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(54) Title: MHC CLASS II T-CELL MODULATORY POLYPEPTIDES FOR TREATING TYPE 1 DIABETES MELLITUS (T1D) AND METHODS OF USE THEREOF

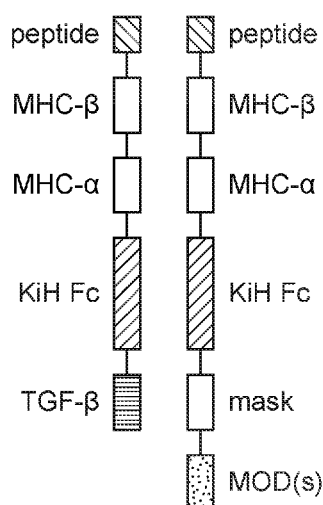


FIG. 1A

(57) Abstract: The present disclosure provides T-cell modulatory polypeptides (TMPs) comprising a type 1 diabetes (T1D)-associated peptide epitope, MHC class II polypeptides, one or more immunomodulatory polypeptides, a TGF-β polypeptide, and a masking polypeptide. A TMP of the present disclosure is useful for modulating activity of a T cell. Thus, the present disclosure provides compositions and methods for modulating the activity of T cells, as well as compositions and methods for treating persons who have T1D.



MHC CLASS II T-CELL MODULATORY POLYPEPTIDES FOR TREATING TYPE 1 DIABETES MELLITUS (T1D) AND METHODS OF USE THEREOF

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/177,641, filed April 21, 2021, which application is incorporated herein by reference in its entirety.

INCORPORATION BY REFERENCE OF SEQUENCE LISTING PROVIDED AS A TEXT FILE

[0002] A Sequence Listing is provided herewith as a text file, "CUEB-142WO_SEQ_LIST_ST25.txt" created on March 25, 2022 and having a size of 498 KB. The contents of the text file are incorporated by reference herein in their entirety.

INTRODUCTION

[0003] Central to the proper functioning of the mammalian immune system are the coordinated activities and communications between two specialized cell types, antigen-presenting cells ("APCs") and T cells. APCs serve to capture and break the proteins from foreign organisms, or abnormal proteins (*e.g.*, from genetic mutation in cancer cells), into smaller fragments suitable as signals for scrutiny by the larger immune system, including T cells. In particular, APCs break down proteins into small peptide fragments, which are then paired with proteins of the major histocompatibility complex ("MHC") and displayed on the cell surface. Cell surface display of an MHC together with a peptide fragment, also known as a T cell epitope, provides the underlying scaffold surveilled by T cells, allowing for specific recognition. The peptide fragments can be pathogen-derived, tumor-derived, or derived from natural host proteins (self-proteins). Moreover, APCs can recognize other foreign components, such as bacterial toxins, viral proteins, viral DNA, viral RNA, etc., whose presence denotes an escalated threat level. The APCs relay this information to T cells through additional costimulatory signals in order to generate a more effective response.

[0004] T cells recognize peptide-major histocompatibility complex ("pMHC") complexes through a specialized cell surface receptor, the T cell receptor ("TCR"). The TCR is unique to each T cell; as a consequence, each T cell is highly specific for a particular pMHC target. In order to adequately address the universe of potential threats, a very large number (~10,000,000) of distinct T cells with distinct TCRs exist in the human body. Further, any given T cell, specific for a particular T cell peptide, is initially a very small fraction of the total T cell population. Although normally dormant and in limited numbers, T cells bearing specific TCRs can be readily activated and amplified by APCs to generate highly potent T cell responses that involve many millions of T cells. Such activated T cell responses are capable of

attacking and clearing viral infections, bacterial infections, and other cellular threats including tumors, as illustrated below. Conversely, the broad, non-specific activation of overly active T cell responses against self or shared antigens can give rise to T cells inappropriately attacking and destroying healthy tissues or cells.

SUMMARY

[0005] The present disclosure provides T-cell modulatory polypeptides (TMPs) comprising a type 1 diabetes (T1D)-associated peptide epitope, MHC class II polypeptides, one or more immunomodulatory polypeptides, a TGF- β polypeptide, and a masking polypeptide. A TMP of the present disclosure is useful for modulating activity of a T cell. Thus, the present disclosure provides compositions and methods for modulating the activity of T cells, as well as compositions and methods for treating persons who have T1D.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] FIG. 1A-1H present schematic depictions of TMPs of the present disclosure.

[0007] FIG. 2A-2D present schematic depictions of TMPs of the present disclosure, in which the immunomodulatory polypeptide is in Position 2.

[0008] FIG. 3A-3D present schematic depictions of TMPs of the present disclosure, in which the immunomodulatory polypeptide is in Position 3.

[0009] FIG. 4 provides an amino acid sequence of an HLA Class II DRA (sometimes referred to as DRA1) α chains (SEQ ID NO:1).

[0010] FIG. 5 provides amino acid sequences of HLA Class II DRB1 β chains.

[0011] FIG. 6 provides amino acid sequences of HLA Class II DRB3 β chains (from top to bottom SEQ ID NOs:37-40).

[0012] FIG. 7 provides an amino acid sequence of an HLA Class II DRB4 β chain (SEQ ID NOs:41-42).

[0013] FIG. 8 provides an amino acid sequence of an HLA Class II DRB5 β chain (SEQ ID NO:43).

[0014] FIG. 9 provides an amino acid sequence of an HLA Class II DMA α chain (SEQ ID NO:44).

[0015] FIG. 10 provides an amino acid sequence of an HLA Class II DMB β chain (SEQ ID NO:45).

[0016] FIG. 11 provides an amino acid sequence of an HLA Class II DOA α chain (SEQ ID NO:46).

[0017] FIG. 12 provides an amino acid sequence of an HLA Class II DOB β chain (SEQ ID NO:47).

[0018] FIG. 13 provides amino acid sequences of HLA Class II DPA1 α chains (SEQ ID NOs:48-49).

[0019] FIG. 14 provides amino acid sequences of HLA Class II DPB1 β chains (from top to bottom SEQ ID NOs:50-61).

[0020] FIG. 15 provides amino acid sequences of HLA Class II DQA1 α chains (from top to bottom SEQ ID NOs:62-72).

[0021] FIG. 16 provides an amino acid sequence of an HLA Class II DQA2 α chain (SEQ ID NO:73).

[0022] FIG. 17 provides amino acid sequences of HLA Class II DQB1 β chains (from top to bottom SEQ ID NOs:74-85).

[0023] FIG. 18A-18B provide amino acid sequences of HLA Class II DQB2 β chains (SEQ ID NO:86 and SEQ ID NO:87, respectively).

[0024] FIG. 19A-19O provide amino acid sequences of wild-type (FIG. 19A) and variant (FIG. 19B-9N) DRA*0101 α chains.

[0025] FIG. 20A-20J provide amino acid sequences of wild-type (FIG. 20A) and variant (FIG. 20B-20J) DRB1*0401 β chains.

[0026] FIG. 21A-21M provide amino acid sequences of immunoglobulin Fc polypeptides.

[0027] FIG. 22A-22F provide amino acid sequences of a wild-type IL-2 polypeptide (FIG. 22A), IL-2R α (FIG. 22B), IL-2R β (FIG. 22C), IL-2R γ (FIG. 22D), a PD-L1 ectodomain polypeptide (FIG. 22E), and a 4-1BBL polypeptide (FIG. 22F).

[0028] FIG. 23A-23G provides amino acid sequences of three different isoforms of TGF- β preproteins (FIG. 23A, FIG. 23C, and FIG. 23E), TGF- β mature form proteins (FIG. 23B, FIG. 23D, and FIG. 23F), and mature form of TGF- β 3 with a C77S substitution (FIG. 23G).

[0029] FIG. 24 provides an alignment of amino acid sequences of TGF- β isoforms 1-3 with the residues corresponding to the mature form of TGF- β 2 bolded, except aa residues Lys 25, Cys 77, Ile 92, and Lys 94 of TGF- β 2 and their corresponding residues in the other forms of TGF- β isoforms 1 and 3 that are underlined and italicized but not bolded.

[0030] FIG. 25A-25N provide amino acid sequences of a type 1 TGF- β receptor (T β RI) (FIG. 25A) and its ectodomain (FIG. 25B); a type 2 TGF- β receptor (T β RII) (FIG. 25C and FIG. 25E), its ectodomain (FIG. 25D and FIG. 25F), and fragments of the ectodomain (FIG. 25G-25J); and a type 3 TGF- β receptor (T β RIII) (FIG. 25K and FIG. 25M) and its ectodomain (FIG. 25L and FIG. 25N).

[0031] FIG. 26A-26B provide amino acid sequences of an exemplary TMP (construct 4415-4417).

[0032] FIG. 27A-27B provide amino acid sequences of an exemplary TMP (construct 4418-4420).

[0033] FIG. 28 provides a schematic depiction of a TMP comprising scaffold polypeptides with interspecific binding sequences.

[0034] FIG. 29A-29B provide amino acid sequences of a TMP lacking MODs (construct 4415-4416).

[0035] FIG. 30A-30B provide amino acid sequences of a TMP lacking MODs (construct 4418-4419).

[0036] FIG. 31A-31B provide amino acid sequences of a TMP lacking MODs (construct 3858-3859).

[0037] FIG. 32A-32B provide amino acid sequences of an exemplary TMP (construct 3858-3869).

[0038] FIG. 33A-33B provide amino acid sequences of an exemplary TMP (construct 3870-3871).

[0039] FIG. 34A-34B provide a schematic depiction of certain TMPs (FIG. 34A) and depict SDS-PAGE analysis of the TMPs.

[0040] FIG. 35 depicts the effect of certain TMPs on the proportion of cells, in a population of T cells, that are FoxP3 positive.

[0041] FIG. 36 depicts SDS-PAGE analysis of certain TMPs.

DEFINITIONS

[0042] The terms “polynucleotide” and “nucleic acid,” used interchangeably herein, refer to a polymeric form of nucleotides of any length, either ribonucleotides or deoxyribonucleotides. Thus, this term includes, but is not limited to, single-, double-, or multi-stranded DNA or RNA, genomic DNA, cDNA, DNA-RNA hybrids, or a polymer comprising purine and pyrimidine bases or other natural, chemically or biochemically modified, non-natural, or derivatized nucleotide bases.

[0043] The terms “peptide,” “polypeptide,” and “protein” are used interchangeably herein, and refer to a polymeric form of amino acids of any length, which can include coded and non-coded amino acids, chemically or biochemically modified or derivatized amino acids, and polypeptides having modified peptide backbones. Furthermore, as used herein, a “polypeptide” refers to a protein that includes modifications, such as deletions, additions, and substitutions (generally conservative in nature as would be known to a person in the art) to the native sequence, as long as the protein maintains the desired activity. These modifications can be deliberate, as through site-directed mutagenesis, or can be accidental, such as through mutations of hosts that produce the proteins, or errors due to polymerase chain reaction (PCR) amplification or other recombinant DNA methods. References herein to a specific residue or residue number in a known polypeptide, e.g., position 72 or 75 of human DRA MHC class II polypeptide, are understood to refer to the amino acid at that position in the wild-type polypeptide (i.e. I72 or K75). To the extent that the sequence of the wild-type polypeptide is altered, either by addition or deletion of one or more amino acids, one of ordinary skill will understand that a reference to the specific residue or residue number will be correspondingly altered so as to refer to the same specific amino acid in the altered polypeptide, which would be understood to reside at an altered position number. For example, if a human DRA MHC class II polypeptide is altered by the addition of one amino acid at the N-terminus, then a reference to position 72 or 75, or to residue I72 or K75, will be understood to indicate the amino acids that are at positions 73 or 76, or to residues I73 and K76. Likewise, a reference herein to substitution of a specific amino acid as a specific position, e.g., I72C, is understood to refer to a substitution of a cysteine for the amino acid at position 72 in the wild-type polypeptide, i.e., isoleucine. If, e.g., the wild-type polypeptide is altered to change the amino acid at position 72 from isoleucine to an alternate amino acid, then the reference to I72C will be understood to refer to the substitution of a

cysteine for the alternate amino acid. If in such case the polypeptide is also altered by the addition or deletion of one or more amino acids, then the reference to I72C will be understood to refer to the substitution of a cysteine for the alternate amino acid at the altered position number. A reference to a “non-naturally occurring Cys residue” in a polypeptide, e.g., a DRA MHC class II polypeptide, means that the polypeptide comprises a Cys residue in a location where there is no Cys in the corresponding wild-type polypeptide. This can be accomplished through routine protein engineering in which a cysteine is substituted for the amino acid that occurs in the wild-type sequence, e.g., at position 72 or 75 of the DRA*0101 polypeptide (see Figs. 13G and H) instead of the isoleucine (I) or lysine (K) residues that are present in the wild-type DRA*0101 polypeptide (see Fig. 13A).

[0044] A polynucleotide or polypeptide has a certain percent “sequence identity” to another polynucleotide or polypeptide, meaning that, when aligned, that percentage of bases or amino acids are the same, and in the same relative position, when comparing the two sequences. Sequence identity can be determined in a number of different ways. To determine sequence identity, sequences can be aligned using various convenient methods and computer programs (e.g., BLAST, T-COFFEE, MUSCLE, MAFFT, etc.), available over the world wide web at sites including ncbi.nlm.nih.gov/BLAST, ebi.ac.uk/Tools/msa/tcoffee/, ebi.ac.uk/Tools/msa/muscle/, mafft.cbrc.jp/alignment/software/. See, e.g., Altschul et al. (1990) *J. Mol. Biol.* 215:403-10. Unless otherwise stated, “sequence identity” as referred to herein is determined by BLAST (Basic Local Alignment Search Tool), as described in Altschul et al. (1990) *J. Mol. Biol.* 215:403.

[0045] As used herein “masked” means that a molecule (e.g., masked polypeptide or masked protein) is bound or otherwise engaged by a masking molecule (e.g., polypeptide, protein or protein fragment) that limits the availability of the masked molecule to other proteins (e.g., cell surface receptors) that also have affinity for the molecule.

[0046] Interspecific binding sequences are dimerization sequences that permit an asymmetric pairing of polypeptides (heterodimer formation). Interspecific binding sequences favor formation of heterodimers with their counterpart interspecific binding sequence(s) (as opposed to forming homodimers), which is their cognate binding partner. Key-in-hole (or key-into-hole) Fc polypeptide pairs are an example of an interspecific binding sequence and its counterpart interspecific binding sequence.

[0047] “Tandem,” as used herein to describe the placement of MOD polypeptides, means having two or more MODs arranged adjacent to each other on a polypeptide separated, at most, by a linker.

[0048] As used herein the term “*in vivo*” refers to any process or procedure occurring inside of the body, e.g., of a T1D patient.

[0049] As used herein, “*in vitro*” refers to any process or procedure occurring outside of the body.

[0050] The term "conservative amino acid substitution" refers to the interchangeability in proteins of amino acid residues having similar side chains. For example, a group of amino acids having aliphatic side chains consists of glycine, alanine, valine, leucine, and isoleucine; a group of amino acids having aliphatic-hydroxyl side chains consists of serine and threonine; a group of amino acids having amide containing side chains consisting of asparagine and glutamine; a group of amino acids having aromatic side chains consists of phenylalanine, tyrosine, and tryptophan; a group of amino acids having basic side chains consists of lysine, arginine, and histidine; a group of amino acids having acidic side chains consists of glutamate and aspartate; and a group of amino acids having sulfur containing side chains consists of cysteine and methionine. Exemplary conservative amino acid substitution groups are: valine-leucine-isoleucine, phenylalanine-tyrosine, lysine-arginine, alanine-valine-glycine, and asparagine-glutamine.

[0051] The term "binding," as used herein (e.g. with reference to binding of a T-cell modulatory antigen-presenting polypeptide to a polypeptide (e.g., a T-cell receptor) on a T cell), refers to a non-covalent interaction between two molecules. Non-covalent binding refers to a direct association between two molecules, due to, for example, electrostatic, hydrophobic, ionic, and/or hydrogen-bond interactions, including interactions such as salt bridges and water bridges. "Covalent binding" or "covalent bond," as used herein, refers to the formation of one or more covalent chemical binds between two different molecules.

[0052] The term "immunological synapse" or "immune synapse" as used herein generally refers to the natural interface between two interacting immune cells of an adaptive immune response including, e.g., the interface between an antigen-presenting cell (APC) or target cell and an effector cell, e.g., a lymphocyte, an effector T cell, a natural killer cell, and the like. An immunological synapse between an APC and a T cell is generally initiated by the interaction of a T cell antigen receptor and major histocompatibility complex molecules, e.g., as described in Bromley et al., *Annu Rev Immunol.* 2001;19:375-96; the disclosure of which is incorporated herein by reference in its entirety.

[0053] "T cell" includes all types of immune cells expressing CD3, including T-helper cells (CD4⁺ cells), cytotoxic T-cells (CD8⁺ cells), T-regulatory cells (Treg), and NK-T cells.

[0054] The term "immunomodulatory polypeptide" (also referred to as a "MOD"), as used herein, includes a polypeptide on an antigen presenting cell (APC) (e.g., a dendritic cell, a B cell, and the like), or a portion of the polypeptide on an APC, that specifically binds a cognate co-immunomodulatory polypeptide on a T cell, thereby providing a signal which, in addition to the primary signal provided by, for instance, binding of a TCR/CD3 complex with a major histocompatibility complex (MHC) polypeptide loaded with peptide, mediates a T cell response, including, but not limited to, proliferation, activation, differentiation, and the like.

[0055] “Heterologous,” as used herein, means a nucleotide or polypeptide that is not found in the native nucleic acid or protein, respectively.

[0056] “Recombinant,” as used herein, means that a particular nucleic acid (DNA or RNA) is the product of various combinations of cloning, restriction, polymerase chain reaction (PCR) and/or ligation steps resulting in a construct having a structural coding or non-coding sequence distinguishable from endogenous nucleic acids found in natural systems. DNA sequences encoding polypeptides can be assembled from cDNA fragments or from a series of synthetic oligonucleotides, to provide a synthetic nucleic acid which is capable of being expressed from a recombinant transcriptional unit contained in a cell or in a cell-free transcription and translation system.

[0057] The terms “recombinant expression vector,” or “DNA construct” are used interchangeably herein to refer to a DNA molecule comprising a vector and at least one insert. Recombinant expression vectors are usually generated for the purpose of expressing and/or propagating the insert(s), or for the construction of other recombinant nucleotide sequences. The insert(s) may or may not be operably linked to a promoter sequence and may or may not be operably linked to DNA regulatory sequences.

[0058] As used herein, the term “affinity” refers to the equilibrium constant for the reversible binding of two agents (e.g., an antibody and an antigen) and is expressed as a dissociation constant (K_D). As used herein, the term “avidity” refers to the resistance of a complex of two or more agents to dissociation after dilution.

[0059] The terms “treatment”, “treating” and the like are used herein to generally mean obtaining a desired pharmacologic and/or physiologic effect. The effect may be prophylactic in terms of completely or partially preventing a disease or symptom thereof and/or may be therapeutic in terms of a partial or complete cure for a disease and/or adverse effect attributable to the disease. “Treatment” as used herein covers any treatment of a disease or symptom in a mammal, and includes: (a) preventing the disease or symptom from occurring in a subject which may be predisposed to acquiring the disease or symptom but has not yet been diagnosed as having it; (b) inhibiting the disease or symptom, i.e., arresting its development; and/or (c) relieving the disease, i.e., causing regression of the disease. The therapeutic agent may be administered before, during or after the onset of disease or injury. The treatment of ongoing disease, where the treatment stabilizes or reduces the undesirable clinical symptoms of the patient, is of particular interest. Such treatment is desirably performed prior to complete loss of function in the affected tissues. The subject therapy will desirably be administered during the symptomatic stage of the disease, and in some cases after the symptomatic stage of the disease.

