1244

gaacacaata aactattttg atgatcttgg gtggaaaaaa aaaaaaaaaa aaaaaaaaaa 1304

aaaaaaaaa 1312

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<210> SEQ ID NO 45
<211> LENGTH: 254
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 45

```

```

Met Ala Ile Ser Gly Val Pro Val Leu Gly Phe Phe Ile Ile Ala Val
 1          5          10          15

Leu Met Ser Ala Gln Glu Ser Trp Ala Ile Lys Glu Glu His Val Ile
    20          25          30

Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met
    35          40          45

Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys
    50          55          60

Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu
    65          70          75          80

Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu
    85          90          95

Ile Met Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro
    100         105         110

Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn
    115         120         125

Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val
    130         135         140

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Thr	Trp	Leu	Arg	Asn	Gly	Lys	Pro	Val	Thr	Thr	Gly	Val	Ser	Glu	Thr
145					150					155					160
Val	Phe	Leu	Pro	Arg	Glu	Asp	His	Leu	Phe	Arg	Lys	Phe	His	Tyr	Leu
				165					170					175	
Pro	Phe	Leu	Pro	Ser	Thr	Glu	Asp	Val	Tyr	Asp	Cys	Arg	Val	Glu	His
			180					185					190		
Trp	Gly	Leu	Asp	Glu	Pro	Leu	Leu	Lys	His	Trp	Glu	Phe	Asp	Ala	Pro
	195						200					205			
Ser	Pro	Leu	Pro	Glu	Thr	Thr	Glu	Asn	Val	Val	Cys	Ala	Leu	Gly	Leu
	210					215					220				
Thr	Val	Gly	Leu	Val	Gly	Ile	Ile	Ile	Gly	Thr	Ile	Phe	Ile	Ile	Lys
225					230					235					240
Gly	Leu	Arg	Lys	Ser	Asn	Ala	Ala	Glu	Arg	Arg	Gly	Pro	Leu		
			245						250						

<210> SEQ ID NO 46

<211> LENGTH: 801

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (1)..(801)

<400> SEQUENCE: 46

atg	gtg	tgt	ctg	aag	ctc	cct	gga	ggc	tcc	tgc	atg	aca	gcg	ctg	aca	48
Met	Val	Cys	Leu	Lys	Leu	Pro	Gly	Gly	Ser	Cys	Met	Thr	Ala	Leu	Thr	
1				5					10					15		
gtg	aca	ctg	atg	gtg	ctg	agc	tcc	cca	ctg	gct	ttg	gct	ggg	gac	acc	96
Val	Thr	Leu	Met	Val	Leu	Ser	Ser	Pro	Leu	Ala	Leu	Ala	Gly	Asp	Thr	
			20					25					30			
cga	cca	cgt	ttc	ttg	tgg	cag	ctt	aag	ttt	gaa	tgt	cat	ttc	ttc	aat	144
Arg	Pro	Arg	Phe	Leu	Trp	Gln	Leu	Lys	Phe	Glu	Cys	His	Phe	Phe	Asn	
		35				40						45				
ggg	acg	gag	cgg	gtg	cgg	ttg	ctg	gaa	aga	tgc	atc	tat	aac	caa	gag	192
Gly	Thr	Glu	Arg	Val	Arg	Leu	Leu	Glu	Arg	Cys	Ile	Tyr	Asn	Gln	Glu	
	50				55					60						
gag	tcc	gtg	cgc	ttc	gac	agc	gac	gtg	ggg	gag	tac	cgg	gcg	gtg	acg	240
Glu	Ser	Val	Arg	Phe	Asp	Ser	Asp	Val	Gly	Glu	Tyr	Arg	Ala	Val	Thr	
65				70					75					80		
gag	ctg	ggg	cgg	cct	gat	gcc	gag	tac	tgg	aac	agc	cag	aag	gac	ctc	288
Glu	Leu	Gly	Arg	Pro	Asp	Ala	Glu	Tyr	Trp	Asn	Ser	Gln	Lys	Asp	Leu	
			85					90						95		
ctg	gag	cag	agg	cgg	gcc	gcg	gtg	gac	acc	tac	tgc	aga	cac	aac	tac	336
Leu	Glu	Gln	Arg	Arg	Ala	Ala	Val	Asp	Thr	Tyr	Cys	Arg	His	Asn	Tyr	
			100				105						110			
ggg	gtt	ggt	gag	agc	ttc	aca	gtg	cag	cgg	cga	gtt	gag	cct	aag	gtg	384
Gly	Val	Gly	Glu	Ser	Phe	Thr	Val	Gln	Arg	Arg	Val	Glu	Pro	Lys	Val	
	115					120					125					
act	gtg	tat	cct	tca	aag	acc	cag	ccc	ctg	cag	cac	cac	aac	ctc	ctg	432
Thr	Val	Tyr	Pro	Ser	Lys	Thr	Gln	Pro	Leu	Gln	His	His	Asn	Leu	Leu	
	130					135					140					
gtc	tgc	tct	gtg	agt	ggg	ttc	tat	cca	ggc	agc	att	gaa	gtc	agg	tgg	480
Val	Cys	Ser	Val	Ser	Gly	Phe	Tyr	Pro	Gly	Ser	Ile	Glu	Val	Arg	Trp	
145				150					155					160		
ttc	cgg	aac	ggc	cag	gaa	gag	aag	gct	ggg	gtg	gtg	tcc	aca	ggc	ctg	528
Phe	Arg	Asn	Gly	Gln	Glu	Glu	Lys	Ala	Gly	Val	Val	Ser	Thr	Gly	Leu	
			165						170					175		

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atc cag aat gga gat tgg acc ttc cag acc ctg gtg atg ctg gaa aca	576
Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr	
180 185 190	
gtt cct cgg agt gga gag gtt tac acc tgc caa gtg gag cac cca agt	624
Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser	
195 200 205	
gtg acg agc cct ctc aca gtg gaa tgg aga gca cgg tct gaa tct gca	672
Val Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala	
210 215 220	
cag agc aag atg ctg agt gga gtc ggg ggc ttc gtg ctg ggc ctg ctc	720
Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu	
225 230 235 240	
ttc ctt ggg gcc ggg ctg ttc atc tac ttc agg aat cag aaa gga cac	768
Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His	
245 250 255	
tct gga ctt cag cca aca gga ttc ctg agc tga	801
Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser	
260 265	

<210> SEQ ID NO 47

<211> LENGTH: 266

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 47

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Thr Ala Leu Thr	
1 5 10 15	
Val Thr Leu Met Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr	
20 25 30	
Arg Pro Arg Phe Leu Trp Gln Leu Lys Phe Glu Cys His Phe Phe Asn	
35 40 45	
Gly Thr Glu Arg Val Arg Leu Leu Glu Arg Cys Ile Tyr Asn Gln Glu	
50 55 60	
Glu Ser Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr	
65 70 75 80	
Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Leu	
85 90 95	
Leu Glu Gln Arg Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr	
100 105 110	
Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Glu Pro Lys Val	
115 120 125	
Thr Val Tyr Pro Ser Lys Thr Gln Pro Leu Gln His His Asn Leu Leu	
130 135 140	
Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp	
145 150 155 160	
Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr Gly Leu	
165 170 175	
Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr	
180 185 190	
Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser	
195 200 205	
Val Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala	
210 215 220	
Gln Ser Lys Met Leu Ser Gly Val Gly Gly Phe Val Leu Gly Leu Leu	
225 230 235 240	

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Phe Leu Gly Ala Gly Leu Phe Ile Tyr Phe Arg Asn Gln Lys Gly His
245 250 255

Ser Gly Leu Gln Pro Thr Gly Phe Leu Ser
260 265

<210> SEQ ID NO 48
<211> LENGTH: 1122
<212> TYPE: DNA
<213> ORGANISM: Homo sapiens
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (87) .. (872)

<400> SEQUENCE: 48

gatctaaggc caccctctcg gggaggagat tggggaagct gggttggctg ggttggttagc 60
tcctacctac tgtgtggcaa gaaggt atg ggt cat gaa cag aac caa gga gct 113
Met Gly His Glu Gln Asn Gln Gly Ala
1 5
gcg ctg cta cag atg tta cca ctt ctg tgg ctg cta ccc cac tcc tgg 161
Ala Leu Leu Gln Met Leu Pro Leu Leu Trp Leu Leu Pro His Ser Trp
10 15 20 25
gcc gtc cct gaa gct cct act cca atg tgg cca gat gac ctg caa aac 209
Ala Val Pro Glu Ala Pro Thr Pro Met Trp Pro Asp Asp Leu Gln Asn
30 35 40
cac aca ttc ctg cac aca gtg tac tgc cag gat ggg agt ccc agt gtg 257
His Thr Phe Leu His Thr Val Tyr Cys Gln Asp Gly Ser Pro Ser Val
45 50 55
gga ctc tct gag gcc tac gac gag gac cag ctt ttc ttc ttc gac ttt 305
Gly Leu Ser Glu Ala Tyr Asp Glu Asp Gln Leu Phe Phe Phe Asp Phe
60 65 70
tcc cag aac act cgg gtg cct cgc ctg ccc gaa ttt gct gac tgg gct 353
Ser Gln Asn Thr Arg Val Pro Arg Leu Pro Glu Phe Ala Asp Trp Ala
75 80 85
cag gaa cag gga gat gct cct gcc att tta ttt gac aaa gag ttc tgc 401
Gln Glu Gln Gly Asp Ala Pro Ala Ile Leu Phe Asp Lys Glu Phe Cys
90 95 100 105
gag tgg atg atc cag caa ata ggg cca aaa ctt gat ggg aaa atc ccg 449
Glu Trp Met Ile Gln Gln Ile Gly Pro Lys Leu Asp Gly Lys Ile Pro
110 115 120
gtg tcc aga ggg ttt cct atc gct gaa gtg ttc acg ctg aag ccc ctg 497
Val Ser Arg Gly Phe Pro Ile Ala Glu Val Phe Thr Leu Lys Pro Leu
125 130 135
gag ttt ggc aag ccc aac act ttg gtc tgt ttt gtc agt aat ctc ttc 545
Glu Phe Gly Lys Pro Asn Thr Leu Val Cys Phe Val Ser Asn Leu Phe
140 145 150
cca ccc atg ctg aca gtg aac tgg cag cat cat tcc gtc cct gtg gaa 593
Pro Pro Met Leu Thr Val Asn Trp Gln His His Ser Val Pro Val Glu
155 160 165
gga ttt ggg cct act ttt gtc tca gct gtc gat gga ctc agc ttc cag 641
Gly Phe Gly Pro Thr Phe Val Ser Ala Val Asp Gly Leu Ser Phe Gln
170 175 180 185
gcc ttt tct tac tta aac ttc aca cca gaa cct tct gac att ttc tcc 689
Ala Phe Ser Tyr Leu Asn Phe Thr Pro Glu Pro Ser Asp Ile Phe Ser
190 195 200
tgc att gtg act cac gaa att gac cgc tac aca gca att gcc tat tgg 737
Cys Ile Val Thr His Glu Ile Asp Arg Tyr Thr Ala Ile Ala Tyr Trp
205 210 215