[0060] The terms “individual,” “subject,” “host,” and “patient,” are used interchangeably herein and refer to any mammalian subject for whom diagnosis, treatment, or therapy is desired. Mammals include,

e.g., humans, non-human primates, rodents (e.g., rats; mice), lagomorphs (e.g., rabbits), ungulates (e.g., cows, sheep, pigs, horses, goats, and the like), etc.

[0061] Unless indicated otherwise, the term “substantially” is intended to encompass both “wholly” and “largely but not wholly”. For example, an Ig Fc that “substantially does not induce cell lysis” means an Ig Fc that induces no cell lysis at all or that largely but not wholly induces no cell lysis.

[0062] As used herein, the term “about” used in connection with an amount indicates that the amount can vary by 10%. For example, “about 100” means an amount of from 90-110. Where about is used in the context of a range, the “about” used in reference to the lower amount of the range means that the lower amount includes an amount that is 10% lower than the lower amount of the range, and “about” used in reference to the higher amount of the range means that the higher amount includes an amount 10% higher than the higher amount of the range. For example, from about 100 to about 1000 means that the range extends from 90 to 1100.

[0063] The terms “purifying”, “isolating”, and the like, refer to the removal of a desired substance, e.g., a TMP, from a solution containing undesired substances, e.g., contaminants, or the removal of undesired substances from a solution containing a desired substance, leaving behind essentially only the desired substance. In some instances, a purified substance may be essentially free of other substances, e.g., contaminants.

[0064] It is to be understood that this disclosure is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the disclosure described in the appended claims will be limited only by the appended claims.

[0065] Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the disclosure. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges, and are also encompassed within the disclosure, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the disclosure.

[0066] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although any methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the present disclosure, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to disclose and describe the methods and/or materials in connection with which the publications are cited.

[0067] It must be noted that as used herein and in the appended claims, the singular forms “a,” “an,” and “the” include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to “an immunomodulatory polypeptide” includes a plurality of such immunomodulatory polypeptides and reference to “the Treg” includes reference to one or more Tregs and equivalents thereof known to those skilled in the art, and so forth. It is further noted that the claims may be drafted to exclude any optional element or any element that is included in a list or other recitation of elements that share a common generic or specific feature, property, or activity. As such, this statement is intended to serve as antecedent basis for use of such exclusive terminology as “solely,” “only” and the like in connection with the recitation of claim elements, or use of a “negative” limitation.

[0068] It is appreciated that certain features of the disclosure, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the disclosure, which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination. All combinations of the embodiments pertaining to the disclosure are specifically embraced by the present disclosure and are disclosed herein just as if each and every combination was individually and explicitly disclosed. In addition, all sub-combinations of the various embodiments and elements thereof are also specifically embraced by the present disclosure and are disclosed herein just as if each and every such sub-combination was individually and explicitly disclosed herein.

[0069] The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present disclosure is not entitled to antedate such publication by virtue of prior disclosure. Further, the dates of publication provided may be different from the actual publication dates which may need to be independently confirmed. The headings of this disclosure are for convenience of reference only and do not define, describe or limit the scope of this disclosure or the scope of the appended claims.

DETAILED DESCRIPTION

[0070] The present disclosure provides T-cell modulatory polypeptides (TMPs) comprising a type 1 diabetes (T1D)-associated peptide epitope, MHC class II polypeptides, one or more optional immunomodulatory polypeptides (“MODs”), a TGF- β polypeptide, and a masking polypeptide (the TGF- β polypeptide and masking polypeptide together comprising a “masked TGF- β MOD”). A TMP of the present disclosure is useful for modulating activity of a T cell. Thus, the present disclosure provides compositions and methods for modulating the activity of T cells, as well as compositions and methods for treating individuals who have T1D. In any of the embodiments described herein, in some cases, a TMP does not include a MOD; such a TMP is useful for delivering TGF β .

T-CELL MODULATORY POLYPEPTIDES (“TMPs”)

[0071] The present disclosure provides TMPs comprising: i) a peptide that displays a Type 1 Diabetes-associated epitope capable of being bound by a T-cell receptor (a “T1D peptide”); ii) a TGF- β polypeptide; iii) a masking polypeptide; iv) MHC class II polypeptides (i.e., an MHC class II α chain polypeptide and an MHC class II β chain polypeptide); and v) optionally, one or more MODs; where the TMP optionally comprises one or more scaffold polypeptides (e.g., one or more immunoglobulin (Ig) Fc polypeptides), and where the TMP optionally comprises one or more independently selected linker polypeptides (e.g., where each of the one or more independently selected linker polypeptides is between any two of the aforementioned polypeptides). TMPs can be in the form of single-chain polypeptides, heterodimeric polypeptides, and dimers or multimers of such single chain and heterodimeric polypeptides, and exemplary configurations are discussed below.

[0072] Further, although the TMPs of this disclosure may comprise both one or more masked TGF- β MODs and one or more additional MODs such as a wt or variant IL-2, PD-L1 and/or a 4-1BBL MOD (as discussed above), if desired, the TMPs of this disclosure may comprise only one or more masked TGF- β MODs. That is, the one or more additional MODs such as the wt or variant IL-2, PD-L1 and/or a 4-1BBL MOD need not be included in a TMP of this disclosure. In the discussion below, therefore, it should be understood that the presence of one or more MODs in addition to the one or more masked TGF- β MODs is optional.

BRIEF OVERVIEW OF EXEMPLARY TMP STRUCTURES

[0073] **A)** A TMP of the present disclosure in some cases comprises a heterodimer comprising scaffold polypeptides (e.g., Ig Fc) with interspecific binding sequences, where the heterodimer comprises: a) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide and iv) a first scaffold polypeptide comprising a first interspecific binding sequence; and b) a second polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide and iv) a second scaffold polypeptide comprising a counterpart interspecific binding sequence to the interspecific binding sequence of the first polypeptide, wherein the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other in the heterodimer; where the first or the second polypeptide comprises a TGF- β polypeptide, where the first or the second polypeptide comprises a masking polypeptide, and where the first and/or the second polypeptide optionally comprises one or more MODs; and where the TMP optionally comprises one or more independently selected linker polypeptides. Examples of such TMPs are depicted schematically in **FIG. 1A-1D**. In some cases, as depicted schematically in **FIG. 1E-1H**, the first and the second polypeptides are linked by a disulfide bond between, e.g., the MHC class II β polypeptide and the MHC class II α polypeptide.

[0074] **B)** A TMP of the present disclosure in some cases comprises one or more heterodimers, where each heterodimer comprises: a) a first polypeptide chain comprising: i) a T1D peptide and a first MHC class II polypeptide; and b) a second polypeptide comprising a second MHC class II polypeptide, where the first and/or the second polypeptide optionally comprises one or more MODs, where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide; wherein the TMP optionally includes one or more independently selected linker polypeptides, and where the first or the second polypeptide chain comprises an Ig Fc polypeptide. A TMP of the present disclosure can be a homodimer comprising two such heterodimers, where the Ig Fc polypeptide of one of the heterodimers is disulfide linked to the Ig Fc polypeptide of the other heterodimer. Examples of such TMPs are depicted schematically in **FIG. 2A-2D**.

[0075] **C)** A TMP of the present disclosure in some cases is a single-chain polypeptide; i.e., a single polypeptide chain comprises: i) a T1D peptide; ii) MHC class II polypeptides (e.g., an MHC class II β polypeptide and an MHC class II α polypeptide); iii) optionally one or more MODS; iv) a TGF- β polypeptide; v) a masking polypeptide; and, optionally, one or more independently selected linker polypeptides, and, optionally, an Ig Fc polypeptide. Examples of such TMPs are depicted schematically in **FIG. 3A-3D**. A TMP of the present disclosure can be a homodimer comprising two copies of such single-chain polypeptides, where the single-chain polypeptide comprises an Ig Fc polypeptide, and where the Ig Fc polypeptide of one of the two single-chain polypeptides is disulfide linked to the Ig Fc polypeptide of the other of the two single-chain polypeptides. Alternatively, a TMP can comprise a heterodimer of two different single-chain TMPs that are joined by polypeptides comprising interspecific binding sequences discussed below.

[0076] The foregoing configurations are discussed in more detail below. References herein to MHC class II α polypeptides may include both the $\alpha 1$ and $\alpha 2$ domains of class II MHC α chains, and references herein to MHC class II β polypeptides may include both the $\beta 1$ and $\beta 2$ domains of class II MHC β chains, which four domains represent all or most of the extracellular class II protein required for presentation of an epitope peptide.

A) HETERODIMERIC TMPs COMPRISING INTERSPECIFIC BINDING SEQUENCES

[0077] A TMP of the present disclosure in some cases comprises a heterodimer comprising scaffold polypeptides (e.g., Ig Fc polypeptides) with interspecific binding sequences, where the heterodimer comprises: a) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; and iv) a first scaffold polypeptide comprising a first interspecific binding sequence; and b) a second polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; and iv) a second scaffold polypeptide comprising a counterpart interspecific binding sequence to the interspecific binding sequence of the first polypeptide, wherein the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other

in the heterodimer; where the first or the second polypeptide comprises a TGF- β polypeptide, where the first or the second polypeptide comprises a masking polypeptide, and where the first and/or the second polypeptide optionally comprises one or more MODs. The TMP optionally comprises one or more independently selected linker polypeptides. Non-limiting examples of such TMPs are depicted schematically in **FIGs. 1A-1D**. Although FIGs 1A-1D illustrate the scaffold polypeptides as Knob-in-Hole (“KiH”) Fc polypeptides, it should be understood that other scaffold polypeptides having interspecific binding sequences may be used.

Arrangement of components

[0078] The components of such a TMP can be arranged in various ways. In some cases, a TMP comprises at least one heterodimer, where the heterodimer comprises: a) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) a first scaffold polypeptide comprising a first interspecific binding sequence; and v) a TGF- β polypeptide; and b) a second polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) a second scaffold polypeptide comprising a counterpart interspecific binding sequence to the interspecific binding sequence of the first polypeptide, wherein the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other in the heterodimer; and v) a masking polypeptide; where the first and/or the second polypeptide comprises one or more MODs. In some cases, the one or more MODs and the TGF- β polypeptide are on the same polypeptide. In some cases, the one or more MODs and the masking polypeptide are on the same polypeptide. In some cases, the interspecific binding sequence and the counterpart interspecific binding sequence comprise KiH sequences.

[0079] In some cases, a TMP comprises at least one heterodimer, where the heterodimer comprises: a) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) a first scaffold polypeptide comprising a first interspecific binding sequence; v) a masking polypeptide; and vi) a TGF- β polypeptide; and b) a second polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; and iv) a second scaffold polypeptide comprising a counterpart interspecific binding sequence to the interspecific binding sequence of the first polypeptide, wherein the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other in the heterodimer; where the first and/or the second polypeptide comprises one or more MODs. In some cases, the one or more MODs are on the first polypeptide. In some cases, the one or more MODs are on the second polypeptide. In some cases, the interspecific binding sequence and the counterpart interspecific binding sequence comprise KiH sequences.

[0080] Further examples of various arrangements of the components of a TMP are depicted schematically in **FIGs. 1A-1D**. In FIGs. 1A-1D, the scaffold polypeptides are KiH Ig Fc polypeptides,

and the masking polypeptide is referred to as “mask.” For example, as depicted schematically in **FIG. 1A**, in some cases, a TMP is a heterodimer comprising: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a first Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence); and v) a TGF- β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a second Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence); v) a masking polypeptide; and vi) one or more MODs, where the first Ig Fc polypeptide dimerizes with the second Ig Fc polypeptide, and where the TMP comprises an optional peptide linker between any two of the components (any two adjacent components) of the TMP.

[0081] As another example, as depicted schematically in **FIG. 1B**, in some cases, a TMP is a heterodimer comprising: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a first Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence); v) a masking polypeptide; and vi) a TGF- β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a second Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence); and v) one or more MODs, where the first Ig Fc polypeptide dimerizes with the second Ig Fc polypeptide, and where the TMP comprises an optional peptide linker between any two of the components (any two adjacent components) of the TMP.

[0082] As another example, as depicted schematically in **FIG. 1C**, in some cases, a TMP is a heterodimer comprising: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a first Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence); and v) a TGF- β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) one or more MODs; v) a second Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence); and vi) a masking polypeptide, where the first Ig Fc polypeptide dimerizes with the second Ig Fc polypeptide, and where the TMP comprises an optional peptide linker between any two of the components (any two adjacent components) of the TMP.

[0083] As another example, as depicted schematically in **FIG. 1D**, in some cases, a TMP is a heterodimer comprising: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a first Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence); v) a masking polypeptide; and vi) a TGF- β polypeptide, and b) a second polypeptide comprising, in order from N-

terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) one or more MODs; and v) a second Ig Fc comprising an interspecific binding sequence (illustrated as a KiH sequence), where the first Ig Fc polypeptide dimerizes with the second Ig Fc polypeptide, and where the TMP comprises an optional peptide linker between any two of the components (any two adjacent components) of the TMP.

[0084] In some cases, as depicted schematically in **FIG. 1E-1H**, in some cases, the MHC class II α chain polypeptide and the MHC class II β chain polypeptide comprise Cys residues not present in naturally-occurring MHC class II α chain and MHC class II β chain polypeptides, where a disulfide bond is formed between the Cys residues, thereby disulfide linking the first polypeptide to the second polypeptide. Suitable MHC class II α chain and MHC class II β chain polypeptides comprising introduced Cys residues are described below. In addition, where the scaffold proteins are Ig Fc polypeptides, one or more disulfide bonds can form between an Ig Fc polypeptide in the first polypeptide and an Ig Fc polypeptide in the second polypeptide. Such disulfide bonds are depicted schematically in **FIG. 28**.

[0085] Amino acid sequences of exemplary TMPs that are heterodimers comprising Ig Fc polypeptides with interspecific binding sequences are depicted in 1) **FIG. 26A** and **FIG. 26B**, where the first polypeptide is “construct 4415” (**FIG. 26A**) and the second polypeptide is “construct 4417” (**FIG. 26B**); 2) **FIG. 27A** and **FIG. 27B**, where the first polypeptide is “construct 4418” (**FIG. 27A**) and the second polypeptide is “construct 4420” (**FIG. 27B**); 3) **FIG. 32A-32B**, where the first polypeptide is “construct 3858” (**FIG. 32A**) and the second polypeptide is “construct 3869” (**FIG. 32B**); and 4) **FIG. 33A-33B**, where the first polypeptide is “construct 3870” (**FIG. 33A**) and the second polypeptide is “construct 3871” (**FIG. 33B**).

TMPs without additional MODs

[0086] As noted above, any of the above-described embodiments can be provided without a MOD other than a masked TGF- β MOD. Non-limiting examples of such TMPs are depicted in: 1) **FIG. 29A-29B**, where the first polypeptide is “construct 4415” (**FIG. 29A**) and the second polypeptide is “construct 4416” (**FIG. 29B**); 2) **FIG. 30A-30B**, where the first polypeptide is “construct 4418” (**FIG. 30A**) and the second polypeptide is “construct 4419” (**FIG. 30B**); and 3) **FIG. 31A-31B**, where the first polypeptide is “construct 3858” (**FIG. 31A**) and the second polypeptide is “construct 3859” (**FIG. 31B**). Such TMPs are useful for, e.g., delivering TGF β selectively to T cells expressing on their surface a TCR specific for the peptide present in the TMP, when complexed with MHC class II polypeptides present in the TMP.

Scaffold polypeptides with interspecific binding sequences

[0087] Scaffold polypeptides serve, among other things, as structural elements providing a framework upon which other components of a TMP are organized. Where the masking polypeptide and the TGF- β polypeptide are located in trans (on different polypeptides of the TMP), scaffolds polypeptides that form

interspecific and non-interspecific duplexes (or higher order structures) can keep the masking polypeptide associated with the TGF- β polypeptide. Depending on the nature of the scaffold, it can also act as an organizational element providing higher order structure in terms of protein folding and dimerization or multimerization (e.g., homodimerization or heterodimerization). The scaffold can also contribute to serum stability, particularly where it is an Ig heavy chain constant region (e.g., an Ig Fc). Suitable scaffold polypeptides will, in some cases, be half-life extending polypeptides. In some cases, a suitable scaffold polypeptide increases the *in vivo* half-life (e.g., the serum half-life) of a TMP, compared to a control TMP having a scaffold polypeptide with a different, non-Ig sequence, by at least about 10%, at least about 15%, at least about 25%, at least about 50%, at least about 2-fold, at least about 5-fold, at least about 10-fold, at least about 25-fold, at least about 50-fold, at least about 100-fold, or more than 100-fold. As an example, in some cases an Ig Fc polypeptide sequence (e.g., including interspecific Ig sequence such as a KiH sequence pairs) increases the stability and/or *in vivo* half-life (e.g., the serum half-life) of a TMP, compared to a control TMP having the Ig Fc polypeptide sequence replaced by a linker (e.g., a GGS aa repeat of equal sequence length; SEQ ID NO:234). The increase in *in vivo* half-life can be by at least about 10%, at least about 15%, at least about 25%, at least about 50%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, at least about 25-fold, at least about 50-fold, at least about 100-fold, or more than 100-fold. Where an Ig Fc polypeptide is employed in a TMP, the Ig Fc can contain mutations that will prevent the spontaneous formation of dimers of the TMP (See, e.g., Tianlei Ying et al., *J. Biol. Chem.*, 287 (23), pp 19399-19408 (June 1, 2012)), and additionally may include mutations (e.g., the LALA mutations discussed below) that reduce or substantially eliminate the ability of the Ig polypeptide to induce cell lysis, e.g., though complement-dependent cytotoxicity (CDC) and/or antibody-dependent cellular cytotoxicity (ADCC).

[0088] Where scaffold polypeptides of a TMP comprise one or more amino acid sequences that permit a scaffold polypeptide to interact (specifically bind) with another scaffold polypeptide, the TMP can form a homodimer. A TMP may also comprise one or more aa sequences that permit scaffold polypeptides to interact (specifically bind) with other scaffold polypeptides, forming higher order structures. Sequences that form higher order multimer structures permit the formation of TMPs of higher order (e.g., trimers, tetramers, pentamers etc.). By way of example, scaffold polypeptides comprising IgM Fc regions permit formation of pentameric (particularly when J-chain sequences are also expressed) or hexameric TMPs. Petrušić et al., *Med Hypotheses*. 77(6):959-61 (2011).

[0089] A variety of polypeptides that specifically bind to each other or themselves with sufficient affinity may be utilized as dimerization sequences in a TMP (see, e.g., U.S. Patent Publication No. 2003/0138440). The polypeptides may be of relatively compact size (e.g., such as less than about 300, 250, 225, 200, 175, 150, 125, 100, 75, or 50 aa). Dimerization/multimerization polypeptides include, but are not limited to: immunoglobulin heavy chain constant region (Ig Fc) polypeptides (polypeptides

comprising CH2-CH3 regions of Igs; see, e.g.); Fc KiH polypeptides; polypeptides of the collectin family (e.g., ACRP30 or ACRP30-like proteins) that contain collagen domains consisting of collagen repeats Gly-Xaa-Yaa; coiled-coil domains; leucine-zipper domains; Fos/Jun binding pairs; Ig heavy chain region 1 (CH1) and light chain constant region CL sequences (CH1/CL pairs such as a CH1 sequence paired with a κ or λ Ig light chain constant region sequence).