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gta ccc cgg aac gca ctg ccc tca gat ctg ctg gag aat gtg ctg tgt      785
Val Pro Arg Asn Ala Leu Pro Ser Asp Leu Leu Glu Asn Val Leu Cys
      220                225                230

ggc gtg gcc ttt ggc ctg ggt gtg ctg ggc atc atc gtg ggc att gtt      833
Gly Val Ala Phe Gly Leu Gly Val Leu Gly Ile Ile Val Gly Ile Val
      235                240                245

ctc atc atc tac ttc cgg aag cct tgc tca ggt gac tga ttcttcaga      882
Leu Ile Ile Tyr Phe Arg Lys Pro Cys Ser Gly Asp
      250                255                260

ccagagtttg atgccagcag ctctgggcat ccaaacagag gatgctcaga ttcttcacat      942

cctgccccagg atctcctctt agggtagaag tctctgggac atccctgggg tgtgtgtgta    1002

gatttccacg ctggggactc tgctgtccct gggcttgcat ccaggggac ccagagtggc    1062

ctgectatca caaccacatc ccttcccccc acaaggcaat aaatctcatt tctttatc     1122

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<210> SEQ ID NO 49

<211> LENGTH: 261

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 49

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Met Gly His Glu Gln Asn Gln Gly Ala Ala Leu Leu Gln Met Leu Pro
1              5              10              15

Leu Leu Trp Leu Leu Pro His Ser Trp Ala Val Pro Glu Ala Pro Thr
      20              25              30

Pro Met Trp Pro Asp Asp Leu Gln Asn His Thr Phe Leu His Thr Val
      35              40              45

Tyr Cys Gln Asp Gly Ser Pro Ser Val Gly Leu Ser Glu Ala Tyr Asp
      50              55              60

Glu Asp Gln Leu Phe Phe Phe Asp Phe Ser Gln Asn Thr Arg Val Pro
      65              70              75              80

Arg Leu Pro Glu Phe Ala Asp Trp Ala Gln Glu Gln Gly Asp Ala Pro
      85              90              95

Ala Ile Leu Phe Asp Lys Glu Phe Cys Glu Trp Met Ile Gln Gln Ile
      100             105             110

Gly Pro Lys Leu Asp Gly Lys Ile Pro Val Ser Arg Gly Phe Pro Ile
      115             120             125

Ala Glu Val Phe Thr Leu Lys Pro Leu Glu Phe Gly Lys Pro Asn Thr
      130             135             140

Leu Val Cys Phe Val Ser Asn Leu Phe Pro Pro Met Leu Thr Val Asn
      145             150             155             160

Trp Gln His His Ser Val Pro Val Glu Gly Phe Gly Pro Thr Phe Val
      165             170             175

Ser Ala Val Asp Gly Leu Ser Phe Gln Ala Phe Ser Tyr Leu Asn Phe
      180             185             190

Thr Pro Glu Pro Ser Asp Ile Phe Ser Cys Ile Val Thr His Glu Ile
      195             200             205

Asp Arg Tyr Thr Ala Ile Ala Tyr Trp Val Pro Arg Asn Ala Leu Pro
      210             215             220

Ser Asp Leu Leu Glu Asn Val Leu Cys Gly Val Ala Phe Gly Leu Gly
      225             230             235             240

Val Leu Gly Ile Ile Val Gly Ile Val Leu Ile Ile Tyr Phe Arg Lys
      245             250             255

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Pro Cys Ser Gly Asp
260

<210> SEQ ID NO 50

<211> LENGTH: 1412

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (264) .. (1055)

<400> SEQUENCE: 50

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atttgtcctt gctactctag ccaatctgtc cctgtttggg acactggact cccgtgagct      60
ggaaggaaca gatttaatat ctaggggctg ggtatcccca catcactcat ttggggggctc    120
aagggaacccg ggcaatatag tattctgtct agtgtctgga gatcatctac ccaggctggg    180
gcttctggga caggcgagga cccacggacc ctggaagagc tggccaggg gactgaactc      240
ccggcatctt tacagagcag agc atg atc aca ttc ctg ccg ctg ctg ctg ggg      293
                Met Ile Thr Phe Leu Pro Leu Leu Leu Gly
                1             5             10

ctc agc ctg ggc tgc aca gga gca ggt ggc ttc gtg gcc cat gtg gaa      341
Leu Ser Leu Gly Cys Thr Gly Ala Gly Gly Phe Val Ala His Val Glu
                15             20             25

agc acc tgt ctg ttg gat gat gct ggg act cca aag gat ttc aca tac      389
Ser Thr Cys Leu Leu Asp Asp Ala Gly Thr Pro Lys Asp Phe Thr Tyr
                30             35             40

tgc atc tcc ttc aac aag gat ctg ctg acc tgc tgg gat cca gag gag      437
Cys Ile Ser Phe Asn Lys Asp Leu Leu Thr Cys Trp Asp Pro Glu Glu
                45             50             55

aat aag atg gcc cct tgc gaa ttt ggg gtg ctg aat agc ttg gcg aat      485
Asn Lys Met Ala Pro Cys Glu Phe Gly Val Leu Asn Ser Leu Ala Asn
                60             65             70

gtc ctc tca cag cac ctc aac caa aaa gac acc ctg atg cag cgc ttg      533
Val Leu Ser Gln His Leu Asn Gln Lys Asp Thr Leu Met Gln Arg Leu
                75             80             85             90

cgc aat ggg ctt cag aat tgt gcc aca cac acc cag ccc ttc tgg gga      581
Arg Asn Gly Leu Gln Asn Cys Ala Thr His Thr Gln Pro Phe Trp Gly
                95             100             105

tca ctg acc aac agg aca cgg cca cca tct gtg caa gta gcc aaa acc      629
Ser Leu Thr Asn Arg Thr Arg Pro Pro Ser Val Gln Val Ala Lys Thr
                110             115             120

act cct ttt aac acg agg gag cct gtg atg ctg gcc tgc tat gtg tgg      677
Thr Pro Phe Asn Thr Arg Glu Pro Val Met Leu Ala Cys Tyr Val Trp
                125             130             135

ggc ttc tat cca gca gaa gtg act atc acg tgg agg aag aac ggg aag      725
Gly Phe Tyr Pro Ala Glu Val Thr Ile Thr Trp Arg Lys Asn Gly Lys
                140             145             150

ctt gtc atg cct cac agc agt gcg cac aag act gcc cag ccc aat gga      773
Leu Val Met Pro His Ser Ser Ala His Lys Thr Ala Gln Pro Asn Gly
                155             160             165             170

gac tgg aca tac cag acc ctc tcc cat tta gcc tta acc ccc tct tac      821
Asp Trp Thr Tyr Gln Thr Leu Ser His Leu Ala Leu Thr Pro Ser Tyr
                175             180             185

ggg gac act tac acc tgt gtg gta gag cac act ggg gct cct gag ccc      869
Gly Asp Thr Tyr Thr Cys Val Val Glu His Thr Gly Ala Pro Glu Pro
                190             195             200

atc ctt cgg gac tgg aca cct ggg ctg tcc ccc atg cag acc ctg aag      917
Ile Leu Arg Asp Trp Thr Pro Gly Leu Ser Pro Met Gln Thr Leu Lys

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205	210	215	
gtt tct gtg tct gca gtg act ctg ggc ctg ggc ctc atc atc ttc tct			965
Val Ser Val Ser Ala Val Thr Leu Gly Leu Gly Leu Ile Ile Phe Ser			
220	225	230	
ctt ggt gtg atc agc tgg cgg aga gct ggc cac tct agt tac act cct			1013
Leu Gly Val Ile Ser Trp Arg Arg Ala Gly His Ser Ser Tyr Thr Pro			
235	240	245	250
ctt cct ggg tcc aat tat tca gaa gga tgg cac att tcc tag			1055
Leu Pro Gly Ser Asn Tyr Ser Glu Gly Trp His Ile Ser			
255	260		
aggcagaatc ctacaacttc cactccaagt gagaaggaga ttcaaactca atgatgctac			1115
catgcctctc caacatcttc aaccctctga cattatcttg gatectatgg tttctccatc			1175
caattctttg aatttcccag tctccctat gtaaaactta gcaacttggg ggacctcatt			1235
cctgggacta tgctgtaacc aaattattgt ccaaggctat atttctggga tgaatataat			1295
ctgaggaagg gagttaaaga cctcctggg gctctcagtg tgccatagag gacagcaact			1355
ggtgattggt tcagagaaat aaactttggt ggaaatattg ttaaaaaaaaa aaaaaaa			1412

<210> SEQ ID NO 51

<211> LENGTH: 263

<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 51

Met Ile Thr Phe Leu Pro Leu Leu Leu Gly Leu Ser Leu Gly Cys Thr	
1 5 10 15	
Gly Ala Gly Gly Phe Val Ala His Val Glu Ser Thr Cys Leu Leu Asp	
20 25 30	
Asp Ala Gly Thr Pro Lys Asp Phe Thr Tyr Cys Ile Ser Phe Asn Lys	
35 40 45	
Asp Leu Leu Thr Cys Trp Asp Pro Glu Glu Asn Lys Met Ala Pro Cys	
50 55 60	
Glu Phe Gly Val Leu Asn Ser Leu Ala Asn Val Leu Ser Gln His Leu	
65 70 75 80	
Asn Gln Lys Asp Thr Leu Met Gln Arg Leu Arg Asn Gly Leu Gln Asn	
85 90 95	
Cys Ala Thr His Thr Gln Pro Phe Trp Gly Ser Leu Thr Asn Arg Thr	
100 105 110	
Arg Pro Pro Ser Val Gln Val Ala Lys Thr Thr Pro Phe Asn Thr Arg	
115 120 125	
Glu Pro Val Met Leu Ala Cys Tyr Val Trp Gly Phe Tyr Pro Ala Glu	
130 135 140	
Val Thr Ile Thr Trp Arg Lys Asn Gly Lys Leu Val Met Pro His Ser	
145 150 155 160	
Ser Ala His Lys Thr Ala Gln Pro Asn Gly Asp Trp Thr Tyr Gln Thr	
165 170 175	
Leu Ser His Leu Ala Leu Thr Pro Ser Tyr Gly Asp Thr Tyr Thr Cys	
180 185 190	
Val Val Glu His Thr Gly Ala Pro Glu Pro Ile Leu Arg Asp Trp Thr	
195 200 205	
Pro Gly Leu Ser Pro Met Gln Thr Leu Lys Val Ser Val Ser Ala Val	
210 215 220	

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Thr Leu Gly Leu Gly Leu Ile Ile Phe Ser Leu Gly Val Ile Ser Trp
225 230 235 240

Arg Arg Ala Gly His Ser Ser Tyr Thr Pro Leu Pro Gly Ser Asn Tyr
245 250 255

Ser Glu Gly Trp His Ile Ser
260

<210> SEQ ID NO 52

<211> LENGTH: 3485

<212> TYPE: DNA

<213> ORGANISM: Homo sapiens

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (77)..(829)

<400> SEQUENCE: 52

cttcttctttt acctccgcct tgttcctgtc ctcaccacac ggactgagac tgatttgatt 60

aaagcaccag agtgta atg gcc ctc aga gca ggg ctg gtc ctg ggg ttc cac 112
Met Ala Leu Arg Ala Gly Leu Val Leu Gly Phe His
1 5 10

acc ctg atg acc ctc ctg agc ccg cag gag gca ggg gcc acc aag gct 160
Thr Leu Met Thr Leu Leu Ser Pro Gln Glu Ala Gly Ala Thr Lys Ala
15 20 25

gac cac atg ggc tcc tac gga ccc gcc ttc tac cag tct tac ggc gcc 208
Asp His Met Gly Ser Tyr Gly Pro Ala Phe Tyr Gln Ser Tyr Gly Ala
30 35 40

tcg ggc cag ttc acc cat gaa ttt gat gag gaa cag ctg ttc tct gtg 256
Ser Gly Gln Phe Thr His Glu Phe Asp Glu Glu Gln Leu Phe Ser Val
45 50 55 60

gac ctg aag aaa agc gag gcc gtg tgg cgt ctg cct gag ttt ggt gac 304
Asp Leu Lys Lys Ser Glu Ala Val Trp Arg Leu Pro Glu Phe Gly Asp
65 70 75