[0090] In some cases, the scaffold polypeptide comprises an Ig heavy chain constant region (CH2-CH3) polypeptide sequence that functions as a dimerization or multimerization sequence (see, e.g., **FIG. 21A-21M**). In some cases, the Ig polypeptide will have a reduced ability to induce cell lysis, e.g., through activation of complement-dependent cytotoxicity (CDC) and/or antibody-dependent cellular cytotoxicity (ADCC), and thus may include mutations that reduce or substantially eliminate the ability of the Ig polypeptide to induce cell lysis. In some cases, the Ig Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to an Ig Fc polypeptide depicted in any one of **FIG. 21A-21M**. Such Ig Fc polypeptides can covalently link the polypeptides of a TMP together, e.g., by forming one or two interchain disulfide bonds. As discussed below, an additional disulfide bond can be introduced to stabilize dimers, particularly where a pair of interspecific Ig sequence such KiH polypeptide pairs are employed.

[0091] In an embodiment, the scaffold polypeptide of a TMP comprises an amino acid sequence that has at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 150 contiguous aas (at least 175, at least 200, at least 225, at least 250, at least 275, at least 300, at least 325, or at least 350 contiguous aas), or all aas, of the IgA Fc sequence depicted in **FIG. 2K**. In an embodiment, the scaffold polypeptide comprises an amino acid sequence that has at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 150 contiguous aas (at least 175, at least 200, at least 225, at least 250, at least 275, at least 300, at least 325, or at least 350 contiguous aas), or all aas, of the IgD Fc sequence depicted in **FIG. 2I**. In an embodiment, the scaffold polypeptide comprises an amino acid sequence that has at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 125 contiguous aas (at least 150, at least 175, or at least 200 contiguous aas), or all aas, of the IgE Fc sequence depicted in **FIG. 21L**. In an embodiment, the scaffold polypeptide comprises an amino acid sequence that has at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 125 contiguous aas (at least 150, at least 175, or at least 200 contiguous aas), or all aas, of a wt IgG Fc polypeptide, such as the IgG1 Fc amino acid sequence depicted in any one of **FIG. 21A-21F**. In an embodiment, the scaffold polypeptide comprises an amino acid sequence that has at least about 70%, at least about 80%, at least about 90%, at

least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 125 contiguous aas (at least 150, at least 175, at least 200, at least 225, at least 250, at least 275, or at least 300), or all aas, of the IgG2 Fc polypeptide amino acid sequence depicted in **FIG. 21G**. In an embodiment, the scaffold polypeptide comprises a sequence that has at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 125 contiguous aas (at least 150, at least 175, at least 200, or at least 225), or all aas, of the IgG3 Fc amino acid sequence depicted in **FIG. 21H**. In an embodiment, the scaffold polypeptide comprises an amino acid sequence that has at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 125 contiguous aas (at least 150, at least 175, at least 200, at least 225, or at least 250), or all aas, of the IgG4 Fc amino acid sequence depicted in **FIG. 21M**. In an embodiment, the scaffold polypeptide comprises an amino acid sequence that has at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to at least 125 contiguous aas (at least 150, at least 175, at least 200, at least 225, or at least 250), or all aas, of the IgM Fc polypeptide sequence depicted in **FIG. 21J**. The above-recited scaffold polypeptides can be covalently linked together by formation of one or two interchain disulfide bonds between cysteines adjacent to their hinge regions.

[0092] In some cases, the dimerization sequence of a scaffold polypeptide present in a TMP has at least about 70% (e.g., at least about 80%, 90%, 95%, 98%, 99% or 100%) aa sequence identity to the human IgG1 Fc polypeptide depicted in **FIG. 21F**, and comprises a substitution of N297 with an alanine (N297A substitution, or N77 as numbered in **FIG. 21F**) substitution. In some cases, the dimerization sequence of a scaffold polypeptide present in a TMP comprises an aa sequence depicted in **FIG. 21A** (human IgG1 Fc), except for a substitution of N297 (N77 of the aa sequence depicted in **FIG. 21A**) with an aa other than asparagine. Substitutions at N297 lead to the removal of carbohydrate modifications and result antibody sequences with reduced complement component 1q ("C1q") binding compared to the wt. protein, and accordingly a reduction in complement-dependent cytotoxicity.

[0093] In some cases, the dimerization sequence of a scaffold polypeptide present in a TMP comprises an aa sequence depicted in **FIG. 21A** (human IgG1 Fc), except for a substitution of L234 (L14 of the aa sequence depicted in **FIG. 21A**) with an aa other than leucine. L234 and other aas in the lower hinge region (e.g., aas 234-LLGGPS-239 (SEQ ID NO:172), which correspond to aas 14-19 of **FIG. 21A**) of IgG are involved in binding to the Fc lambda receptor (FcλR), and accordingly, mutations at that location reduce binding to the receptor (relative to the wt. protein). In some cases, the dimerization sequence of a scaffold polypeptide present in a TMP comprises an aa sequence depicted in **FIG. 21A** (human IgG1 Fc), except for a substitution of L235 (L15 of the aa sequence depicted in **FIG. 21A**) with an aa other than leucine. In some cases, the dimerization sequence of a scaffold polypeptide present in a TMP

comprises an aa sequence depicted in **FIG. 21A** (e.g., the wt. human IgG1 sequence) with L234A and L235A(“LALA”) substitutions (the positions corresponding to positions 14 and 15 of the wt. aa sequence depicted in **FIG. 21A**; see, e.g., SEQ ID NO:113). See **FIG. 21B**. These two mutations will reduce or substantially eliminate the ability of the IgG1 Fc to induce cell lysis, e.g., through activation of complement-dependent cytotoxicity (CDC) and/or antibody-dependent cellular cytotoxicity (ADCC).

[0094] In some cases, the dimerization sequence of a scaffold polypeptide present in TMP comprises an aa sequence depicted in **FIG. 21A** (human IgG1 Fc), having a substitution of P331 (P111 of the aa sequence depicted in **FIG. 21A**) with an aa other than proline; in some cases, the substitution is a P331S substitution. Substitutions at P331, like those at N297, lead to reduced binding to C1q relative to the wt. protein, and thus a reduction in complement-dependent cytotoxicity. Substitutions of D270, K322, and/or P329 (corresponding to D50, K122, and P119 of **FIG. 21A**), for example with alanine, may be utilized alone or in place of a P331 substitution to reduce binding to C1q. As noted above, in some cases, the dimerization sequence of a scaffold polypeptide present in a TMP is an IgG1 Fc polypeptide that comprises L234A and/or L235A substitutions (substitutions of leucines at L14 and/or L15 of the aa sequences depicted in **FIG. 21A** with Ala). See **FIG. 21B**. In some cases, the dimerization sequence of a scaffold polypeptide present in a TMP comprises the aa sequence depicted in **FIG. 21A** (wt. human IgG1 Fc), except for substitutions at L234 and/or L235 (L14 and/or L15 of the aa sequence depicted in **FIG. 21A**) with aas other than leucine, and a substitution of P331 (P111 of the aa sequence depicted in **FIG. 2D**) with an aa other than proline. In some cases, the dimerization sequence of a scaffold polypeptide present in a TMP comprises the “Triple Mutant” aa sequence depicted in **FIG. 21E** (human IgG1 Fc) comprising L234F, L235E, and P331S substitutions (corresponding to aa positions 14, 15, and 111 of the aa sequence depicted in **FIG. 21E**).

[0095] As noted above, the Ig Fc polypeptides of each polypeptide chain of a heterodimeric TMP may comprise interspecific dimerization sequences, e.g., KiH sequences that permit the two chains to selectively dimerize. Interspecific binding sequences favor formation of heterodimers with their cognate polypeptide sequence (i.e., the interspecific sequence and its counterpart interspecific sequence), particularly those based on Ig Fc sequence variants. Such interspecific polypeptide sequences include KiH, and KiH sequences that facilitate the formation of one or more disulfide bonds. For example, one interspecific binding pair comprises a T366Y and Y407T mutant pair in the CH3 domain interface of IgG1, or the corresponding residues of other immunoglobulins. See Ridgway et al., *Protein Engineering* 9:7, 617-621 (1996). A second interspecific binding pair involves the formation of a knob by a T366W substitution, and a hole by the triple substitutions T366S, L368A and Y407V on the complementary Ig Fc sequence. See Xu et al. *mAbs* 7:1, 231-242 (2015). Another interspecific binding pair has a first Fc polypeptide with Y349C, T366S, L368A, and Y407V substitutions and a second Ig Fc polypeptide with S354C, and T366W substitutions (disulfide bonds can form between the Y349C and the S354C). See,

e.g., Brinkmann and Konthermann, *mAbs* 9:2, 182–212 (2015). Ig Fc polypeptide sequences, either with or without KiH modifications, can be stabilized by the formation of disulfide bonds between the Ig Fc polypeptides (e.g., the hinge region disulfide bonds).

[0096] Several interspecific binding sequences based upon immunoglobulin sequences are summarized in Table 1, below, with cross reference to the numbering of the aa positions as they appear in the wt IgG1 sequence set forth in **FIG. 21A** shown in brackets “{ }”. In **FIG. 21A**: i) hinge: amino acids 1-10; ii) CH2: amino acids 11-120; iii) CH3: amino acids 121-227; iv) Fc amino acids 11-227.

Table 1. Interspecific immunoglobulin sequences and their cognate counterpart interspecific sequences

Interspecific Pair Name	Substitutions in the first interspecific polypeptide sequence	Substitutions in the second (counterpart) interspecific polypeptide sequence	Comments
KiH	T366W {T146W}	T366S/L368A/Y407V {T146S/L148A/Y187V}	Hydrophobic/steric complementarity
KiHs-s	T366W/S354C* {T146W/S134C*}	T366S/L368A/Y407V/Y349C {T146S/L148A/Y187V/Y129C}	KiH + inter-CH3 domain S-S bond
HA-TF	S364H/F405A {S144H/F185A}	Y349T/T394F {Y129T/T174F}	Hydrophobic/steric complementarity
ZW1	T350V/L351Y/F405A/ Y407V {T130V/L131Y/F185A/Y187V}	T350V/T366L/K392L/T394W {T130V/T146L/K172L/T174W}	Hydrophobic/steric complementarity
7.8.60	K360D/D399M/Y407A {K140D/D179M/Y187A}	E345R/Q347R/T366V/K409V {E125R/Q127R/T146V/K189V}	Hydrophobic/steric complementarity + electrostatic complementarity
DD-KK	K409D/K392D {K189D/K172D}	D399K/E356K {D179K/E136K}	Electrostatic complementarity
EW-RVT	K360E/K409W {K140E/K189W}	Q347R/D399V/F405T {Q127R/D179V/F185T}	Hydrophobic/steric complementarity & long-range electrostatic interaction
EW-RVTs-s	K360E/K409W/Y349C* {K140E/K189W/Y129C*}	Q347R/D399V/F405T/S354C {Q127R/D179V/F185T/S134C}	EW-RVT + inter-CH3 domain S-S bond
A107	K370E/K409W {K150E/K189W}	E357N/D399V/F405T {E137N/D179V/F185T}	Hydrophobic/steric complementarity + hydrogen bonding complementarity

Table 1 modified from Ha et al., *Frontiers in Immunol.* 7:1-16 (2016).

* aa forms a stabilizing disulfide bond.

[0097] In addition to the interspecific pairs of sequences in Table 1, Ig Fc polypeptides may include interspecific “SEED” sequences having 45 residues derived from IgA in an IgG1 CH3 domain of the interspecific sequence, and 57 residues derived from IgG1 in the IgA CH3 in its counterpart interspecific sequence. See Ha et al., *Frontiers in Immunol.* 7:1-16 (2016).

[0098] An Ig Fc polypeptide present in a TMP may comprise an interspecific binding sequence or its counterpart interspecific binding sequence selected from the group consisting of: knob-in-hole (KiH); knob-in-hole with a stabilizing disulfide (KiHs-s); HA-TF; ZW-1; 7.8.60; DD-KK; EW-RVT; EW-RVTs-s; A107; or SEED sequences.

[0099] A TMP may comprise an Ig Fc polypeptide comprising a T146W KiH sequence substitution, and its counterpart interspecific binding partner polypeptide comprises an Ig Fc polypeptide having T146W, L148A, and Y187V KiH sequence substitutions, where the Ig Fc polypeptides comprise a sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of **FIG. 21A**. One or both of the Ig Fc polypeptides optionally comprising substitutions at one or more of: L234 and L235 (e.g., L234A/L235A “LALA” or L234F/L235E); N297 (e.g., N297A); P331 (e.g., P331S); L351 (e.g., L351K); T366 (e.g., T366S); P395 (e.g., P395V); F405 (e.g., F405R); Y407 (e.g., Y407A); and K409 (e.g., K409Y). Those substitutions appear at: L14 and L15 (e.g., L14A/L15A “LALA” or L14F/L15E); N77 (e.g., N77A); P111 (e.g., P111S); L131 (e.g., L131K); T146 (e.g., T146S); P175 (e.g., P175V); F185 (e.g., F185R); Y187 (e.g., Y187A); and K189 (e.g., K189Y) in the wt IgG1 sequence of **FIG. 21A**.

[00100] A TMP in some cases comprises an Ig Fc polypeptide comprising a T146W KiH sequence substitution, and its counterpart interspecific binding partner Ig Fc polypeptide comprises T146S, L148A, and Y187V KiH sequence substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt. IgG1 of **FIG. 21A**; where one or both of the Ig Fc polypeptides may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A), and/or N77 (N297 e.g., N297A or N297G).

[00101] A TMP in some cases comprises an Ig Fc polypeptide comprising T146W and S134C KiHs-s substitutions, and its counterpart interspecific binding partner Ig Fc polypeptide comprises T146S, L148A, Y187V and Y129C KiHs-s substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of **FIG. 21A**; where one or both of the Ig Fc polypeptides may comprise additional substitutions such as L14

and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A), and/or N77 (N297 e.g., N297A or N297G).

[00102] A TMP in some cases comprises an Ig Fc polypeptide comprising S144H and F185A HA-TF substitutions, and its counterpart interspecific binding partner Ig Fc polypeptide comprises Y129T and T174F HA-TF substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of FIG. 21A; where one or both of the Ig Fc polypeptides may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A), and/or N77 (N297 e.g., N297A or N297G).

[00103] A TMP in some cases comprises an Ig Fc polypeptide comprising T130V, L131Y, F185A, and Y187V ZW1 substitutions, and its counterpart interspecific binding partner Ig Fc polypeptide comprises T130V, T146L, K172L, and T174W ZW1 substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of FIG. 21A; where one or both of the Ig Fc polypeptide sequences may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A), and/or N77 (N297 e.g., N297A or N297G).

[00104] A TMP in some cases comprises an Ig Fc polypeptide comprising K140D, D179M, and Y187A 7.8.60 substitutions, and its counterpart interspecific binding partner Ig Fc polypeptide comprises T130V E125R, Q127R, T146V, and K189V 7.8.60 substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of FIG. 21A; where one or both of the Ig Fc polypeptide sequences may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A), and/or N77 (N297 e.g., N297A or N297G).

[00105] A TMP in some cases comprises an Ig Fc polypeptide comprising K189D and K172D DD-KK substitutions, and its counterpart interspecific binding partner Ig Fc polypeptide comprises an IgG1 sequence having T130V D179K and E136K DD-KK substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of FIG. 21A; where one or both of the Ig Fc polypeptides may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A), and/or N77 (N297 e.g., N297A or N297G).

[00106] A TMP in some cases comprises an Ig Fc polypeptide comprising K140E and K189W EW-RVT substitutions, its counterpart interspecific binding partner Ig Fc polypeptide comprises T130V Q127R, D179V, and F185T EW-RVT substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of FIG. 21A; where one or both of the Ig Fc polypeptides may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A; corresponding to L14 and L15 of the amino acid sequence depicted in FIG. 21A), and/or N77 (N297 e.g., N297A or N297G).

[00107] A TMP in some cases comprises an Ig Fc polypeptide comprising K140E, K189W, and Y129C EW-RVTs-s substitutions, its counterpart interspecific binding partner Ig Fc polypeptide comprises T130V Q127R, D179V, F185T, and S134C EW-RVTs-s substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of **FIG. 21A**. One or both of the Ig Fc polypeptides may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A; corresponding to L14 and L15 of the amino acid sequence depicted in FIG. 21A), and/or N77 (N297 e.g., N297A or N297G).

[00108] A TMP in some cases comprises an Ig Fc polypeptide comprising K150E and K189W A107 substitutions, its counterpart interspecific binding partner Ig Fc polypeptide comprises T130V E137N, D179V, and F185T A107 substitutions, where the Ig Fc polypeptides comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, or at least 97% sequence identity to at least 100 (e.g., at least 125, 150, 170, 180, 190, 200, 210, 220, or all 227) contiguous aas of the wt IgG1 of **FIG. 21A**; where one or both of the Ig Fc polypeptides may comprise additional substitutions such as L14 and/or L15 substitutions (e.g., “LALA” substitutions L234A and L235A), and/or N77 (N297 e.g., N297A or N297G).

[00109] As one non-limiting example, in some cases: a) the first polypeptide of a TMP comprises an Ig Fc polypeptide (referred to in FIG. 26A as “IgG Fc (LALA) KiH Chain A (S354C; T366W)” comprising an amino acid sequence having at least 90%, at least 95%, or at least 98%, to the following amino acid sequence:

DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ
VYTLPPCREMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:173), where amino acid 14 is
Leu, amino acid 15 is Leu, amino acid 134 is Cys, and amino acid 146 is Trp.

[00110] and b) the second polypeptide of the TMP comprises an Ig Fc polypeptide (referred to in FIG. 26B as “IgG Fc (LALA) KiH Chain B (Y349C, T366S, L368A, Y407V)”) comprising an amino acid sequence having at least 90%, at least 95%, or at least 98%, to the following amino acid sequence: DKHTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPSSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFNFSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:174), where amino acid 14 is Leu, amino acid 15 is Leu, amino acid 129 is Cys, amino acid 146 is Ser, amino acid 148 is Ala, and amino acid 187 is Val.

[00111] In some cases, a) the first polypeptide of a TMP comprises an Ig Fc polypeptide (referred to in FIG. 26A as “IgG Fc (LALA) KiH Chain A (S354C; T366W)”) having the following amino acid sequence:

DKHTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFNFSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:173); and b) the second the second polypeptide of the TMP comprises an Ig Fc polypeptide (referred to in FIG. 26B as “IgG Fc (LALA) KiH Chain B (Y349C, T366S, L368A, Y407V)”) having the following amino acid sequence: DKHTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFNFSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:173).

B) HETERODIMERIC TMPs COMPRISING DISULFIDE LINKAGES

[00112] A TMP of the present disclosure in some cases comprises one or more heterodimers, where each heterodimer comprises: a) a first polypeptide chain comprising: i) a T1D peptide; and a first MHC class II polypeptide; and b) a second polypeptide comprising a second MHC class II polypeptide, where the first and/or the second polypeptide comprises one or more MODs, where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide; where the TMP optionally includes one or more independently selected linker polypeptides, and where the first or the second polypeptide chain comprises an Ig Fc polypeptide. In some cases, the first polypeptide comprises the TGF- β polypeptide and the second polypeptide comprises the masking polypeptide. In some cases, the first polypeptide comprises the masking polypeptide and the second polypeptide comprises the TGF- β polypeptide. In some cases, the first polypeptide comprises the TGF- β polypeptide and the masking polypeptide, and the second polypeptide does not comprise a TGF- β polypeptide or a masking polypeptide. In some cases, the first

polypeptide does not comprise a TGF- β polypeptide or a masking polypeptide, and the second polypeptide comprises the TGF- β polypeptide and the masking polypeptide. A TMP of the present disclosure can be a homodimer comprising two such heterodimers, where the Ig Fc polypeptide of one of the heterodimers is disulfide linked to the Ig Fc polypeptide of the other heterodimer. Non-limiting examples of such TMPs are depicted schematically in **FIG. 2A-2D**. A TMP can comprise two disulfide-linked heterodimers. When both heterodimers include Ig Fc polypeptides, disulfide bonds will spontaneously form between the respective Ig Fc polypeptides to covalently link the two heterodimers to one another. Alternatively, a TMP of the present disclosure can be a heterodimer comprising two such heterodimers, where the Ig Fc polypeptide of one of the heterodimers is disulfide linked to the Ig Fc polypeptide of the other heterodimer using interspecific binding sequences as discussed above.

Arrangement of components

[00113] In some cases, a TMP comprise at least one heterodimer, wherein each heterodimer comprises: a) a first polypeptide comprising: i) a T1D peptide; and ii) a first MHC class II polypeptide; and iii) optionally a linker that links the T1D peptide to the first MHC class II polypeptide; and b) a second polypeptide comprising the second MHC class II polypeptide, wherein the first and/or the second polypeptide comprises the one or more MODs, wherein the first or the second polypeptide comprises the TGF- β polypeptide, and wherein the first or the second polypeptide comprises the masking polypeptide, and optionally where the first polypeptide and the second polypeptide of the heterodimer are covalently linked to one another via at least one disulfide bond.

[00114] In some cases, a TMP comprise at least one heterodimer, wherein each heterodimer comprises: a) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II α chain polypeptide or an MHC class II β chain polypeptide; ii) optionally a linker that links the T1D peptide to the first MHC class II polypeptide; and b) a second polypeptide comprising i) an MHC class II α chain polypeptide if the first polypeptide comprises an MHC class II β chain polypeptide, or ii) an MHC class II β chain polypeptide if the first polypeptide comprises an MHC class II α chain polypeptide, wherein: i) the first and/or the second polypeptide comprises the one or more MODs; ii) the first or the second polypeptide comprises the TGF- β polypeptide; and iii) the first or the second polypeptide comprises the masking polypeptide; optionally wherein the first polypeptide and the second polypeptide of the heterodimer are covalently linked to one another via at least one disulfide bond; and optionally where the TMP optionally comprises one or more independently selected linker polypeptides (e.g., where each of the one or more independently selected linker polypeptides is between any two of the aforementioned polypeptides).

[00115] As a first non-limiting example, in some cases a TMP comprises: a1) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; and b1) a second polypeptide comprising: i) an MHC class II α polypeptide; ii) a TGF- β polypeptide; iii) a masking polypeptide; iv)

one or more MODs; and v) an Ig Fc polypeptide. In some cases, the components of the first polypeptide are joined by one or more independently selected linkers, and in some cases the components of the second polypeptide are joined by one or more independently selected linkers.

[00116] As a second non-limiting example, in some cases a TMP comprises: a2) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; and iii) a TGF- β polypeptide or a masking polypeptide, and b2) a second polypeptide comprising: i) an MHC class II α polypeptide; ii) a masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or a TGF- β polypeptide if the first polypeptide comprises the masking polypeptide; iii) one or more MODs; and iv) an Ig Fc polypeptide. In some cases, the components of the first polypeptide are joined by one or more independently selected linkers, and in some cases the components of the second polypeptide are joined by one or more independently selected linkers.

[00117] As a third non-limiting example, in some cases a TMP comprises: a3) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) a TGF- β polypeptide or a masking polypeptide; and iv) an Ig Fc polypeptide, and b3) a second polypeptide comprising: i) an MHC class II α polypeptide; ii) a masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or a TGF- β polypeptide if the first polypeptide comprises the masking polypeptide; iii) one or more MODs. In some cases, the components of the first polypeptide are joined by one or more independently selected linkers, and in some cases the components of the second polypeptide are joined by one or more independently selected linkers.

[00118] As a fourth non-limiting example, in some cases a TMP comprises: a4) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) a TGF- β polypeptide or a masking polypeptide; and iv) one or more MODs, and b4) a second polypeptide comprising: i) an MHC class II α polypeptide; ii) a masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or a TGF- β polypeptide if the first polypeptide comprises the masking polypeptide; iii) an Ig Fc polypeptide. In some cases, the components of the first polypeptide are joined by one or more independently selected linkers, and in some cases the components of the second polypeptide are joined by one or more independently selected linkers.

[00119] As a fifth non-limiting example, in some cases a TMP comprises: a5) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) a TGF- β polypeptide or a masking polypeptide; and iv) one or more MODs; and v) an Ig Fc polypeptide; and b5) a second polypeptide comprising: i) an MHC class II α polypeptide; and ii) a masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or a TGF- β polypeptide if the first polypeptide comprises the masking polypeptide. In some cases, the components of the first polypeptide are joined by one or more independently selected linkers, and in some cases the components of the second polypeptide are joined by one or more independently selected linkers.

[00120] As a sixth non-limiting example, in some cases a TMP comprises: a6) a first polypeptide comprising: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) a TGF- β polypeptide; iv) a masking polypeptide; v) one or more MODs; and vi) an Ig Fc polypeptide; and b6) a second polypeptide comprising an MHC class II α polypeptide. In some cases, the components of the first polypeptide are joined by one or more independently selected linkers.

[00121] In some cases, as depicted schematically in **FIG. 2A**, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a masking polypeptide; and iv) an Ig Fc polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) an MHC class II α chain polypeptide; ii) a TGF- β polypeptide; and iii) one or more MODs, where the TMP optionally includes one or more independently selected linker polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

[00122] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a TGF- β polypeptide; and iv) an Ig Fc polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) an MHC class II α chain polypeptide; ii) a masking polypeptide; and iii) one or more MODs, where the TMP optionally includes one or more independently selected linker polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

[00123] In some cases, as depicted schematically in **FIG. 2B**, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a masking polypeptide; iv) an Ig Fc polypeptide; and v) one or more MODs; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) an MHC class II α chain polypeptide; ii) a TGF- β polypeptide, where the TMP optionally includes one or more independently selected linker polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

[00124] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a TGF- β polypeptide; iv) an Ig Fc polypeptide; and v) one or more MODs; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) an MHC class II α chain polypeptide; ii) a masking polypeptide, where the TMP optionally includes one or more independently selected linker

polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

[00125] In some cases, as depicted schematically in **FIG. 2C**, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a masking polypeptide; and iv) an Ig Fc polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) an MHC class II α chain polypeptide; and iii) a TGF- β polypeptide, where the TMP optionally includes one or more independently selected linker polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

[00126] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a TGF- β polypeptide; and iv) an Ig Fc polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) an MHC class II α chain polypeptide; and iii) a masking polypeptide, where the TMP optionally includes one or more independently selected linker polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

[00127] In some cases, as depicted schematically in **FIG. 2D**, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a masking polypeptide; and iv) a TGF- β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) an MHC class II α chain polypeptide; and iii) an Ig Fc polypeptide, where the TMP optionally includes one or more independently selected linker polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

[00128] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) a TGF- β polypeptide; and iv) a masking polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) an MHC class II α chain polypeptide; and iii) an Ig Fc polypeptide, where the TMP optionally includes one or more independently selected linker polypeptides between any two of the components. The first and the second polypeptides are covalently linked to one another by disulfide bonds, e.g., disulfide bonds formed between Cys residues in the MHC class II α and β chains, as described below.

DISULFIDE LINKAGES

[00129] As noted above, the first polypeptide and the second polypeptide of a heterodimer of a TMP are covalently linked to one another via at least one disulfide bond. For example, the at least one disulfide bond is present between: i) a Cys present in the first MHC class II polypeptide and a Cys present in the second MHC class II polypeptide; or ii) a Cys present in a peptide linker in the first polypeptide and a Cys present in an MHC class II polypeptide present in the second polypeptide; or iii) a Cys present in a peptide linker in the second polypeptide and a Cys present in an MHC class II polypeptide present in the first polypeptide; or iv) a Cys present in a linker in the first polypeptide and a Cys present in a linker in the second polypeptide.

1) Disulfide Bond Between the Two MHC class II Polypeptides

[00130] As noted above, in some cases, the first polypeptide of a heterodimer of a TMP comprises a first MHC class II polypeptide comprising an amino acid substitution that results in a Cys (a “first Cys”); and the second polypeptide comprises a second MHC class II polypeptide comprising an amino acid substitution that results in a Cys (a “second Cys”); where the heterodimer comprises a disulfide bond formed between the first Cys and the second Cys. For example, in some cases, the first polypeptide comprises an MHC class II β polypeptide comprising an amino acid substitution that results in a Cys (a “first Cys”); and the second polypeptide comprises an MHC class II α polypeptide comprising an amino acid substitution that results in a Cys (a “second Cys”); where the heterodimer comprises a disulfide bond formed between the first Cys and the second Cys.

Arrangement of components

[00131] In some cases, for example, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; and ii) a first MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “first Cys”), the components of the first polypeptide optionally being joined by a linker that does not comprise a Cys; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) a second MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “second Cys”); and iii) optionally an Ig Fc polypeptide, the components of the second polypeptide optionally being joined by one or more linkers that do not comprise a Cys; where the first polypeptide and the second polypeptide are linked via a disulfide bond between the first Cys and the second Cys; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In

some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the first MHC class II polypeptide is an MHC class II β chain polypeptide and the second MHC class II polypeptide is an MHC class II α chain polypeptide.

[00132] As another example, in some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; and ii) a first MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “first Cys”), the components of the first polypeptide optionally being joined by a linker that does not comprise a Cys; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “second Cys”); ii) one or more MODs; and iii) optionally an Ig Fc polypeptide, the components of the second polypeptide optionally being joined by one or more linkers that do not comprise a Cys; where the first polypeptide and the second polypeptide are linked via a disulfide bond between the first Cys and the second Cys; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the first MHC class II polypeptide is an MHC class II β chain polypeptide and the second MHC class II polypeptide is an MHC class II α chain polypeptide.

[00133] As another example, in some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; and ii) a first MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “first Cys”), the components of the first polypeptide optionally being joined by a linker that does not comprise a Cys; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “second Cys”); ii) an Ig Fc polypeptide; and iii) one or more MODs, the components of the second polypeptide optionally being joined by a linker that does not comprise a Cys; where the first polypeptide and the second polypeptide are linked via a disulfide bond between the first Cys and the second Cys; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above

embodiments, in some cases, the first MHC class II polypeptide is an MHC class II β chain polypeptide and the second MHC class II polypeptide is an MHC class II α chain polypeptide.

[00134] As another example, in some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) a T1D peptide; and iii) a first MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “first Cys”), the components of the first polypeptide optionally being joined by one or more linkers that do not comprise a Cys; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “second Cys”); and ii) optionally an Ig Fc polypeptide, where when the optional Ig Fc is present, the components of the second polypeptide are optionally joined by a linker that does not comprise a Cys; where the first polypeptide and the second polypeptide are linked via a disulfide bond between the first Cys and the second Cys; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the first MHC class II polypeptide is an MHC class II β chain polypeptide and the second MHC class II polypeptide is an MHC class II α chain polypeptide.

[00135] As another example, in some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) a first MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “first Cys”); and iii) one or more MODs, the components of the first polypeptide optionally being joined by one or more linkers that do not comprise a Cys; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) a second MHC class II polypeptide comprising a substitution of an amino acid (other than a Cys) with a Cys (a “second Cys”); and ii) optionally an Ig Fc polypeptide, where when the optional Ig Fc is present, the components of the second polypeptide are optionally joined by a linker that does not comprise a Cys; where the first polypeptide and the second polypeptide are linked via a disulfide bond between the first Cys and the second Cys; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some

cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the first MHC class II polypeptide is an MHC class II β chain polypeptide and the second MHC class II polypeptide is an MHC class II α chain polypeptide.

Location of Cys residues

[00136] As noted above, in some cases, a TMP in some cases comprises a heterodimer comprising a first polypeptide chain comprising: i) a T1D peptide; and ii) a first MHC class II polypeptide; and b) a second polypeptide comprising a second MHC class II polypeptide, where the first and/or the second polypeptides comprise one or more MODs, where the first or the second polypeptide comprises a masking polypeptide, and where the first or the second polypeptide comprises a TGF- β polypeptide, optionally wherein the first and/or the second polypeptide comprises an Ig Fc polypeptide; where the first MHC class II polypeptide comprises a substitution of an amino acid (other than a Cys) with a Cys (a “first Cys”), and the second MHC class II polypeptide comprises a substitution of an amino acid (other than a Cys) with a Cys (a “second” Cys), where the first polypeptide and the second polypeptide are joined by a disulfide bond formed between the first Cys and the second Cys.

[00137] The first MHC class II polypeptide can be a DRB MHC class II polypeptide comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 5 or FIG. 20A** and having an amino acid substitution selected from P5C, F7C, Q10C, N19C, G20C, H33C, G151C, D152C, and W153C. The second MHC class II polypeptide can be a DRA MHC class II polypeptide comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in **FIG. 4 or FIG. 19A** and having an amino acid substitution selected from E3C, E4C, F12C, G28C, D29C, I72C, K75C, T80C, P81C, I82C, T93C, N94C, and S95C.

[00138] As one example, in some cases, the first MHC class II polypeptide is a DRB MHC class II polypeptide comprising a substitution at a residue selected from the group consisting of P5C, H33C, G151C, and W153, and the second MHC class II polypeptide is a DRA MHC class II polypeptide comprising a substitution selected from the group consisting of P81C, I82C, and D29C. For example, the MHC class II β chain polypeptide can comprise an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 5 or FIG. 20A**, where the polypeptide comprises a Cys at a residue position selected from the group consisting of 5, 33, 151, and 153; and the MHC class II α chain polypeptide can comprise an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence

depicted in **FIG. 4 or FIG. 19A**, where the polypeptide comprises a Cys at a residue selected from the group consisting of 81, 82, and 29.

[00139] As another example, the disulfide can be formed between one of the specific pairs of Cys residues in Table 2, below:

Table 2

DRB MHC Class II Polypeptide Substitution	DRA MHC Class II Polypeptide Substitution
N19C	E3C
G20C	E3C
N19C	E4C
G20C	E4C
F7C	F12C
Q10C	F12C
G151C	G28C
D152C	G28C
W153C	G28C
G151C	D29C
D152C	D29C
W153C	D29C
F7C	T80C
P5C	T80C
H33C	T80C
P5C	P81C
H33C	P81C
F7C	P81C
H33C	I82C
F7C	I82C
P5C	I82C
Q156C	T93C
W153C	T93C
Q156C	N94C
N120C	N94C
Q156C	S95C
N120C	S95C

[00140] For example, the DRB MHC class II polypeptide can comprise an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 5** or **FIG. 20A**, and the DRA MHC class II polypeptide can comprise an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 4** or **FIG. 19A**, wherein the β chain polypeptide and α chain polypeptides are joined by a disulfide formed between a pair of Cys residues selected from the group consisting of: β chain polypeptide residue 5 and α chain polypeptide residue 81; β chain polypeptide residue 33 and α chain polypeptide residue 81; β chain polypeptide residue 33 and α chain polypeptide residue 82; β chain polypeptide residue 151 and α chain polypeptide residue 29; and β chain polypeptide residue 153 and α chain polypeptide residue 29.

[00141] In some cases, a TMP comprises a DRB MHC class II polypeptide comprising a P5C substitution and a DRA MHC class II polypeptide comprising a P81C substitution; where the first polypeptide and the second polypeptide of the TMP are linked via a disulfide bond between the Cys at residue 5 in the DRB MHC class II polypeptide and the Cys at residue 81 in the DRA MHC class II polypeptide. In some cases, linkers that do not comprise a Cys optionally can be used to connect the components of the first or second polypeptide. In some cases, the one or more MODs present in the TMP is a PD-L1 polypeptide or variant thereof, an IL-2 polypeptide or variant thereof, or a FasL polypeptide or variant thereof. In some cases, the TMP comprises an Ig Fc polypeptide, and in some cases, the IgFc polypeptide is a human IgG1 Fc polypeptide, optionally comprising L234A and L235A substitutions (L14A and L15A of the amino acid sequence depicted in **FIG. 21A**). In some cases, the DRB MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 20B**, and comprises a Cys at position 5. In some cases, the DRA MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 19J**, and comprises a Cys at position 81. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90). In some cases, the T1D peptide is a GAD peptide. In some cases, the T1D peptide is a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).

[00142] In some cases, a TMP comprises a DRB MHC class II polypeptide comprising an H33C substitution and a DRA MHC class II polypeptide comprising a P81C substitution, where the first

polypeptide and the second polypeptide of the TMP are linked via a disulfide bond between the Cys at residue 33 in the DRB MHC class II polypeptide and the Cys at residue 81 in the DRA MHC class II polypeptide. In some cases, linkers that do not comprise a Cys optionally can be used to connect the components of the first or second polypeptide. In some cases, the one or more MODs present in the TMP is a PD-L1 polypeptide or variant thereof, an IL-2 polypeptide or variant thereof, or a FasL polypeptide or variant thereof. In some cases, the TMP comprises an Ig Fc polypeptide, and in some cases, the IgFc polypeptide is a human IgG1 Fc polypeptide, optionally comprising L234A and L235A substitutions (L14A and L15A of the amino acid sequence depicted in **FIG. 21A**). In some cases, the DRB MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 20G**, and comprises a Cys at position 33. In some cases, the DRA MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 19J**, and comprises a Cys at position 81. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90). In some cases, the T1D peptide is a GAD peptide. In some cases, the T1D peptide is a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).

[00143] In some cases, a TMP comprises a DRB MHC class II polypeptide comprising an H33C substitution and a DRA MHC class II polypeptide comprising a I82C substitution, where the first polypeptide and the second polypeptide of the TMP are linked via a disulfide bond between the Cys at residue 33 in the DRB MHC class II polypeptide and the Cys at residue 81 in the DRA MHC class II polypeptide. In some cases, linkers that do not comprise a Cys optionally can be used to connect the components of the first or second polypeptide. In some cases, the one or more MODs present in the TMP is a PD-L1 polypeptide or variant thereof, an IL-2 polypeptide or variant thereof, or a FasL polypeptide or variant thereof. In some cases, the TMP comprises an Ig Fc polypeptide, and in some cases, the IgFc polypeptide is a human IgG1 Fc polypeptide, optionally comprising L234A and L235A substitutions (L14A and L15A of the amino acid sequence depicted in **FIG. 21A**). In some cases, the DRB MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 20G**, and comprises a Cys at position 33. In some cases, the DRA MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 19K**, and comprises a Cys at position 82. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the

T1D peptide is a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90). In some cases, the T1D peptide is a GAD peptide. In some cases, the T1D peptide is a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).

[00144] In some cases, a TMP comprises a DRB MHC class II polypeptide comprising an G151C substitution and a DRA MHC class II polypeptide comprising a D29C substitution, where the first polypeptide and the second polypeptide of the TMP are linked via a disulfide bond between the Cys at residue 33 in the DRB MHC class II polypeptide and the Cys at residue 81 in the DRA MHC class II polypeptide. In some cases, linkers that do not comprise a Cys optionally can be used to connect the components of the first or second polypeptide. In some cases, the one or more MODs present in the TMP is a PD-L1 polypeptide or variant thereof, an IL-2 polypeptide or variant thereof, or a FasL polypeptide or variant thereof. In some cases, the TMP comprises an Ig Fc polypeptide, and in some cases, the IgFc polypeptide is a human IgG1 Fc polypeptide, optionally comprising L234A and L235A substitutions (L14A and L15A of the amino acid sequence depicted in **FIG. 21A**). In some cases, the DRB MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 20H**, and comprises a Cys at position 151. In some cases, the DRA MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 19F**, and comprises a Cys at position 29. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175 proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90). In some cases, the T1D peptide is a GAD peptide. In some cases, the T1D peptide is a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).