ttt gcc cgc ttt gac ccg cag ggc ggg ctg gcc ggc atc gcc gca atc 352
Phe Ala Arg Phe Asp Pro Gln Gly Gly Leu Ala Gly Ile Ala Ala Ile
80 85 90

aaa gcc cat ctg gac atc ctg gtg gag cgc tcc aac cgc agc aga gcc 400
Lys Ala His Leu Asp Ile Leu Val Glu Arg Ser Asn Arg Ser Arg Ala
95 100 105

atc aac gtg cct cca cgg gtg acc gtg ctc ccc aag tct cgg gtg gag 448
Ile Asn Val Pro Pro Arg Val Thr Val Leu Pro Lys Ser Arg Val Glu
110 115 120

ctg ggc cag ccc aac atc ctc atc tgc atc gtg gac aac atc ttc ccc 496
Leu Gly Gln Pro Asn Ile Leu Ile Cys Ile Val Asp Asn Ile Phe Pro
125 130 135 140

cct gtg atc aat atc acc tgg ctg cgc aac ggc caa act gtc act gag 544
Pro Val Ile Asn Ile Thr Trp Leu Arg Asn Gly Gln Thr Val Thr Glu
145 150 155

gga gtg gcc cag acc agc ttc tat tcc cag cct gac cat ttg ttc cgc 592
Gly Val Ala Gln Thr Ser Phe Tyr Ser Gln Pro Asp His Leu Phe Arg
160 165 170

aag ttc cac tac ctg ccc ttc gtg ccc tca gcc gag gac gtc tat gac 640
Lys Phe His Tyr Leu Pro Phe Val Pro Ser Ala Glu Asp Val Tyr Asp
175 180 185

tgc cag gtg gag cac tgg ggc ctg gat gcg cca ctc ctc agg cat tgg 688
Cys Gln Val Glu His Trp Gly Leu Asp Ala Pro Leu Leu Arg His Trp
190 195 200

gag ctc cag gtg cct att cca cca cca gat gcc atg gag acc ctg gtc 736
Glu Leu Gln Val Pro Ile Pro Pro Pro Asp Ala Met Glu Thr Leu Val

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205	210	215	220	
tgt gcc ctg ggc ctg gcc atc ggc ctg gtg ggc ttc ctc gtg ggc acc				784
Cys Ala Leu Gly Leu Ala Ile Gly Leu Val Gly Phe Leu Val Gly Thr				
	225	230	235	
gtc ctc atc atc atg ggc aca tat gtg tcc agt gtc ccc agg taa				829
Val Leu Ile Ile Met Gly Thr Tyr Val Ser Ser Val Pro Arg				
	240	245	250	
tgatccttct gagagaaatg acttgtggga gacaccctgc agatcctcat gggtttgtga				889
cagccctctgc gtgctcagtg cctttaagt gcacccctgc gtgctgactt tgagtgggat				949
caacatctgt cctacgggctc cctctttttt tggccccagt attcatggca gggtttgttg				1009
gacacctact agcttccctt cccattcaac acacacacac attcttcttc taccctaaagc				1069
tctggctggc agcactaaat gctttgttggtg tgtttgcact gtgtcctttc caggccttgg				1129
ccagttcttc caggggtgag gcatgtggtg ctggggattg gcagccatcc tggggccac				1189
acaggtgtgt cttgtcccat ttggcccatg gtgtgttact ttgtgaatga gccatttcac				1249
atggacttca tgaaatttgc ctctctgagt caggtttacc ctgaaaggga tgcagattat				1309
cctgttcctc acgacccctt cagctaacaa cagttctgaa ggggtgctggg acaggacagg				1369
ctcatgggga ctccactctt gcctgggttt actctgtatg aagaggccac tggatcctg				1429
ccatgatgtt atctcctttt tctacttttc cctagagtcc catgcatgat aaagagaggc				1489
ccaaggcttg gataaggttg ccaacttcct cagtggagtc agtcatgtta ggtaggaggt				1549
ggtagagtgc gtctgcgagg tatctcgtaa gaggggaggt ccacctagac acactctaaa				1609
tatgtggcct agaagatttt ggtctacttt tctgtgaaca gaatttaaaa catacaaaga				1669
gataaatcac cataccacat agtttatgtc aggacccaaa tgagcaatac agattacggt				1729
tttcaaacca gaatgcacat aagaactgct tgggatcctt ttaaaagtac aggcattggc				1789
ctggtgcagt ggctcattcc tgtaatccca gcactttggg aggccaaagg gacaggactg				1849
cttgaggcca agagggtgaa accatcttgg gctacataga gagaccccat ctctacaaag				1909
aaagatttaa aaattaacca ggcattggtg ctgcacctg tattcccagc cactggggag				1969
gctgaggccg gaggagtgtc tgagcccagg agttcaaggc tgcagtgagc caagattgcg				2029
ccactgcact ccagcctagg tgacagagtg agaccctgct tctaaataaa taaataaata				2089
aaatataaaa ataacagtca tcaccagac ctactgaatt agaatctcgg gagtgcaggg				2149
ggcagcaaca gggaggctgt cttttctgag atggggtctc actctgtcac caggctggag				2209
tgccatggca tgatctcagc tcaactgcaac ctccacctcc tgagttcaag ccattctcct				2269
gcctcagcct cctgagtagc tgggactaca ggtgtgcgcc actacactca gctaattttt				2329
gtattttaag tagagacggg gtttcatcat gttggccagg atggcctcca tctcttgacc				2389
tcgtgatcca cccaccttcc ctcccaaagt actggaatta caggcattag ccactgtgcc				2449
cagccgaggc tgtcattttt aaccggctct ggatgactct gatgcagcca tctggacct				2509
tggtgtggt ctggttaactg gaaccagtg acgtaatcag gtgccatcgg gggatcatggg				2569
aaagggggat ccccaaggtc tgaggtggac taggaaggct ttctgaagaa cctgggtctg				2629
ttagggcatc agccaatcaa ggtacaagta aatagaggca aatgagggt ttgaactgtg				2689
agcagttggt cctggaaaag aaagaaacca agagattatg gggactcaat gggcttctta				2749
agagagaata agttgaaatc aatgaccaga agaccctgat ggaagtggag gagaatcatc				2809