[00145] In some cases, a TMP comprises a DRB MHC class II polypeptide comprising a W153C substitution and a DRA MHC class II polypeptide comprising a D29C substitution, where the first polypeptide and the second polypeptide of the TMP are linked via a disulfide bond between the Cys at residue 33 in the DRB MHC class II polypeptide and the Cys at residue 81 in the DRA MHC class II polypeptide. In some cases, linkers that do not comprise a Cys optionally can be used to connect the components of the first or second polypeptide. In some cases, the one or more MODs present in the TMP is a PD-L1 polypeptide or variant thereof, an IL-2 polypeptide or variant thereof, or a FasL polypeptide or variant thereof. In some cases, the TMP comprises an Ig Fc polypeptide, and in some cases, the IgFc polypeptide is a human IgG1 Fc polypeptide, optionally comprising L234A and L235A substitutions

(L14A and L15A of the amino acid sequence depicted in **FIG. 21A**). In some cases, the DRB MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 20J**, and comprises a Cys at position 153. In some cases, the DRA MHC class II polypeptide comprises an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the amino acid sequence depicted in **FIG. 19F**, and comprises a Cys at position 29. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90). In some cases, the T1D peptide is a GAD peptide. In some cases, the T1D peptide is a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).

2) Disulfide Bond Between a Peptide Linker and an MHC class II Polypeptide

[00146] In some cases, the TMP comprises a peptide linker between the T1D peptide and the MHC class II polypeptide. Where desired, the linker can comprise a Cys that can be used to form a disulfide bond between the two polypeptides in the heterodimer.

Arrangement of components

[00147] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) a peptide linker comprising a Cys; iii) an MHC class II β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus (optionally including one or more linkers that do not comprise a Cys): i) one or more MODs; ii) an MHC class II α chain; and (optionally) iii) an Ig Fc polypeptide; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. The peptide linker comprising a Cys can comprise an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). In any of the above embodiments, in some cases the MOD is a PD-L1 polypeptide or variant thereof, in some cases the MOD is an IL-2 polypeptide or variant thereof, and in some cases the MOD is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the MHC class II α chain comprises an amino acid substitution of an amino acid (other than a Cys) with a Cys, such that the Cys in the MHC class II α chain forms a disulfide bond with the Cys in the first polypeptide linker.

[00148] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) a peptide linker comprising a Cys; and iii) an MHC class II β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus (optionally including one or more linkers that do not comprise a Cys): i) an MHC class II α chain; ii) one or more MODs; and iii) an Ig Fc polypeptide; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. The peptide linker comprising a Cys can comprise, e.g., an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). Other peptide linkers comprising a Cys may be used. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the MHC class II α chain comprises an amino acid substitution of an amino acid (other than a Cys) with a Cys, such that the Cys in the MHC class II α chain forms a disulfide bond with the Cys in the linker.

[00149] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) a peptide linker comprising a Cys; and iii) an MHC class II β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus (optionally including one or more linkers that do not comprise a Cys): i) an MHC class II α chain; and ii) one or more MODs; where the first or the second polypeptide comprises an Ig Fc polypeptide, where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. The peptide linker comprising a Cys can comprise, e.g., an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). Other peptide linkers comprising a Cys may be used. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the MHC class II α

chain comprises an amino acid substitution of an amino acid (other than a Cys) with a Cys, such that the Cys in the MHC class II α chain forms a disulfide bond with the Cys in the linker.

[00150] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) a T1D peptide; ii) a peptide linker comprising a Cys; and iii) an MHC class II β polypeptide; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) an MHC class II α chain; and (optionally) ii) an Ig Fc polypeptide, optionally joined by a linker that does not comprise a Cys; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. The peptide linker comprising a Cys can comprise, e.g., an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). Other peptide linkers comprising a Cys may be used. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the MHC class II α chain comprises an amino acid substitution of an amino acid (other than a Cys) with a Cys, such that the Cys in the MHC class II α chain forms a disulfide bond with the Cys in the linker.

[00151] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) a peptide linker comprising a Cys; iii) an MHC class II β polypeptide; and iv) one or more MODs; and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) an MHC class II α chain; and (optionally) ii) an Ig Fc polypeptide, optionally joined by a linker that does not comprise a Cys; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. The peptide linker comprising a Cys can comprise, e.g., an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). Other peptide linkers comprising a Cys may be used. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any

of the above embodiments, in some cases, the MHC class II α chain comprises an amino acid substitution of an amino acid (other than a Cys) with a Cys, such that the Cys in the MHC class II α chain forms a disulfide bond with the Cys in the linker.

Location of Cys residues

[00152] As noted above, in some cases, a TMP comprises a heterodimer comprising a first polypeptide chain comprising: i) a T1D peptide; ii) a peptide linker comprising a Cys; and iii) a first MHC class II polypeptide; and b) a second polypeptide comprising a second MHC class II polypeptide, where the first and/or the second polypeptides comprise one or more MODs, where the first or the second polypeptide comprises a TGF- β polypeptide, where the first or the second polypeptide comprises a masking polypeptide, optionally wherein the first or the second polypeptide comprises an Ig Fc polypeptide, where the second MHC class II polypeptide comprises a substitution of an amino acid (other than a Cys) with a Cys; and where the first and the second polypeptides are linked via a disulfide bond between the Cys in the peptide linker and the Cys provided by the substitution in the second MHC class II polypeptide.

[00153] For example, in some cases, the peptide linker can comprise an amino acid sequence selected from: (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, with n = 2 or 3 generally being useful); the first MHC class II polypeptide is a DRB MHC class II polypeptide; and the second MHC class II polypeptide is a DRA MHC class II polypeptide that comprises a substitution of an amino acid (other than a Cys) with a Cys.

[00154] Specific examples of the Cys-containing linkers between the T1D peptide and a DRB MHC class II polypeptide and Cys residues in the DRA MHC class II polypeptide that can form a disulfide bond are provided in Table 3, below:

Table 3

Cys-Containing Linker Between the T1D peptide and the DRB MHC Class II Polypeptide	DRA MHC class II polypeptide substitution
(CGGGS)(GGGGS) _n (SEQ ID NO:178)	I72C
(GCGGS)(GGGGS) _n (SEQ ID NO:179)	I72C
(GGCGS)(GGGGS) _n (SEQ ID NO:180)	I72C

Cys-Containing Linker Between the T1D peptide and the DRB MHC Class II Polypeptide	DRA MHC class II polypeptide substitution
(GGGCS)(GGGGS) _n (SEQ ID NO:181)	I72C
(GGGGC)(GGGGS) _n (SEQ ID NO:182)	I72C
(CGGGS)(GGGGS) _n (SEQ ID NO:178)	K75C
(GCGGS)(GGGGS) _n (SEQ ID NO:179)	K75C
(GGCGS)(GGGGS) _n (SEQ ID NO:180)	K75C
(GGGCS)(GGGGS) _n (SEQ ID NO:181)	K75C
(GGGGC)(GGGGS) _n (SEQ ID NO:182)	K75C

[00155] In some cases, where the first and second MHC class II polypeptides are DRB and DRA polypeptides, respectively, the DRB MHC class II polypeptide can comprise an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the amino acid sequence depicted in **FIG. 5** or **FIG. 20A**. The DRA MHC class II polypeptide can comprise an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in **FIG. 4** or **FIG. 19A**, and can comprise a Cys at, e.g., position 72 or position 75. In any of the above embodiments, $n = 0, 1, 2, 3, 4$ or more, with 2 or 3 typically being used to create a total linker length of 15 or 20 amino acids, although longer lengths may be possible. In any of the above embodiments, linkers that do not comprise a Cys optionally can be used to connect the other components of the first or second polypeptide. In some cases, the Ig Fc polypeptide is present and is a human IgG1 Fc polypeptide, optionally comprising L234A and L235A substitutions (L14A and L15A of the amino acid sequence depicted in **FIG. 21A**). In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90). In some cases, the T1D peptide is a GAD peptide. In some cases, the T1D peptide is a GAD peptide selected from NFFRMVISNPAAT (SEQ ID

NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I). In any of the above embodiments, in some cases, the one or more MODs is a PD-L1 polypeptide or variant thereof, a 4-1BBL polypeptide or variant thereof, an IL-2 polypeptide or variant thereof, or a FasL polypeptide or variant thereof.

3) Disulfide Bond Between Peptide Linkers in the First and Second Polypeptides

[00156] In some cases, the TMP comprises a first Cys-containing peptide linker between the T1D peptide and the MHC class II polypeptide in the first polypeptide, and a second Cys-containing peptide linker between two of the components in the second polypeptide. In such cases, the Cys residues in the first and second Cys-containing linkers can be used to form a disulfide bond between the two polypeptides in the heterodimer.

[00157] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) a first peptide linker comprising a Cys; and iii) an MHC class II β polypeptide (e.g., a DRB MHC class II polypeptide comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% amino acid sequence identity to the amino acid sequence depicted in **FIG. 5** or **FIG. 20A**); and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) one or more MODs; ii) an MHC class II α chain (e.g., a DRA MHC class II polypeptide comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% amino acid sequence identity to the amino acid sequence depicted in **FIG. 4** or **FIG. 19A**); and (optionally) iii) an Ig Fc polypeptide; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. The second polypeptide comprises a second peptide linker that comprises a Cys, where the second peptide linker is positioned either between the MOD(s) and the MHC class II α chain or between the MHC class II α chain and the Ig Fc, if present. The second polypeptide optionally may include one or more linkers that do not comprise a Cys. The peptide linkers comprising a Cys can comprise an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide.

[00158] In some cases, a TMP comprises: a) a first polypeptide comprising, in order from N-terminus to C-terminus: i) a T1D peptide; ii) a first peptide linker comprising a Cys; and iii) an MHC class II β polypeptide (e.g., a DRB MHC class II polypeptide comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% amino acid sequence identity to the amino acid sequence depicted in **FIG. 5** or **FIG. 20A**); and b) a second polypeptide comprising, in order from N-terminus to C-terminus: i) an MHC class II α chain (e.g., a DRA MHC class II polypeptide comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% amino acid sequence identity to the amino acid sequence depicted in **FIG. 4** or **FIG. 19A**); ii) an Ig Fc polypeptide; and iii) one or more MODs; where the first or the second polypeptide comprises a TGF- β polypeptide, and where the first or the second polypeptide comprises a masking polypeptide. The second polypeptide comprises a second peptide linker that comprises a Cys, where the second peptide linker is positioned either between the MHC class II α chain and the Ig Fc or between the Ig Fc and the one or more MODs. The second polypeptide optionally may include one or more linkers that do not comprise a Cys. The peptide linkers comprising a Cys can comprise an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is a proinsulin peptide. In some cases, the T1D peptide is a GAD peptide.

C) SINGLE-CHAIN TMPs

[00159] As noted above, in some cases, a TMP of the present disclosure is a single-chain (a single polypeptide chain) TMP. A single-chain TMP comprises: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) one or more MODs; v) a TGF- β polypeptide; and vi) a masking polypeptide; and optionally one or more independently selected linker polypeptides. A single-chain TMP of the present disclosure can also include an Ig Fc polypeptide. A single-chain TMP can comprise two or more MODs, where the two or more MODs can have the same amino acid sequence or different amino acid sequences. Non-limiting examples single-chain TMPs are depicted schematically in **FIG. 3A-3D**.

Arrangement of components

[00160] The arrangement of the components of a single-chain TMP can vary. As a first non-limiting example, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus:

i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) a TGF- β polypeptide or a masking polypeptide; v) a masking polypeptide or a TGF- β polypeptide; vi) an Ig Fc polypeptide; and vii) one or more MODs. The components of the single-chain TMP may be joined by one or more independently selected linkers.

[00161] As a second non-limiting example, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) a TGF- β polypeptide or a masking polypeptide; v) a masking polypeptide or a TGF- β polypeptide; vi) one or more MODs; and vii) an Ig Fc polypeptide. The components of the first polypeptide may be joined by one or more independently selected linkers.

[00162] As a third non-limiting example, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) one or more MODs; v) a TGF- β polypeptide or a masking polypeptide; vi) a masking polypeptide or a TGF- β polypeptide; and vii) an Ig Fc polypeptide. The components of the single-chain TMP may be joined by one or more independently selected linkers.

[00163] As a fourth non-limiting example, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) one or more MODs; v) an Ig Fc polypeptide; vi) a TGF- β polypeptide or a masking polypeptide; and vii) a masking polypeptide or a TGF- β polypeptide. The components of the single-chain TMP may be joined by one or more independently selected linkers.

[00164] As a fifth non-limiting example, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) an Ig Fc polypeptide; v) one or more MODs; vi) a TGF- β polypeptide or a masking polypeptide; and vii) a masking polypeptide or the TGF- β polypeptide. The components of the single-chain TMP may be joined by one or more independently selected linkers.

[00165] As a sixth non-limiting example, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) one or more MODs; v) a TGF- β polypeptide or a masking polypeptide; vi) a masking polypeptide or a TGF- β polypeptide; and vii) an Ig Fc polypeptide. The components of the single-chain TMP may be joined by one or more independently selected linkers.

[00166] As a seventh non-limiting example, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; iv) an Ig Fc polypeptide; v) a TGF- β polypeptide or a masking polypeptide; vi) a masking polypeptide or the TGF- β polypeptide; and vii) one or more MODs. The components of the single-chain TMP may be joined by one or more independently selected linkers.

[00167] In some cases, as depicted schematically in **FIG. 3A**, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a masking polypeptide; v) a TGF- β polypeptide; vi) an Ig Fc polypeptide; and vii) one or more MODs; and optionally one or more independently selected linker polypeptides. In some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) a TGF- β polypeptide; v) a masking polypeptide; vi) an Ig Fc polypeptide; and vii) one or more MODs; and optionally one or more independently selected linker polypeptides. In some cases, as depicted schematically in **FIG. 3B**, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) one or more MODs; v) an Ig Fc polypeptide; vi) a masking polypeptide; and vii) a TGF- β polypeptide; and optionally one or more independently selected linker polypeptides. In some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) one or more MODs; v) an Ig Fc polypeptide; vi) a TGF- β polypeptide; and vii) a masking polypeptide; and optionally one or more independently selected linker polypeptides. In some cases, as depicted schematically in **FIG. 3C**, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) an Ig Fc polypeptide; v) a masking polypeptide; vi) a TGF- β polypeptide; and vii) one or more MODs; and optionally one or more independently selected linker polypeptides. In some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) an Ig Fc polypeptide; v) a TGF- β polypeptide; vi) a masking polypeptide; and vii) one or more MODs; and optionally one or more independently selected linker polypeptides. In some cases, as depicted schematically in **FIG. 3D**, in some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) an Ig Fc polypeptide; v) one or more MODs; vi) a masking polypeptide; and vii) a TGF- β polypeptide; and optionally one or more independently selected linker polypeptides. In some cases, a single-chain TMP comprises, in order from N-terminus to C-terminus: i) a T1D peptide; ii) an MHC class II β chain polypeptide; iii) an MHC class II α chain polypeptide; iv) an Ig Fc polypeptide; v) one or more MODs; vi) a TGF- β polypeptide; and vii) a masking polypeptide; and optionally one or more independently selected linker polypeptides. In any one of the above embodiments, the TMP can include a single MOD. In any one of the above embodiments, the TMP can include 2 copies of a MOD; the 2 copies can be in tandem, or can be separated by a linker. In any one of the above embodiments, the TMP can include 3 copies of the MOD; the 3 copies can be in tandem, or can be separated by a linker.

[00168] In any one of the above embodiments, the TMP can comprise a peptide linker between one or more of: i) the T1D peptide and the MHC class II β chain polypeptide; ii) between the MHC class II β chain polypeptide and the MHC class II α chain polypeptide; iii) between the MHC class II α chain polypeptide and the masking polypeptide; iv) between the MHC class II α chain polypeptide and a MOD; v) between the MHC class II α chain polypeptide and an Ig Fc polypeptide; vi) between the masking polypeptide and the TGF- β polypeptide; vii) between the TGF- β polypeptide and the Ig Fc polypeptide; viii) between the Ig Fc polypeptide and a MOD; ix) between a MOD and an Ig Fc polypeptide; or between any other two components of the TMP. Exemplary suitable linkers include (GGGGS) n (SEQ ID NO:183), where n is 1, 2, 3, 4, 5, 6, 7, or 8; AAAGG (SEQ ID NO:184), and GGSAAAGG (SEQ ID NO:162). In any of the above embodiments, in some cases, the Ig Fc is an IgG1 Fc polypeptide or a variant thereof. In any of the above embodiments, in some cases, the Ig Fc is an IgG4 Fc polypeptide or a variant thereof. In any of the above embodiments, in some cases the one or more MODs is a PD-L1 polypeptide or variant thereof, in some cases the one or more MODs is a 4-1BBL polypeptide or variant thereof, in some cases the one or more MODs is an IL-2 polypeptide or variant thereof, and in some cases the one or more MODs is a FasL polypeptide or variant thereof. In some cases, the T1D peptide is proinsulin peptide. In some cases, the T1D peptide is a GAD peptide. In any of the above embodiments, in some cases, the TMP includes one or more intrachain disulfide bonds.

[00169] In some cases, a single-chain TMP comprises one or more intrachain disulfide bonds, where an intrachain disulfide bond can form between: a) a Cys present in an MHC class II α chain polypeptide and a Cys present in an MHC class II β chain polypeptide; b) a Cys present in a peptide linker and an MHC class II polypeptide.

[00170] A TMP can comprise a homodimer of two identical single-chain TMPs. Where the single-chain TMP comprises an Ig Fc polypeptide, the homodimer can comprise one or more disulfide bonds formed between the Ig Fc polypeptides of each of the two single-chain TMPs present in the homodimer. Alternatively, a TMP can comprise a heterodimer of two different single-chain TMPs that comprise polypeptides having interspecific binding sequences as discussed above, e.g., Ig Fc polypeptides comprising KiH sequences.

HOMODIMERS AND HETERODIMERS

[00171] The present disclosure provides a protein comprising two of the TMPs of the present disclosure. In some cases, the protein is a homodimer comprising two TMP heterodimers. In some cases, the protein is a homodimer comprising two single-chain TMPs. In some cases, the protein is a heterodimer comprising two TMP heterodimers. In some cases, the protein is a heterodimer comprising two single-chain TMPs.

[00172] The present disclosure provides a protein that is a homodimer comprising two TMP heterodimers, e.g., a first TMP heterodimer and a second TMP heterodimer, where the first TMP heterodimer and the second TMP heterodimer are the same (i.e., the first polypeptide of the first TMP heterodimer and the second TMP heterodimer have the same amino acid sequence; and the second polypeptide of the first TMP heterodimer and the second TMP heterodimer have the same amino acid sequence). The first TMP heterodimer and the second TMP heterodimer can be covalently linked to one another via one or more disulfide bonds between, e.g., an Ig Fc polypeptide present in the first TMP heterodimer and an Ig Fc polypeptide present in the second TMP heterodimer.

[00173] The present disclosure provides a protein that is a heterodimer comprising two TMP heterodimers, e.g., a first TMP heterodimer and a second TMP heterodimer, where the first TMP heterodimer and the second TMP heterodimer are not the same (i.e., the first polypeptide of the first TMP heterodimer and the second TMP heterodimer have different amino acid sequences; and/or the second polypeptide of the first TMP heterodimer and the second TMP heterodimer have different amino acid sequences). In some cases, the first and the second polypeptides of the first and second TMP heterodimers are identical except that the MODs are different. For example, in some case, the first TMP heterodimer comprises one or more MODs, where the one or more MODs comprise IL-2 polypeptides; and the second TMP heterodimer comprises, one or more MODs, where the one or more MODs comprise one or more PD-L1 polypeptides. As another example, in some case, the first TMP heterodimer comprises one or more MODs, where the one or more MODs comprise IL-2 polypeptides; and the second TMP heterodimer comprises, one or more MODs, where the one or more MODs comprise one or more 4-1BBL polypeptides.

[00174] The present disclosure provides a protein that is a homodimer comprising two single-chain TMPs, e.g., a first single-chain TMP and a second single-chain TMP, where the first single-chain TMP and the second single-chain TMP are the same (have the same amino acid sequence). The first single-chain TMP and the second single-chain TMP can be covalently linked to one another via one or more disulfide bonds between, e.g., an Ig Fc polypeptide present in the first single-chain TMP and an Ig Fc polypeptide present in the second single-chain TMP.

[00175] The present disclosure provides a protein that is a heterodimer comprising two single-chain TMPs, e.g., a first single-chain TMP and a second single-chain TMP, where the first single-chain TMP and the second single-chain TMP are not the same (have different amino acid sequences). In such cases, the two single-chain TMPs can comprise polypeptides having interspecific binding sequences as discussed above, e.g., Ig Fc polypeptides comprising KiH sequences. In some cases, the first and the second polypeptides of the first and second single-chain TMPs are identical except that the MODs are different. For example, in some case, the first single-chain TMP comprises one or more MODs, where the one or more MODs comprise IL-2 polypeptides; and the second single-chain TMP comprises, one or

more MODs, where the one or more MODs comprise one or more PD-L1 polypeptides. As another example, in some case, the first single-chain TMP comprises one or more MODs, where the one or more MODs comprise IL-2 polypeptides; and the second single-chain TMP comprises, one or more MODs, where the one or more MODs comprise one or more 4-1BBL polypeptides. The first single-chain TMP and the second single-chain TMP can be covalently linked to one another via one or more disulfide bonds between, e.g., an Ig Fc polypeptide present in the first single-chain TMP and an Ig Fc polypeptide present in the second single-chain TMP.

IMMUNOMODULATORY POLYPEPTIDES (“MODS”)

[00176] MODs that are suitable for inclusion in a TMP of the present disclosure include, but are not limited to, IL-2, CD7, B7-1 (CD80), B7-2 (CD86), PD-L1, PD-L2, 4-1BBL, OX40L, Fas ligand (FasL), inducible costimulatory ligand (ICOS-L), intercellular adhesion molecule (ICAM), CD30L, CD40, CD70, CD83, HLA-G, MICA, MICB, HVEM, lymphotoxin beta receptor, 3/TR6, ILT3, ILT4, and HVEM. In some cases, the MOD is selected from an IL-2 polypeptide, a 4-1BBL polypeptide, an ICOS-L polypeptide, an OX-40L polypeptide, a CD80 polypeptide, a CD86 polypeptide, a PD-L1 polypeptide, a FasL polypeptide, a and a PD-L2 polypeptide. In some cases, the MOD is selected from an IL-2 polypeptide, a PD-L1 polypeptide, a 4-1BBL polypeptide and a FasL polypeptide.

[00177] As also noted above, the MOD can comprise a wild-type amino acid sequence, or can comprise one or more amino acid substitutions relative to a wild-type amino acid sequence. The MOD can comprise only the extracellular portion of a full-length MOD. Thus, for example, the MOD can in some cases exclude one or more of a signal peptide, a transmembrane domain, and an intracellular domain normally found in a naturally-occurring MOD.

[00178] In some cases, a MOD suitable for inclusion in a TMP comprises all or a portion of (e.g., an extracellular portion of) the amino acid sequence of a naturally-occurring MOD. In other instances, a MOD suitable for inclusion in a TMP is a variant MOD that comprises at least one amino acid substitution compared to the amino acid sequence of a naturally-occurring MOD. In some instances, a variant MOD exhibits a binding affinity for a co-immunomodulatory polypeptide (“co-MOD”) that is lower than the affinity of a corresponding naturally-occurring MOD (e.g., a MOD not comprising the amino acid substitution(s) present in the variant) for the co-MOD.

[00179] Suitable MODs that exhibit reduced affinity for a co-MOD can have from 1 amino acid (aa) to 20 aa differences from a wild-type MOD. For example, in some cases, a variant MOD present in a TMP differs in amino acid sequence by 1 aa, 2 aa, 3 aa, 4 aa, 5 aa, 6 aa, 7 aa, 8 aa, 9 aa, or 10 aa, from a corresponding wild-type MOD. As another example, in some cases, a variant MOD present in a TMP differs in amino acid sequence by 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, or 20 aa, from a corresponding wild-type MOD. As an example, in some cases, a variant MOD present in a TMP

includes 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acid substitutions, compared to a corresponding reference (e.g., wild-type) MOD.

[00180] A variant MOD suitable for inclusion in a TMP exhibits reduced affinity for a cognate co-MOD, compared to the affinity of a corresponding wild-type MOD for the cognate co-MOD.

[00181] Exemplary pairs of MOD and cognate co-MOD include, but are not limited to those set out in Table 4, below:

Table 4

Immunomodulatory Polypeptide (MOD)	Cognate Co-Immunomodulatory Polypeptide (co-MOD)
4-1BBL	4-1BB
PD-L1	PD-1
IL-2	IL-2 receptor
CD80	CD28
CD86	CD28
OX40L (CD252)	OX40 (CD134)
Fas ligand	Fas
ICOS-L	ICOS
ICAM	LFA-1
CD30L	CD30
CD40	CD40L
CD83	CD83L
HVEM (CD270)	CD160
JAG1 (CD339)	Notch
JAG1	CD46
CD80	CTLA4
CD86	CTLA4
CD70	CD27
TGF β	TGF β receptor

[00182] Binding affinity between a MOD and its cognate co-MOD can be determined by bio-layer interferometry (BLI) using purified MOD and purified cognate co-MOD, following the procedure set forth in published PCT Application WO 2020/132138 A1.

[00183] MODs and variants, including reduced affinity variants, such as PD-L1, CD80, CD86, 4-1BBL, and IL-2 are described in the published literature, e.g., published PCT application

WO2020132138A1 and WO2019/051091, the disclosures of which as they pertain to MODs and specific variant MODs of PD-L1, CD80, CD86, 4-1BBL, IL-2 are expressly incorporated herein by reference, including specifically paragraphs [00260]-[00455] of WO2020132138A1 and paragraphs [00157]-[00352] of WO2019/051091.

[00184] Of specific interest are MODs that are variants of the cytokine IL-2. Wild-type IL-2 binds to IL-2 receptor (IL-2R) on the surface of a T cell. Wild-type IL-2 has a strong affinity for IL-2R and will bind to activate most or substantially all CD8+ T cells. For this reason, synthetic forms of wild type IL-2 such as the drug Aldesleukin (trade name Proleukin®) are known to have severe side-effects when administered to humans for the treatment of cancer because the IL-2 indiscriminately activates both target and non-target T cells.

[00185] An IL-2 receptor is in some cases a heterotrimeric polypeptide comprising an alpha chain (IL-2R α ; also referred to as CD25), a beta chain (IL-2R β ; also referred to as CD122; and a gamma chain (IL-2R γ ; also referred to as CD132). Amino acid sequences of human IL-2, human IL-2R α , IL2R β , and IL-2R γ are known. See, e.g., published PCT applications WO2020132138A1 and WO2019/051091, discussed above. For example, a wild-type IL-2 polypeptide can have the amino acid sequence depicted in **FIG. 22A**. Amino acid sequences of human IL-2R α , human IL-2R β , and human IL-2R γ are depicted in **FIG. 22B, 22C, and 22D**, respectively.

[00186] In some cases, an IL-2 variant MOD of this disclosure exhibits decreased binding to IL-2R α , thereby minimizing or substantially reducing the activation of Tregs by the IL-2 variant. Alternatively, or additionally, in some cases, an IL-2 variant MOD of this disclosure exhibits decreased binding to IL-2R β and/or IL-2R γ such that the IL-2 variant MOD exhibits an overall reduced affinity for IL-2R. In some cases, an IL-2 variant MOD of this disclosure exhibits both properties, i.e., it exhibits decreased or substantially no binding to IL-2R α , and also exhibits decreased binding to IL-2R β and/or IL-2R γ such that the IL-2 variant polypeptide exhibits an overall reduced affinity for IL-2R. For example, IL-2 variants having substitutions at H16 and F42 have shown decreased binding to IL-2R α and IL-2R β . See, Quayle et al., Clin Cancer Res; 26(8) April 15, 2020, which discloses that the binding affinity of an IL-2 polypeptide with H16A and F42A substitutions for human IL-2R α and IL-2R β was decreased 110- and 3-fold, respectively, compared with wild-type IL2 binding, predominantly due to a faster off-rate for each of these interactions. TMPs comprising such variants, including variants that exhibit decreased binding to IL-2R α and IL-2R β , have shown the ability to preferentially bind to and activate IL-2 receptors on T cells that contain the target TCR that is specific for the peptide epitope on the TMP, and are thus less likely to deliver IL-2 to non-target T cells, i.e., T cells that do not contain a TCR that specifically binds the peptide epitope on the TMP. That is, the binding of the IL-2 variant MOD to its costimulatory polypeptide on the T cell is substantially driven by the binding of the MHC-epitope moiety rather than by the binding of the IL-2.

[00187] Suitable IL-2 variant MODs thus include a polypeptide that comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, or at least 99% amino acid sequence identity to the wild-type IL-2 amino acid sequence depicted in **FIG. 22A**; and that have one or more amino acid differences from the wild-type IL-2 amino acid sequence depicted in **FIG. 22A**. In some cases, such a variant IL-2 polypeptide of this disclosure exhibits reduced binding affinity to IL-2R, compared to the binding affinity of an IL-2 polypeptide comprising the wild-type IL-2 amino acid sequence depicted in **FIG. 22A**. For example, in some cases, a variant IL-2 polypeptide binds IL-2R with a binding affinity that is at least 10% less, at least 15% less, at least 20% less, at least 25%, at least 30% less, at least 35% less, at least 40% less, at least 45% less, at least 50% less, at least 55% less, at least 60% less, at least 65% less, at least 70% less, at least 75% less, at least 80% less, at least 85% less, at least 90% less, at least 95% less, or more than 95% less, than the binding affinity of an IL-2 polypeptide comprising the wild-type IL-2 amino acid sequence depicted in **FIG. 22A** for an IL-2R (e.g., an IL-2R comprising polypeptides comprising the amino acid sequences depicted in **FIG. 22B-22D**), when assayed under the same conditions.

[00188] In some cases, a suitable variant IL-2 polypeptide comprises an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100% amino acid sequence identity to the amino acid sequence: APTSSSTKKT QLQLEALLLD LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLEEELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNRWITFCQSIIS TLT (SEQ ID NO:185), i.e., the variant IL-2 polypeptide has the amino acid sequence of wild-type IL-2 but with H16A and F42A substitutions (shown in bold). Alternatively, the foregoing sequence, but with substitutions other than Ala at H16 and/or F42 may be employed, e.g., H16T may be employed instead of H16A. In some cases, a variant IL-2 polypeptide present in a TMP comprises the amino acid sequence: APTSSSTKKT QLQLEALLLD LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLEEELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNRWITFCQSIIS TLT (SEQ ID NO:185). In some cases, a variant IL-2 polypeptide present in a TMP comprises the amino acid sequence: APTSSSTKKT QLQLETLLLD LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLEEELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNRWITFCQSIIS TLT (SEQ ID NO:186). In some cases, a TMP comprises two copies of such a variant IL-2 polypeptide.

[00189] In some cases, a MOD present in a TMP is a PD-L1 polypeptide. PD-L1 variants that may be suitable as MODs are disclosed in Published PCT applications WO 2019/051091 and WO 2017/201131. In some cases, a PD-L1 polypeptide of a TMP comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following PD-L1 ectodomain amino acid sequence: FT VTPKDL YVV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG EEDLKVQHSS

YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR
ILVDPVTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVSTSLRIN
TTTNEIFYCT FRRLDPEENH TAEVIPGNI LNVSIIKI (SEQ ID NO:130). See also FIG. 22E.

[00190] In some cases, a MOD present in a TMP is a 4-1BBL polypeptide. In some cases, a 4-1BBL polypeptide of a TMP comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following 4-1BBL amino acid sequence: DPAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ GATVLGLFRV TPEIPA (SEQ ID NO:131). See also FIG. 22F.

[00191] In some cases, a MOD present in a TMP is a FasL polypeptide, e.g., the extracellular domain of a FasL polypeptide. In some cases, a FasL polypeptide of a TMP comprises an amino acid sequence having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to the following FasL extracellular domain amino acid sequence: QLFHLQKE LAELRESTSQ MHTASSLEKQ IGHPSPPPEK KELRKVAHLT GKSNSRSMPL EWEDTYGIVL LSGVKYKKGG LVINETGLYF VYSKVYFRGQ SCNNLPLSHK VYMRNSKYPQ DLVMMEGKMM SYCTTGQMW A RSSYLGAVFN LTSADHLYVN VSELSLVNFE ESQTFFGLYK L (SEQ ID NO:187).

CLASS II MHC POLYPEPTIDES

[00192] As noted above, a TMP of the present disclosure includes MHC class II polypeptides. A TMP can include MHC class II polypeptides of various species, including human MHC polypeptides (HLA polypeptides), rodent (*e.g.*, mouse, rat, *etc.*) MHC polypeptides, and MHC polypeptides of other mammalian species (*e.g.*, lagomorphs, non-human primates, canines, felines, ungulates (*e.g.*, equines, bovines, ovines, caprines, *etc.*), and the like. Examples of MHC class II polypeptides are presented in **FIG. 4-18, FIG. 19A-19N, and FIG. 20A-20J.**

[00193] MHC proteins are referred to as human leukocyte antigens (HLA) in humans. HLA class II gene loci include 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).

[00194] For the purpose of this disclosure, the term “MHC polypeptide” is meant to include class II MHC polypeptides, including the α - and β -chains or portions thereof. More specifically, MHC class II

polypeptides include the $\alpha 1$ and $\alpha 2$ domains of class II MHC α chains, and the $\beta 1$ and $\beta 2$ domains of class II MHC β chains, which represent all or most of the extracellular class II protein required for presentation of an epitope peptide. In some cases, both the α and β class II MHC polypeptide sequences in a TMP are of human origin, or variants of such polypeptides.

[00195] Unless expressly stated otherwise, MHC class II polypeptides in a TMP are not intended to include membrane anchoring domains (transmembrane regions) of MHC class II α and β chains, or a part of any thereof sufficient to anchor the resulting TMP, or a peptide thereof, in the membrane of a cell (e.g., a eukaryotic cell such as a mammalian cell such as a Chinese Hamster Ovary or “CHO” cell) in which the TMP is expressed. Similarly, unless expressly stated otherwise, MHC class II polypeptides in a TMP described herein do not include the leader and/or intracellular portions (e.g., cytoplasmic tails) that may be present in some naturally-occurring MHC class II proteins.

[00196] TMPs of the present disclosure comprise MHC class II polypeptides. Naturally occurring class II MHC polypeptides comprise an α chain and a β chain (e.g., HLA α - and β -chains). MHC Class II polypeptides include MHC Class II DP α and β polypeptides, DM α and β polypeptides, DO α and β polypeptides, DQ α and β polypeptides, and DR α and β polypeptides. As used herein, a “Class II MHC polypeptide” can comprise a class II MHC α chain polypeptide, a class II MHC β chain polypeptide, or only a portion of a class II MHC α and/or β chain polypeptide. For example, a “Class II MHC polypeptide” can be a polypeptide that includes: i) only the $\alpha 1$ domain of a class II MHC α chain; ii) only the $\alpha 2$ domain of a class II MHC α chain; iii) only the $\alpha 1$ domain and the $\alpha 2$ domain of a class II MHC α chain; iv) only the $\beta 1$ domain of a class II MHC β chain; v) only the $\beta 2$ domain of a class II MHC β chain; vi) only the $\beta 1$ domain and the $\beta 2$ domain of a class II MHC β chain; vii) the $\alpha 1$ domain of a class II MHC α chain, the $\beta 1$ domain of a class II MHC β chain, and the $\beta 2$ domain of a class II MHC; and the like. In many instances, an MHC class II α chain polypeptide will include only the $\alpha 1$ domain and the $\alpha 2$ domain of a class II MHC α chain polypeptide; and an MHC class II β chain polypeptide will include only the $\beta 1$ domain and the $\beta 2$ domain of a class II MHC β chain polypeptide.

[00197] The human MHC or HLA locus is highly polymorphic in nature, and the HLA Nomenclature site run by the Anthony Nolan Research Institute, available on the world wide web at hla.alleles.org/nomenclature/index.html indicates that, as of April 8, 2019, there are 7 DRA alleles, 2,479 DRB1 alleles, 1 DRB2 allele, 225 DRB3 alleles, 121 DRB4 alleles, 85 DRB5 alleles, 3 DRB6 alleles, 2 DRB7 alleles, 1 DRB8 allele, 6 DRB9 alleles, 149 DQA1 alleles, 1,561 DQB1 alleles, 106 DPA1, 1,360 DPB1 alleles, 7 DMA alleles, 13 DMB alleles, 12 DOA alleles and 13 DOB alleles. As used herein, the term “Class II MHC polypeptide” includes allelic forms of any known Class II MHC polypeptide.

[00198] A TMP may comprise a Class II MHC α chain, without the leader, transmembrane, and intracellular portions (e.g., cytoplasmic tails) that may be present in a naturally-occurring Class II MHC α chain. Thus, a TMP may comprise only the $\alpha 1$ and $\alpha 2$ portions of a Class II MHC α chain; and does

not include the leader, transmembrane, and intracellular portions (e.g., cytoplasmic tails) that may be present in a naturally-occurring Class II MHC α chain.

[00199] A TMP may comprise a Class II MHC β chain, without the leader, transmembrane, and intracellular portions (e.g., cytoplasmic tails) that may be present in a naturally-occurring Class II MHC β chain. Thus, a TMP may comprise only the $\beta 1$ and $\beta 2$ domain portions of a Class II MHC β chain; and does not include the leader, transmembrane, and intracellular portions (e.g., cytoplasmic tails) that may be present in a naturally-occurring Class II MHC β chain.

a) MHC Class II alpha chains

[00200] MHC Class II alpha chains comprise an $\alpha 1$ domain and an $\alpha 2$ domain. In some cases, the $\alpha 1$ and $\alpha 2$ domains present in an antigen-presenting cell are from the same MHC Class II α chain polypeptide. In some cases, the $\alpha 1$ and $\alpha 2$ domains present in an antigen-presenting cell are from two different MHC Class II α chain polypeptides. As noted above, References herein to MHC class II α polypeptides may include both the $\alpha 1$ and $\alpha 2$ domains of class II MHC α chains.

[00201] MHC Class II alpha chains suitable for inclusion in a TMP may lack a signal peptide. An MHC Class II alpha chain suitable for inclusion in a TMP can have a length of from about 60 amino acids (aas) to about 200 aas; for example, an MHC Class II alpha chain suitable for inclusion in a TMP can have a length of from about 60 amino acids to about 80 amino acids, 80 aas to about 100 aas, from about 100 aas to about 140 aas, from about 140 aas to about 170 aas, from about 170 aas to about 200 aas. An MHC Class II $\alpha 1$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 95 aas; for example, an MHC Class II $\alpha 1$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 50 aas, from about 50 aas to about 70 aas, or from about 70 aas to about 95 aas. In an embodiment, an MHC Class II $\alpha 1$ domain of TMP is from about 70 aas to about 95 aas. An MHC Class II $\alpha 2$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 95 aas; for example, an MHC Class II $\alpha 2$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 50 aas, from about 50 aas to about 70 aas, or from about 70 aas to about 95 aas. In an embodiment, an MHC Class II $\alpha 2$ domain of a TMP is from about 70 aas to about 95 aas.