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tcaggcaaac tttttgtgtg ccagtaacag aaacctctt tgtgtgatca catgcaaagt 2869
ataggatatt tgcaatatag ccattggggag gaggcaggg cccaagggtg gatatttagcc 2929
aggcctccca ggaacagaac tcggatccga aaagcccaga gaagctagag ctgcccctcc 2989
aacactctcg gatccacatg gtctgtgttc tctagacccc cctgcatgtt agcgggtgttc 3049
tctctctgtg gactgactgt ccttctcagt gaacatgtcc acccgacagc tcctgagttt 3109
atatcatctc aacctcaca acccagagag gctgtgtctc ctatgcacag ctttaaatta 3169
ctggaaaaat aaatgactgg ccaaacttgg agcagggtgc catcccagcc ctgtgtagtt 3229
agagcaggaa tcaagatctc aacacaaatg tggctgccaa gcactcagcc ccggggcgag 3289
gggtcaagtt cttctcagag aaagaggaat aagttggttc tcagaagaca tcacaagata 3349
cgtgtgtacc caacaatctc tgatctctgc tgatcttttg cttagacgtt aacttgatgc 3409
atcattggaa aggtgtttct ctcactctcg tctaaggct tgataaagtc attaaaattg 3469
tggtcttttg actaaa 3485

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<210> SEQ ID NO 53
<211> LENGTH: 250
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

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<400> SEQUENCE: 53

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Met Ala Leu Arg Ala Gly Leu Val Leu Gly Phe His Thr Leu Met Thr
1      5      10      15
Leu Leu Ser Pro Gln Glu Ala Gly Ala Thr Lys Ala Asp His Met Gly
20     25     30
Ser Tyr Gly Pro Ala Phe Tyr Gln Ser Tyr Gly Ala Ser Gly Gln Phe
35     40     45
Thr His Glu Phe Asp Glu Glu Gln Leu Phe Ser Val Asp Leu Lys Lys
50     55     60
Ser Glu Ala Val Trp Arg Leu Pro Glu Phe Gly Asp Phe Ala Arg Phe
65     70     75     80
Asp Pro Gln Gly Gly Leu Ala Gly Ile Ala Ala Ile Lys Ala His Leu
85     90     95
Asp Ile Leu Val Glu Arg Ser Asn Arg Ser Arg Ala Ile Asn Val Pro
100    105    110
Pro Arg Val Thr Val Leu Pro Lys Ser Arg Val Glu Leu Gly Gln Pro
115    120    125
Asn Ile Leu Ile Cys Ile Val Asp Asn Ile Phe Pro Pro Val Ile Asn
130    135    140
Ile Thr Trp Leu Arg Asn Gly Gln Thr Val Thr Glu Gly Val Ala Gln
145    150    155    160
Thr Ser Phe Tyr Ser Gln Pro Asp His Leu Phe Arg Lys Phe His Tyr
165    170    175
Leu Pro Phe Val Pro Ser Ala Glu Asp Val Tyr Asp Cys Gln Val Glu
180    185    190
His Trp Gly Leu Asp Ala Pro Leu Leu Arg His Trp Glu Leu Gln Val
195    200    205
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210    215    220
Leu Ala Ile Gly Leu Val Gly Phe Leu Val Gly Thr Val Leu Ile Ile
225    230    235    240

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				Met Gly Ser Gly Trp Val			
				1	5		
ccc tgg gtg gtg gct ctg cta gtg aat ctg acc cga ctg gat tcc tcc						163	
Pro Trp Val Val Ala Leu Leu Val Asn Leu Thr Arg Leu Asp Ser Ser							
	10			15	20		
atg act caa ggc aca gac tct cca gaa gat ttt gtg att cag gca aag						211	
Met Thr Gln Gly Thr Asp Ser Pro Glu Asp Phe Val Ile Gln Ala Lys	25			30	35		
gct gac tgt tac ttc acc aac ggg aca gaa aag gtg cag ttt gtg gtc						259	
Ala Asp Cys Tyr Phe Thr Asn Gly Thr Glu Lys Val Gln Phe Val Val	40			45	50		
aga ttc atc ttt aac ttg gag gag tat gta cgt ttc gac agt gat gtg						307	
Arg Phe Ile Phe Asn Leu Glu Glu Tyr Val Arg Phe Asp Ser Asp Val	55		60	65	70		
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Trp Asn Ser Arg Leu Asp Leu Leu Glu Arg Ser Arg Gln Ala Val Asp	90			95	100		
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Gly Val Cys Arg His Asn Tyr Arg Leu Gly Ala Pro Phe Thr Val Gly	105			110	115		
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Arg Lys Val Gln Pro Glu Val Thr Val Tyr Pro Glu Arg Thr Pro Leu	120			125	130		
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Gly Asp Ile Lys Ile Lys Trp Phe Leu Asn Gly Gln Glu Glu Arg Ala	155			160	165		
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Thr Val Val Met Leu Glu Met Thr Pro Glu Leu Gly His Val Tyr Thr	185			190	195		
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Cys Leu Val Asp His Ser Ser Leu Leu Ser Pro Val Ser Val Glu Trp	200			205	210		
aga gct cag tct gaa tat tct tgg aga aag atg ctg agt ggc att gca						787	
Arg Ala Gln Ser Glu Tyr Ser Trp Arg Lys Met Leu Ser Gly Ile Ala	215		220	225	230		