DRA Polypeptides

[00202] In some cases, a suitable MHC Class II α chain polypeptide is a DRA polypeptide. A DRA polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 150, at least 160, or at least 170 contiguous amino acids of the aa sequence from aa 26 to aa 203 of the DRA aa sequence depicted in **FIG. 4** including-naturally occurring allelic variants thereof. In some cases, the DRA polypeptide has a length of about 178 aas (e.g., 175, 176, 177, 178, 179, or 180 aas).

[00203] A “DRA polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DRA polypeptide comprises aas 26-203 of DRA*01:02:01 (see **FIG. 4**), or an allelic variant thereof. In some cases, the allelic variant is the DRA*01:01:01:01 allelic variant that differs from DRA*01:02 by having a valine in place of the leucine at position 242 (see **FIG. 4**).

[00204] A suitable DRA for inclusion in a TMP can have at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with at least 160, at least 170, or at least 180 contiguous aas of the sequence from aa 26 to aa 216 of the DRA*01:02 sequence depicted in **FIG. 4**. A “DRA polypeptide” includes allelic variants, e.g., naturally occurring allelic variants.

[00205] Thus, in some cases, a suitable DRA polypeptide comprises the following amino acid sequence: IKEEH VIIQAEFYLN PDQSGEFMFD FDGDEIFHVD MAKKETVWRL EEFGRFASFE AQGALANIAV DKANLEIMTK RSNYTPITNV PPEVTVLNTS PVELREPNVL ICFIDKFTTP VVNVTWLRNG KPVTTGVSET VFLPREDHLF RKFHYLPFLP STEDVYDCRV EHWGLDEPLL KHW (SEQ ID NO:188, amino acids 26-203 of DRA*01:02, see **FIG. 4**), or an allelic variant thereof. In some cases, the allelic variant is the DRA*01:01:01:01 allelic variant that differs from DRA*01:02:01 by having a valine in place of the leucine at position 242 of the sequence in **FIG. 4**. In some cases, a DRA polypeptide suitable for inclusion in a TMP comprises an amino acid substitution, relative to a wild-type DRA polypeptide, where the amino acid substitution replaces an amino acid (other than a Cys) with a Cys.

[00206] A TMP may comprise a variant DRA polypeptide that comprises a non-naturally occurring Cys residue. For example, a TMP may comprise a variant DRA polypeptide that comprises an amino acid substitution selected from E3C, E4C, F12C, G28C, D29C, I72C, K75C, T80C, P81C, I82C, T93C, N94C, and S95C.

[00207] A suitable DRA α 1 domain for inclusion in a TMP, including naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: VIIQAEFYLN PDQSGEFMFD FDGDEIFHVD MAKKETVWRL EEFGRFASFE AQGALANIAV DKANLEIMTK RSNYTPITN (SEQ ID NO:189); and can have a length of about 84 aas (e.g., 80, 81, 82, 83, 84, 85, or 86 aas).

[00208] A suitable DRA α 2 domain for inclusion in a TMP, including naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: V PPEVTVLNTSPVELREPNVL ICFIDKFTTP VVNVTWLRNG KPVTTGVSET VFLPREDHLF RKFHYLPFLP STEDVYDCRV EHWGLDEPLL KHW (SEQ ID NO:190); and can have a length of about 94 aas (e.g., 90, 91, 92, 93, 94, 95, 96, 97, or 98 aas).

DMA Polypeptides

[00209] In some cases, a suitable MHC Class II α chain polypeptide is a DMA polypeptide. A DMA polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 27-217 of the DMA*01:01 aa sequence depicted in **FIG. 9**, including-naturally occurring allelic variants thereof. In some cases, the DMA polypeptide has a length of about 191 aas (e.g., 188, 189, 190, 191, 192, or 193 aas).

[00210] A “DMA polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DMA polypeptide comprises aas 27-217 of DMA*01:01:01 (see **FIG. 9**), or an allelic variant thereof.

[00211] A suitable DMA α 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: VPEA PTPMWPDDLQ NHTFLHTVYC QDGSPSVGLS EAYDEDQLFF FDFSQNTRVP RLPEFADWAQ EQGDAPAILF DKEFCEWMIQ QIGPKLDGKI PVSR (SEQ ID NO:191); and can have a length of about 98 aas (e.g., 94, 95, 96, 97, 98, 99, 100, or 101 aas).

[00212] A suitable DMA α 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: GFPIAE VFTLKPLEFG KPNTLVCFVS NLFPPMLTVN WQHHSVPVEG FGPTFVSAVD GLSFQAFSYL NFTPEPSDIF SCIVTHEIDR YTAIAYW (SEQ ID NO:192); and can have a length of about 93 aas (e.g., 90, 91, 92, 93, 94, 95, 96, or 97 aas).

DOA Polypeptides

[00213] In some cases, a suitable MHC Class II α chain polypeptide is a DOA polypeptide. A DOA polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 26-204 of the DOA*01:01 aa sequence depicted in **FIG. 11**. In some cases, the DOA polypeptide has a length of about 179 aas (e.g., 175, 176, 177, 178, 179, 180, 181, or 182 aas).

[00214] A “DOA polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DOA polypeptide comprises aas 26-204 of DOA*01:011 (see **FIG. 11**), or an allelic variant thereof. In some cases, the allelic variant may be the DOA*01:02 by having an arginine in place of the cysteine (R80C) at position 80 or the DOA*01:03 variant having a valine in place of the leucine at position 74 (L74V) relative to DOA*01:01.

[00215] A suitable DOA α 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at

least 99%, or 100% aa sequence identity to the following aa sequence: TKADH MGSYGPAFYQ SYGASGQFTH EFDEEQLFSV DLKKSEAVWR LPEFGDFARF DPQGGLAGIA AIKAHLDILV ERSNRSRAIN (SEQ ID NO:193); and can have a length of about 85 aas (e.g., 83, 84, 85, 86, 87, or 88 aas). Suitable $\alpha 1$ domain sequences may incorporate the L74V and/or R80C substitutions found in DOA*01:02 and DOA*01:03 (the aas corresponding to L74 and R 80 are shown italicized and bolded).

[00216] A suitable DOA $\alpha 2$ domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: VPPRVTVLPK SRVELGQPNI LICIVDNIFP PVINITWLRN GQTVTEGVAQ TSFYSQPDHL FRKFHYLPFV PSAEDVYDCQ VEHWGLDAPL LRHW (SEQ ID NO:194); and can have a length of about 94 aas (e.g., 91, 92, 93, 94, 95, 96, or 97 aas).

DPA1 Polypeptides

[00217] In some cases, a suitable MHC Class II α chain polypeptide is a DPA1 polypeptide. A DPA1 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 29-209 of the DPA1 aa sequence depicted in **FIG. 13**. In some cases, the DPA1 polypeptide has a length of about 181 aas (e.g., 178, 179, 180, 181, 182, 183, or 184 aas).

[00218] A “DPA1 polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DPA1 polypeptide comprises aas 29-209 of DPA1*01:03 (see **FIG. 13**), or an allelic variant thereof.

[00219] A suitable DPA1 $\alpha 1$ domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: AIKADHVSTY AAFVQTHRPT GEFMFEFDED EMFYVDLDDK ETVWHLEEFQ QAFSFEAQGG LANIAILNNN LNTLIQRSNH TQATN (SEQ ID NO:195); and can have a length of about 87 aas (e.g., 84, 85, 86, 87, 88, or 89 aas).

[00220] A suitable DPA1 $\alpha 2$ domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: DPPEV TVFPKEPVEL GQPNTLICH I DKFFPPVLNV TWLCNGELVT EGVAESLFLP RTDYSFHKFH YLTFVPSAED FYDCRVEHWG LDQPLLKHW (SEQ ID NO:196); and can have a length of about 97 aas (e.g., 91, 92, 93, 94, 95, 96, or 97 aas).

[00221] Another DPA1 polypeptide comprises aas 29-209 of DPA1*02:01 (see **FIG. 13**), or a variant thereof having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity. A suitable DPA1 $\alpha 1$ domain, including-naturally occurring allelic variants thereof,

may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to aas 29-115 of DPA1*02:01; and can have a length of about 87 aas (e.g., 84, 85, 86, 87, 88, or 89 aas). A suitable DPA1 α 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to aas 116 to 209 of DPA1*02:01:01:01; and can have a length of about 97 aas (e.g., 91, 92, 93, 94, 95, 96, or 97 aas).

DQA1 Polypeptides

[00222] In some cases, a suitable MHC Class II α chain polypeptide is a DQA1 polypeptide. A suitable DQA1 polypeptide, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of any of the DQA1 aa sequences depicted in **FIG. 15**. In some cases, the DQA1 polypeptide has a length of about 181 aas (e.g., 177, 178, 179, 180, 181, 182, or 183 aas). In an embodiment, a DQA1 α chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA1*01:01 α chain aa sequence in **FIG. 15**, ImMunoGeneTics (“IMGT”)/HLA Acc No:HLA00601. In an embodiment, a DQA1 α chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA1*01:02 α chain aa sequence in **FIG. 15**, IMGT/HLA Acc No:HLA00603, GenBank NP_002113. In an embodiment, a DQA1 α chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA1*02:01 α chain aa sequence in **FIG. 15**, IMGT/HLA Acc No:HLA00607. In an embodiment, a DQA1 α chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA1*03:01 α chain aa sequence in **FIG. 15**, IMGT/HLA Acc No:HLA00609. In an embodiment, a DQA1 α chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA1*04:01 α chain aa sequence in **FIG. 15**, IMGT/HLA Acc No:HLA00612. In an embodiment, a DQA1 α chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA1*05:01 α chain aa sequence in **FIG. 15**, IMGT/HLA Acc No:HLA00613. In an embodiment, a DQA1 α chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA1*06:01 α chain aa sequence in **FIG. 15**, IMGT/HLA Acc No:HLA00620.

[00223] A “DQA1 polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DQA1 polypeptide comprises the following aa sequence: EDIVADH

VASCGVNLYQ FYGPSGQYTH EFDGDEQFYV DLERKETAWR WPEFSKFGGF DPQGALRNMA VAKHNLNIMI KRYNSTAATN EVPEVTVFSK SPVTLGQPNT LICLVDNIFP PVVNITWLSN GQSVTEGVSE TSFLSKSDHS FFKISYLTFL PSADEIYDCK VEHWGLDQPL LKHW (SEQ ID NO:197), or an allelic variant thereof.

[00224] A suitable DQA1 α 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: EDIVADH VASCGVNLYQ FYGPSGQYTH EFDGDEQFYV DLERKETAWR WPEFSKFGGF DPQGALRNMA VAKHNLNIMI KRYNSTAATN (SEQ ID NO:198); and can have a length of about 87 aas (e.g., 84, 85, 86, 87, 88, or 89 aas).

[00225] A suitable DQA1 α 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: EVPEVTVFSK SPVTLGQPNT LICLVDNIFP PVVNITWLSN GQSVTEGVSE TSFLSKSDHS FFKISYLTFL PSADEIYDCK VEHWGLDQPL LKHW (SEQ ID NO:199); and can have a length of about 94 aas (e.g., 91, 92, 93, 94, 95, 96, or 97 aas).

DQA2 Polypeptides

[00226] In some cases, a suitable MHC Class II α chain polypeptide is a DQA2 polypeptide. A DQA2 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 24-204 of the DQA2 aa sequence depicted in **FIG. 16**. In some cases, the DQA2 polypeptide has a length of about 181 aas (e.g., 177, 178, 179, 180, 181, 182, or 183 aas).

[00227] A “DQA2 polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DQA2 polypeptide comprises the following aa sequence: EDIVADH VASYGVNFYQ SHGPSGQYTH EFDGDEEFYV DLETKETVWQ LPMFSKFISF DPQSALRNMA VGKHTLEFMM RQSNSTAATN EVPEVTVFSK FPVTLGQPNT LICLVDNIFP PVVNITWLSN GHSVTEGVSE TSFLSKSDHS FFKISYLTFL PSADEIYDCK VEHWGLDEPL LKHW (SEQ ID NO:200), or an allelic variant thereof.

[00228] A suitable DQA2 α 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: EDIVADH VASYGVNFYQ SHGPSGQYTH EFDGDEEFYV DLETKETVWQ LPMFSKFISF DPQSALRNMA VGKHTLEFMM RQSNSTAATN (SEQ ID NO:201); and can have a length of about 87 aas (e.g., 84, 85, 86, 87, 88, or 89 aas).

[00229] A suitable DQA2 $\alpha 2$ domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: EVPEVTVFSK FPVTLGQPNT LICLVDNIFP PVVNITWLSN GHSVTEGVSE TSFLSKSDHS FFKISYLTFL PSADEIYDCK VEHWGLDEPL LKHW (SEQ ID NO:202); and can have a length of about 94 aas (e.g., 91, 92, 93, 94, 95, 96, or 97 aas).

b) MHC Class II beta chains

[00230] MHC Class II beta chains comprise a $\beta 1$ domain and a $\beta 2$ domain. In some cases, the $\beta 1$ and $\beta 2$ domains present in a TMP are from the same MHC Class II β chain polypeptide. In some cases, the $\beta 1$ and $\beta 2$ domains present in a TMP are from two different MHC Class II β chain polypeptides. As noted above, references herein to MHC class II β polypeptides may include both the $\beta 1$ and $\beta 2$ domains of class II MHC β chains.

[00231] MHC Class II beta chain sequences suitable for inclusion in a TMP lack a signal peptide. An MHC Class II beta chain suitable for inclusion in a TMP can have a length of from about 60 aas to about 210 aas; for example, an MHC Class II beta chain suitable for inclusion in a TMP can have a length of from about 60 aas to about 90 aas, from about 90 aas to about 120 aas, from about 120 aas to about 150 aas, from about 150 aas to about 180 aas, from about 180 aas to 210 aas. An MHC Class II $\beta 1$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 105 aas; for example, an MHC Class II $\beta 1$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 50 aas, from about 50 aas to about 70 aas, from about 70 aas to about 90 aas, from about 90 aas to about 105 aas. An MHC Class II $\beta 2$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 105 aas; for example, an MHC Class II $\beta 2$ domain suitable for inclusion in a TMP can have a length of from about 30 aas to about 50 aas, from about 50 aas to about 70 aas, from about 70 aas to about 90 aas, from about 90 aas to about 105 aas.

[00232] MHC class II β chain polypeptide suitable for inclusion in a TMP may comprises an aa substitution, relative to a wild-type MHC class II β chain polypeptide, where the aa substitution replaces an aa (other than a Cys) with a Cys. For example, in some cases, the MHC class II β chain polypeptide is a variant DRB1 MHC class II polypeptide that comprises an aa substitution selected from the group consisting of P5C, F7C, Q10C, N19C, G20C, H33C, G151C, D152C, and W153C. In some cases, the MHC class II β chain polypeptide is a variant DRB1 polypeptide comprising an aa sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, or at least 99%, aa sequence identity to the following DRB1 aa sequence:

GDTRPRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELGRPDAEYWNS
QKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKTQPLQHHNLLVCSVNGFYPA

SIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLV MLETVPRSGEVYTCQVEHPSLTSP LTVIEWR ARSESAQSKM (SEQ ID NO:103), and comprising an aa substitution selected from the group consisting of P5C, F7C, Q10C, N19C, G20C, H33C, G151C, D152C, and W153C. In some cases, the MHC class II β chain polypeptide is a variant DRB3 polypeptide, a variant DRB4 polypeptide, or a variant DRB5 polypeptide comprising an aa substitution corresponding to any of the foregoing aa substitutions in a variant DRB1 polypeptide. For example, as depicted in **FIG. 7B**: i) an aa corresponding to P5 of DRB1 would be P5 of a mature DRB3 polypeptide (lacking the N-terminal signal peptide MVCLKLPGGSSLAALTVTL MVLSSRLAFA (SEQ ID NO:203)); ii) an aa corresponding to F7 of DRB1 would be F7 of a mature DRB3 polypeptide; iii) an aa corresponding to Q10 of DRB1 would be L10 of a mature DRB3 polypeptide; iv) an aa corresponding to N19 of DRB1 would be N19 of a mature DRB3 polypeptide; v) an aa corresponding to G20 of DRB1 would be G20 of a mature DRB3 polypeptide; vi) an aa corresponding to H33 of DRB1 would be N33 of a mature DRB3 polypeptide; vii) an aa corresponding to G151 of DRB1 would be G151 of a mature DRB3 polypeptide; viii) an aa corresponding to D152 of DRB1 would be D152 of a mature DRB3 polypeptide; and ix) an aa corresponding to W153 of DRB1 would be W153 of a mature DRB3 polypeptide. As another example, as depicted in **FIG. 7C**, i) an aa corresponding to P5 of DRB1 would be P15 of a mature DRB4 polypeptide (lacking the N-terminal signal peptide MVCLKLPGGSCMAALTVTL (SEQ ID NO:204)); ii) an aa corresponding to F7 of DRB1 would be F17 of a mature DRB4 polypeptide; iii) an aa corresponding to Q10 of DRB1 would be Q20 of a mature DRB4 polypeptide; iv) an aa corresponding to N19 of DRB1 would be N29 of a mature DRB4 polypeptide; v) an aa corresponding to G20 of DRB1 would be G30 of a mature DRB4 polypeptide; vi) an aa corresponding to H33 of DRB1 would be N43 of a mature DRB4 polypeptide; vii) an aa corresponding to G151 of DRB1 would be G161 of a mature DRB4 polypeptide; viii) an aa corresponding to D152 of DRB1 would be D162 of a mature DRB4 polypeptide; and ix) an aa corresponding to W153 of DRB1 would be W153 of a mature DRB4 polypeptide. As another example, as depicted in **FIG. 7D**, i) an aa corresponding to P5 of DRB1 would be P15 of a mature DRB5 polypeptide (lacking the N-terminal signal peptide MVCLKLPGGSYMAKLT VTL (SEQ ID NO:205)); ii) an aa corresponding to F7 of DRB1 would be F17 of a mature DRB5 polypeptide; iii) an aa corresponding to Q10 of DRB1 would be Q20 of a mature DRB5 polypeptide; iv) an aa corresponding to N19 of DRB1 would be N29 of a mature DRB5 polypeptide; v) an aa corresponding to G20 of DRB1 would be G30 of a mature DRB5 polypeptide; vi) an aa corresponding to H33 of DRB1 would be N43 of a mature DRB5 polypeptide; vii) an aa corresponding to G151 of DRB1 would be G161 of a mature DRB5 polypeptide; viii) an aa corresponding to D152 of DRB1 would be D162 of a mature DRB5 polypeptide; and ix) an aa corresponding to W153 of DRB1 would be W163 of a mature DRB5 polypeptide.

DRB1 Polypeptides

[00233] In some cases, a suitable MHC Class II β chain polypeptide is a DRB1 polypeptide. In an embodiment, a DRB1 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of any DRB1 aa sequence depicted in **FIG. 5**, including naturally occurring allelic variants. **FIG. 5** displays the DRB1 precursor proteins in which aas 1-29 are the signal sequence (underlined), 30-124 form the β 1 region (bolded), 125-227 for the β 2 region (bolded and underlined), and 228-250 the transmembrane region. In some cases, a DRB1 polypeptide suitable for inclusion in a TMP comprises an aa substitution, relative to a wild-type DRB1 polypeptide, where the aa substitution replaces an aa (other than a Cys) with a Cys.