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gcc ttc cta ctt ggg cta atc ttc ctt ctg gtg gga atc gtc atc cag      835
Ala Phe Leu Leu Gly Leu Ile Phe Leu Leu Val Gly Ile Val Ile Gln
                235                240                245

cta agg gct cag aaa gga tat gtg agg acg cag atg tct ggt aat gag      883
Leu Arg Ala Gln Lys Gly Tyr Val Arg Thr Gln Met Ser Gly Asn Glu
                250                255                260

gtc tca aga gct gtt ctg ctc cct cag tca tgc taa ggtcctcact          929
Val Ser Arg Ala Val Leu Leu Pro Gln Ser Cys
                265                270

gaagctttctc tctctggagc ctgaagtagt gatgagtagt ctgggccctg ggtgaggtaa    989

aggacattca tgagggtcaat gttctgggaa taactctctt ccctgatcct tggaggagcc  1049

cgaactgatt ctggagctct gtgttctgag atcatgcac tcccacccat ctgcccttct  1109

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aagtcatgat ctccaaagct ttctgtcttc caactgcagt ctccacagtc ttcagaagac  1289

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<212> TYPE: PRT

<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 55

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Phe Val Ile Gln Ala Lys Ala Asp Cys Tyr Phe Thr Asn Gly Thr Glu
          35          40          45

Lys Val Gln Phe Val Val Arg Phe Ile Phe Asn Leu Glu Glu Tyr Val
          50          55          60

Arg Phe Asp Ser Asp Val Gly Met Phe Val Ala Leu Thr Lys Leu Gly
65          70          75          80

Gln Pro Asp Ala Glu Gln Trp Asn Ser Arg Leu Asp Leu Leu Glu Arg
          85          90          95

Ser Arg Gln Ala Val Asp Gly Val Cys Arg His Asn Tyr Arg Leu Gly
          100         105         110

Ala Pro Phe Thr Val Gly Arg Lys Val Gln Pro Glu Val Thr Val Tyr
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Pro Glu Arg Thr Pro Leu Leu His Gln His Asn Leu Leu His Cys Ser
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Val Thr Gly Phe Tyr Pro Gly Asp Ile Lys Ile Lys Trp Phe Leu Asn
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Gly Gln Glu Glu Arg Ala Gly Val Met Ser Thr Gly Pro Ile Arg Asn
          165         170         175

Gly Asp Trp Thr Phe Gln Thr Val Val Met Leu Glu Met Thr Pro Glu
          180         185         190

Leu Gly His Val Tyr Thr Cys Leu Val Asp His Ser Ser Leu Leu Ser
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Pro	Val	Ser	Val	Glu	Trp	Arg	Ala	Gln	Ser	Glu	Tyr	Ser	Trp	Arg	Lys
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Met	Leu	Ser	Gly	Ile	Ala	Ala	Phe	Leu	Leu	Gly	Leu	Ile	Phe	Leu	Leu
225					230					235				240	
Val	Gly	Ile	Val	Ile	Gln	Leu	Arg	Ala	Gln	Lys	Gly	Tyr	Val	Arg	Thr
			245						250					255	
Gln	Met	Ser	Gly	Asn	Glu	Val	Ser	Arg	Ala	Val	Leu	Leu	Pro	Gln	Ser
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Cys

<210> SEQ ID NO 56
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gctcgtgggg aggtgagtg acctcctgga tcgatttagg aggtcgggtt gggactggga    360
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c g a a c a t c t a c a c c a c a c a a c a c c g c c t c g a c c a g g g t g a g a t a t c g g c c g g g g a c g c g g	1680
c g g t g g t a a t g a c a a g c g c c c a g a t a a c a a t g g g c a t g c c t t a t g c c g t g a c c g a c g c c g	1740
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c c c t c a t c t t c g a c c g c c a t c c c a t c g c c g c c c t c c t g t g c t a c c c g g c c g c g c g g t a c c	1860
t t a t g g g c a g c a t g a c c c c c c a g g c c g t g c t g g c g t t c g t g g c c c t c a t c c c g c c g a c c t	1920
t g c c c g g c a c c a a c a t c g t g c t t g g g g c c c t t c c g g a g g a c a g a c a c a t c g a c c g c c t g g	1980
c c a a a c g c c a g c g c c c c g g c g a g c g g c t g g a c c t g g c t a t g c t g g c t g c g a t t c g c c g c g	2040
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c g g g c c c a c g a c c c c a t a t c g g g g a c a c g t t a t t t a c c c t g t t t c g g g c c c c c g a g t t g c	2220
t g g c c c c c a a c g g c g a c c t g t a t a a c g t g t t t g c c t g g g c c t t g g a c g t c t t g g c c a a a c	2280
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a c g c c c t g c t g c a a c t t a c c t c c g g g a t g g t c c a g a c c c a c g t c a c c a c c c c c g g c t c c a	2400
t a c c g a c g a t a t g c g a c c t g g c g c g c a c g t t t g c c c g g g a g a t g g g a t c g g c c a t t g a a c	2460
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g g g c a c a a c a g a c a a t c g g c t g c t c t g a t g c c g c c g t g t t c c g g c t g t c a g c g c a g g g g c	2580
g c c c g g t t c t t t t t g t c a a g a c c g a c c t g t c c g g t g c c c t g a a t g a a c t g c a g g a c g a g g	2640
c a g c g c g g c t a t c g t g g c t g g c c a c g a c g g g c g t t c c t t g c g c a g c t g t g c t c g a c g t t g	2700
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t c t g a g g g t c t c t a g a t a a c t t c g t a t a a t g t a t g c t a t a c g a a g t t a t a a t a a a a g a t	3300
c c t t a t t t t c a t t g g a t c t g t g t g t t g g t t t t t t g t g t g g g a t c c g t t g a c t g a g t c g a c	3360
g g a g c t t a c c c a g c c t g c a g a a g a c c t c a t c c a g a c c c a g c a g a c c c c t g c c t c a g a a c t	3420
t g g g g a c c c t g a a g a c c c c g g a g a g g a g g c t g c a g a t g g c t c a g a c a c t g t g g t c c t c a g	3480
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a c a g g g t a g g a t a c c t c c t c t g g g a t t a g c c c t c t g g g a t t c c a t g a t g a t g g a a t g t c a	3600
g g c c t c a c a t g g a a c c t g t g t c t t g c t t t c g t t t t t g t t t t g t t t t g t t t t g t t g t t t t t	3660
t g a g a t g g a g t t t t g c t c t t g t t g c c c a t g c t g g a g t g c a a t g g c g t g a t c t c a g c t c a c	3720
t g c a a c c t c t g c c t c c t g g g t t c a a c t g a t t c t c c t g t c t c a g c c t c c t g a g t a g c t g g g	3780
a t t a c a g g c t t c c g c c a c t a c g c c c a g c t a a t t t t t t g g g t a t t t t t a g t a g a g a c g g g g	3840

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cgcgag	4507

1. An isolated cell comprising a genetically engineered disruption in a human leukocyte antigen (HLA) class II-related gene, wherein the cell is a primate cell.

2. The cell of claim 1, wherein the HLA class II-related gene is selected from the group consisting of regulatory factor X-associated ankyrin-containing protein (RFXANK) (SEQ ID NO: 24-27), regulatory factor 5 (RFX5) (SEQ ID NO: 28-31), regulatory factor X-associated protein (RFXAP) (SEQ ID NO: 32-33), class II transactivator (CIITA) (SEQ ID NO: 34-35), HLA-DPA (α chain) (SEQ ID NO: 36-37), HLA-DPB (β chain) (SEQ ID NO: 38-39), HLA-DQA (SEQ ID NO: 40-41), HLA-DQB (SEQ ID NO: 42-43), HLA-DRA (SEQ ID NO: 44-45), HLA-DRB (SEQ ID NO: 46-47), HLA-DMA (SEQ ID NO: 48-49), HLA-DMB (SEQ ID NO: 50-51), HLA-DOA (SEQ ID NO: 52-53) and HLA-DOB (SEQ ID NO: 54-55).

3. The cell of claim 2, wherein the cell comprises genetically engineered disruptions in at least two, at least three, or in all four of the HLA class II-related genes.

4. The cell of claim 1, wherein the HLA class II-related gene is regulatory factor X-associated ankyrin-containing protein (RFXANK) (SEQ ID NO: 24-27).

5. The cell of claim 1, wherein the cell comprises genetically engineered disruptions in all copies of the HLA class II-related gene.

6. The cell of claim 1, wherein the cell further comprises one or more recombinant immunomodulatory genes, each capable of expressing an immunomodulatory polypeptide in the human cell.

7. The cell of claim 6, wherein the one or more immunomodulatory genes comprise a polynucleotide capable of encoding a single chain fusion HLA class II protein, or an HLA class II protein.

8. The cell of claim 1, wherein the cell further comprises a genetically engineered disruption in the β 2-microglobulin (B2M) gene (SEQ ID NO: 1).

9. An isolated cell comprising

(a) a genetically engineered disruption in a beta-2 microglobulin (B2M) gene (SEQ ID NO: 1); and

(b) one or more polynucleotides capable of encoding a single chain fusion HLA class II protein or an HLA class II protein;

wherein the cell is a primate cell.

10. (canceled)

11. The cell of claim 7, wherein the one or more immunomodulatory genes comprise a polynucleotide capable of encoding one or more single chain fusion HLA class II proteins, and wherein the one or more single chain fusion HLA class II proteins comprises at least a portion of an HLA class II gene α chain covalently linked to at least a portion of an HLA class II gene β chain, wherein the HLA class II gene is selected from the group consisting of HLA-DP (SEQ ID NO: 36-39), HLA-DQ (SEQ ID NO: 40-43), HLA-DR (SEQ ID NO: 44-47), HLA-DM (SEQ ID NO: 48-51), and HLA-DO (SEQ ID NO: 52-55).

12. The cell of claim 11, wherein the single chain fusion HLA class II protein comprises a plurality of different single chain fusion HLA class II proteins

13. The cell of claim 11, wherein the single chain fusion HLA class II protein comprises one or more of:

a. at least a portion of HLA-DQ α chain (SEQ ID NO: 41) and at least a portion of HLA-DQ (3 chain (SEQ ID NO: 43); and

b. at least a portion of HLA-DQ α chain allele HLA-DQA1*01 (SEQ ID NO: 41) and at least a portion of HLA-DQ β chain allele HLA-DQB1*02 (SEQ ID NO: 43).

14. (canceled)

15. The cell of claim 11 wherein the single chain fusion HLA class II protein presents a first target peptide antigen on the cell surface.

16. The cell of claim 15 wherein the first target peptide antigen is covalently linked to the single chain fusion HLA class II protein.

17. (canceled)

18. The cell of claim 8, wherein the cell further comprises a polynucleotide capable of encoding a single chain fusion HLA class I protein.

19. The cell of claim 18, wherein the single chain fusion HLA class I protein comprises one or more of:

- a. at least a portion of B2M (SEQ ID NO: 2) covalently linked to at least a portion of an HLA class I α chain selected from the group consisting of HLA-A (SEQ ID NO: 4), HLA-B (SEQ ID NO: 6), HLA-C (SEQ ID NO: 8), HLA-E (SEQ ID NO: 10), HLA-F (SEQ ID NO: 12) and HLA-G (SEQ ID NO: 14);
- b. at least a portion of B2M (SEQ ID NO: 2) covalently linked to at least a portion of HLA-A (SEQ ID NO: 3); and
- c. at least a portion of B2M covalently linked to at least a portion of HLA-A0201 (SEQ ID NO: 4).

20.-27. (canceled)

28. The cell of any claim **1**, wherein the cell is a stem cell.

29-32. (canceled)

33. The cell of claim **1**, wherein the cell is a human cell.

34. A vaccine comprising the cell of claim **16**, wherein the vaccine is capable of eliciting in a primate an immune response specific for the first and/or second target peptide antigen.

35. (canceled)

36. A method of transplantation in a patient in need thereof comprising the step of administering to the patient an effective amount of the cell of claim **1**.

37-39. (canceled)

* * * * *