[00234] In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-1 (DRB1*01:01) beta chain aa sequence Swiss-Prot/UniProt reference (“sp”) P04229.2 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-3 (DRB1*03:01) beta chain aa sequence sp P01912.2 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-4 (DRB1*04:01) beta chain aa sequence sp P13760.1 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-7 (DRB1*07:01) beta chain aa sequence sp P13761.1 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-8 (DRB1*08:01) beta chain aa sequence sp Q30134.2 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-9 (DRB1*09:01) beta chain aa sequence sp Q9TQE0.1 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa

30 to aa 227 of the DRB1-10 (DRB1*10:01) beta chain aa sequence sp Q30167.2 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-11 (DRB1*11:01) beta chain aa sequence sp P20039.1 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-12 (DRB1*12:01) beta chain aa sequence sp Q95IE3.1 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-13 (DRB1*13:01) beta chain aa sequence sp Q5Y7A7.1 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-14 (DRB1*14:01) beta chain aa sequence sp Q9GIY3.1 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-15 (DRB1*15:01) beta chain aa sequence sp P01911 in **FIG. 5**. In an embodiment, a DRB1 β chain polypeptide of a TMP can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB1-16 (DRB1*16:01) beta chain aa sequence sp Q29974.1 in **FIG. 5**. In some cases, the DRB1 β chain polypeptide has a length of about 198 aas (e.g., 195, 196, 197, 198, 199, 200, 201, or 202 aas).

[00235] A suitable “DRB1 polypeptide” for inclusion in a TMP may include allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DRB1 polypeptide comprises aas 31-227 of DRB1*04:01 (DRB1-4) provided in **FIG. 5** or an allelic variant thereof.

[00236] Another suitable DRB1 polypeptide may comprise a sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to at least 170, at least 180, or at least 190 contiguous aas of the following DRB1*04:01 aa sequence:

GDTRPRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELGRPDAEYWNS
QKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTYVPAKTQPLQHHNLLVCSVNGFYPA
SIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVMLETVPRSGEVYTCQVEHPSLTSP LTV EWR
ARSESAQSKM (SEQ ID NO:103), which may bear one or more cysteine substitutions. In an

embodiment the cysteine substitution is a P5C substitution. In an embodiment the cysteine substitution is a G151C substitution. In an embodiment the cysteine substitution is a W153C substitution.

[00237] A suitable DRB1 β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence:

DTRPRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELGRPDAEYWNSQ
KDLLEQKRAAVDTYCRHNYGVGESFTVQRRV (SEQ ID NO:206); and can have a length of about 95 aas (e.g., 92, 93, 94, 95, 96, 97, or 98 aas).

[00238] A suitable DRB1 β 1 domain can comprise the following amino acid sequence:

GDTRCRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELGRPDAEYWNS
QKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV (SEQ ID NO:207), where P5 is substituted with a Cys (shown in bold and italics text).

[00239] A suitable DRB1 β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence:

YPEVTVYPAKTQPLQHNNLLVCSVNGFYPGSIEVRWFRNGQEEKTGTVVSTGLIQNGDWTFTQL
VMLETVPRSGEVYTCQVEHPSLTSPLEWRARSESAQSK (SEQ ID NO:208); and can have a length of about 103 aas (e.g., 100, 101, 102, 103, 104, 105, or 106 aas).

[00240] A suitable DRB1 β 2 domain can comprise the following amino acid sequence:

YPEVTVYPAKTQPLQHNNLLVCSVNGFYPASIEVRWFRNGQEEKTGTVVSTGLIQNGDCTFTQLV
MLETVPRSGEVYTCQVEHPSLTSPLEWRARSESAQSKM (SEQ ID NO:209), where W153 is substituted with a Cys (shown in bold and italics text).

DRB3 Polypeptides

[00241] In some cases, a suitable MHC Class II β chain polypeptide is a DRB3 polypeptide. In an embodiment, a DRB3 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 30-227 of any DRB3 aa sequence depicted in **FIG. 6**, which displays the DRB3 precursor proteins in which aas 1-29 are the signal sequence (underlined), 30-124 form the β 1 region (shown bolded), 125-227 form the β 2 region, and 228-250, the transmembrane region. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 30-227 of the DRB1-3 (DRB3*01:01) beta chain aa sequence GenBank NP_072049.1 in FIG. 6. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 30-227 of the DRB1-3 beta chain aa sequence in GenBank accession EAX03632.1 in FIG. 6. In an

embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 30-227 of the DRB1-3 (DRB3*02:01) beta chain aa sequence GenBank CAA23781.1 in FIG. 6. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 30-227 of the DRB1-3 (DRB3*03:01) beta chain aa sequence GenBank AAN15205.1 in FIG. 6. In some cases, a DRB3 polypeptide suitable for inclusion in a TMP comprises an aa substitution, relative to a wild-type DRB3 polypeptide, where the aa substitution replaces an aa (other than a Cys) with a Cys.

[00242] A suitable “DRB3 polypeptide” for incorporation into a TMP may include allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DRB3 polypeptide comprises aas 30 to 227 of DRB3*01:01 provided in FIG. 6, or an allelic variant thereof. Thus, in some cases, a suitable DRB3 polypeptide comprises a sequence having at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% sequence identity to at least 170, at least 180, or at least 190 contiguous aas of the following sequence: DTRPRFLELR KSECHFFNGT ERVRYLDRYF HNQEEFLRFD SDVGEYRAVT ELGRPVAESW NSQKDLLEQK RGRVDNYCRH NYGVGESFTV QRRVHPQVTV YPAKTQPLQH HNLLVCSVSG FYPGSIEVRW FRNGQEEKAG VVSTGLIQNG DWTFQTLVML ETVPRSGEVY TCQVEHPSVT SALTVEWRAR SESAQSK (SEQ ID NO:210), or an allelic variant thereof. In some cases, a DRB3 polypeptide suitable for inclusion in a TMP comprises an aa substitution, relative to a wild-type DRB3 polypeptide, where the aa substitution replaces an aa (other than a Cys) with a Cys. Thus, e.g., in some cases, the MHC class II β chain polypeptide is a variant DRB3 MHC class II polypeptide that comprises a non-naturally occurring Cys at an aa selected from the group consisting of P5C, F7C, L10C, N19C, G20C, N33C, G151C, D152C, and W153C (of a mature DRB3 polypeptide (lacking the N-terminal signal peptide MVCLKLPGGSSLAALTVTLMLSSRLAFA (SEQ ID NO:203) depicted in FIG. 6).

[00243] A suitable DRB3 β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: DTRPRFLELR KSECHFFNGT ERVRYLDRYF HNQEEFLRFD SDVGEYRAVT ELGRPVAESW NSQKDLLEQK RGRVDNYCRH NYGVGESFTV QRRV (SEQ ID NO:211); and can have a length of about 95 aas (e.g., 93, 94, 95, 96, 97, or 98 aas). A suitable DRB3 β 1 domain can comprise the following aa sequence: DTRPRFLELR KSECHFFNGT ERVRYLDRYF HNQEEFLRFD SDVGEYRAVT ELGRPVAESW NSQKDLLEQK RGRVDNYCRH NYGVGESFTV QRRV (SEQ ID NO:211), or a naturally-occurring allelic variant A suitable DRB3 β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: HPQVTV YPAKTQPLQH HNLLVCSVSG

FYPGSIEVRW FRNGQEEKAG VVSTGLIQNG DWTFQTLVML ETVPRSGEVY TCQVEHPSVT SALTVEWRAR SESAQSK (SEQ ID NO:212); and can have a length of about 103 aas (e.g., 100, 101, 102, 103, 104, or 105 aas). A suitable DRB3 β 2 domain can comprise the following aa sequence: HPQVTV YPAKTQPLQH HNLLVCSVSG FYPGSIEVRW FRNGQEEKAG VVSTGLIQNG DWTFQTLVML ETVPRSGEVY TCQVEHPSVT SALTVEWRAR SESAQSK (SEQ ID NO:212), or a naturally-occurring allelic variant thereof.

DRB4 Polypeptides

[00244] In some cases, a suitable MHC Class II β chain polypeptide is a DRB4 polypeptide. A DRB4 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity with aas 30-227 of a DRB4 aa sequence depicted in **FIG. 7**. In some cases, the DRB4 polypeptide has a length of about 198 aas (e.g., 195, 196, 197, 198, 199, 200, 201, or 202 aas). In some cases, a DRB4 polypeptide suitable for inclusion in a TMP comprises an amino acid substitution, relative to a wild-type DRB4 polypeptide, where the amino acid substitution replaces an amino acid (other than a Cys) with a Cys.

[00245] A suitable “DRB4 polypeptide” for inclusion in a TMP may include allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DRB4 polypeptide comprises aas 30 to 227 of DRB4*01:01 (SEQ ID NO:41) or DRB4*01:03 (SEQ ID NO:42) provided in **FIG. 7**, or an allelic variant thereof. In some cases, a DRB4 polypeptide suitable for inclusion in a TMP comprises an amino acid substitution, relative to a wild-type DRB4 polypeptide, where the amino acid substitution replaces an amino acid (other than a Cys) with a Cys. Thus, e.g., in some cases, the MHC class II β chain polypeptide is a variant DRB4 MHC class II polypeptide that comprises a non-naturally occurring Cys residue; e.g., where the variant DRB4 MHC class II polypeptide comprises an amino acid substitution selected from the group consisting of P15C, F17C, Q20C, N29C, G30C, N43C, G161C, D162C, and W163C of a mature DRB4 polypeptide (lacking the N-terminal signal peptide MVCLKLPGGSCMAALTVTL (SEQ ID NO:204) depicted in **FIG. 7**).

[00246] A suitable DRB4 β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: T VLSSPLALAG DTQPRFLEQA KCECHFLNGT ERVWNLIRYI YNQEEYARYN SDLGEYQAVT ELGRPDAEYW NSQKDLLERR RAEVDITYCRY NYGVVESFTV QRRV (SEQ ID NO:213); and can have a length of about 95 aas (e.g., 93, 94, 95, 96, 97, or 98 aas).

[00247] A suitable DRB4 β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100% aa sequence identity to the following aa sequence: QPKVTV YPSKTQPLQH HNLLVCSVNG FYPGSIEVRW FRNGQEEKAG VVSTGLIQNG DWTFQTLVML ETVPRSGEVY

TCQVEHPSMM SPLTVQWSAR SESAQSK (SEQ ID NO:214); and can have a length of about 103 aas (e.g., 100, 101, 102, 103, 104, or 105 aas).

DRB5 Polypeptides

[00248] A TMP may comprise an MHC Class II β chain polypeptide of a DRB5 allele. In some cases, the DRB5 polypeptide has a length of about 198 aas (e.g., 195, 196, 197, 198, 199, 200, 201, or 202 aas). In some cases, a DRB5 polypeptide suitable for inclusion in a TMP comprises an aa substitution, relative to a wild-type DRB5 polypeptide, where the aa substitution replaces an aa (other than a Cys) with a Cys.

DRB5*01:01

[00249] A TMP may comprise a DRB5*01:01 polypeptide comprising an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB5*01:01 aa sequence provided in **FIG. 8**. In some cases, a DRB5 polypeptide suitable for inclusion in a TMP comprises an aa substitution, relative to a wild-type DRB5 polypeptide, where the aa substitution replaces an aa (other than a Cys) with a Cys. Thus, e.g., in some cases, the MHC class II β chain polypeptide is a variant DRB5 MHC class II polypeptide that comprises a non-naturally occurring Cys residue; e.g., where the variant DRB5 MHC class II polypeptide comprises an aa substitution selected from the group consisting of P15C, F17C, Q20C, N29C, G30C, N43C, G161C, D162C, and W163C (of a mature DRB5 polypeptide (lacking the N-terminal signal peptide MVCLKLPGGSYMAKLTVTTL (SEQ ID NO:205) depicted in **FIG. 8**), or a naturally-occurring allelic variant thereof.

[00250] A TMP may comprise a DRB5*01:01 β 1 domain polypeptide comprising an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to aas 30-124 of the DRB5*01:01 aa sequence provided in **FIG. 8**. A TMP may comprise a DRB5*01:01 polypeptide comprising an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 170, at least 180, or at least 190, contiguous aas of the sequence from aa 30 to aa 227 of the DRB5*01:01 β 2 domain aa sequence depicted in **FIG. 8**, or a naturally-occurring allelic variant thereof.

DMB Polypeptides

[00251] In some cases, a suitable MHC Class II β chain polypeptide is a DMB polypeptide. A DMB polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 19-207 of the DMB aa sequence depicted in **FIG. 10**. In some cases, the DMB polypeptide has a length of about 189 aas (e.g., 187, 188, 189, 190, or 191 aas).

[00252] A “DMB polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DMB polypeptide comprises aas 19 to 207 of DMB*01:03 (SEQ ID NO:45) provided in **FIG. 10**, or an allelic variant thereof.

[00253] A suitable DMB β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: GG FVAHVESTCL LDDAGTPKDF TYCISFNKDL LTCWDPEENK MAPCEFGVLN SLANVLSQHL NQKDTLMQRL RNGLQNCATH TQPFWGSALTN RT (SEQ ID NO:215); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, 96, or 97 aas).

[00254] A suitable DMB β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: RPPSVQVA KTTFPNTREP VMLACYVWGF YPAEVTITWR KNGKLVMPHS SAHKTAQPNG DWTYQTLNHL ALTPSYGDTY TCVVEHTGAP EPILRDW (SEQ ID NO:216); and can have a length of about 95 aas (e.g., 93, 94, 95, 96, 97, or 98 aas).

DOB Polypeptides

[00255] In some cases, a suitable MHC Class II β chain polypeptide is a DOB polypeptide. A DOB polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 27-214 of the DOB aa sequence depicted in **FIG. 12**. In some cases, the DOB polypeptide has a length of about 188 aas (e.g., 186, 187, 188, 189, or 190 aas).

[00256] A “DOB polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DOB polypeptide comprises aas 27-214 of DOB*01:01 (SEQ ID NO:47) provided in **FIG. 12**, or an allelic variant thereof.

[00257] A suitable DOB β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: TDSP EDFVIQAKAD CYFTNGTEKV QFVVRFIFNL EEYVRFDSDV GMFVALTKLG QPDAEQWNSR LDLLERSRQA VDGVCRRHNYR LGAPFTVGRK (SEQ ID NO:217); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, 96, or 97 aas).

[00258] A suitable DOB β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: VQPEVTVYPE RTPLHQNHL LHCSVTGFYP GDIKIKWFLN GQEERAGVMS TGPIRNGDWT FQTVVMLEMT PELGHVYTCL

VDHSSLLSPV SVEW (SEQ ID NO:218); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, 96, or 97 aas).

DPB1 Polypeptides

[00259] In some cases, a suitable MHC Class II β chain polypeptide is a DPB1 polypeptide. A DPB1 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-215 of any of the DPB1 aa sequences depicted in **FIG. 14**. In some cases, the DPB1 polypeptide has a length of about 186 aas (e.g., 184, 185, 186, 187, or 188 aas). In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*01:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA00514. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*02:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA00517. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*03:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA00520. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*04:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA00521, GenBank NP_002112.3. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*06:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA00524. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*11:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA00528. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*71:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA00590. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*104:01 β chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA02046. In an embodiment, a DRB3 β chain polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 30-227 of the DPB1*141:01 beta chain aa sequence in FIG. 14, IMGT/HLA Acc No: HLA10364.

[00260] A “DPB1 polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DPB1 polypeptide comprises the following aa sequence: R ATPENYLFQG

RQECYAFNGT QRFLERYIYN REEFARFSD VGEFRAVTEL GRPAAEYWNS QKDILEEKRA VPDRMCRHNY ELGGPMTLQR RVQPRVNVSP SKKGPLQHHN LLVCHVTDFY PGSIQVRWFL NGQEETAGVV STNLIRNGDW TFQILVMLEM TPQQGDVYTC QVEHTSLDSP VTVEW (SEQ ID NO:219), or an allelic variant thereof.

[00261] A suitable DPB1 β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: R ATPENYLFQG

RQECYAFNGT QRFLERYIYN REEFARFSD VGEFRAVTEL GRPAAEYWNS QKDILEEKRA VPDRMCRHNY ELGGPMTLQR R (SEQ ID NO:220); and can have a length of about 92 aas (e.g., 90, 91, 92, 93, or 94 aas).

[00262] A suitable DPB1 β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: VQPRVNVSP SKKGPLQHHN LLVCHVTDFY PGSIQVRWFL NGQEETAGVV STNLIRNGDW TFQILVMLEM TPQQGDVYTC QVEHTSLDSP VTVEW (SEQ ID NO:221); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, 96, or 97 aas).

DQB1 Polypeptides

[00263] In some cases, a suitable MHC Class II β chain polypeptide is a DQB1 polypeptide. A DQB1 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 33-220 of the DQB1 aa sequence depicted in **FIG. 17**. In some cases, the DQB1 polypeptide has a length of about 188 aas (e.g., 186, 187, 188, 190, 191, or 192 aas).

[00264] A “DQB1 polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DQB1 polypeptide comprises aas 33-220 of DQB1*06:02 provided in **FIG. 17** (SEQ ID NO:85), or an allelic variant thereof.

[00265] A suitable DQB1 β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: RDSPEDFV FQFKGMCYFT NGTERVRLVT RYIYNREEYA RFDSVGVYR AVTPQGRPDA EYWNSQKEVL EGTRAELDTV CRHNYEVAFR GILQRR (SEQ ID NO:222); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, or 96 aas).

[00266] A suitable DQB1 β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: VEPT VTISPSRTEA

LNHHNLLVCS VTDFYPGQIK VRWFRNDQEE TAGVVSTPLI RINGDWTQIL VMLEMPQGRG DVYTCHVEHP SLQSPITVEW (SEQ ID NO:223); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, or 96 aas).

DQB2 Polypeptides

[00267] In some cases, a suitable MHC Class II β chain polypeptide is a DQB2 polypeptide. A DQB2 polypeptide can have at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity with aas 33-215 of the DQB2 aa sequence depicted in **FIG. 18A** or **FIG. 18B**. In some cases, the DQB2 polypeptide has a length of about 182 aas (e.g., 175, 176, 177, 178, 179, 180, 181, or 182 aas).

[00268] A “DQB2 polypeptide” includes allelic variants, e.g., naturally occurring allelic variants. Thus, in some cases, a suitable DQB2 polypeptide comprises the following aa sequence: DFLVQFK GMCYFTNGTE RVRGVARYIY NREEYGRFDS DVGEFQAVTE LGRSIEDWNN YKDFLEQERA AVDKVCRHNY EAELRTTLQR QVEPTVTISP SRTEALNHHN LLVCSVTDFY PAQIKVRWFR NDQEETAGVV STSLIRNGDW TFQILVMLEI TPQRGDIYTC QVEHPSLQSP ITVEW (SEQ ID NO:224), or an allelic variant thereof.

[00269] A suitable DQB2 β 1 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: DFLVQFK GMCYFTNGTE RVRGVARYIY NREEYGRFDS DVGEFQAVTE LGRSIEDWNN YKDFLEQERA AVDKVCRHNY EAELRTTLQR QVEPTV (SEQ ID NO:225); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, 96, or 97 aas).

[00270] A suitable DQB2 β 2 domain, including-naturally occurring allelic variants thereof, may comprise an aa sequence having at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to the following aa sequence: TISP SRTEALNHHN LLVCSVTDFY PAQIKVRWFR NDQEETAGVV STSLIRNGDW TFQILVMLEI TPQRGDIYTC QVEHPSLQSP ITVEW (SEQ ID NO:226); and can have a length of about 94 aas (e.g., 92, 93, 94, 95, 96, or 97 aas).

MHC Class II disease risk-associated alleles and haplotypes

[00271] Certain alleles and haplotypes of MHC class II have been associated with disease, e.g., increased risk of developing a particular disease. See, e.g., Erlich et al. (2008) *Diabetes* 57:1084; Gough and Simmonds (2007) *Curr. Genomics* 8:453; Mitchell et al. (2007) *Robbins Basic Pathology* Philadelphia: Saunders, 8th ed.; Margaritte-Jeannin et al. (2004) *Tissue Antigens* 63:562; and Kurko et al. (2013) *Clin. Rev. Allergy Immunol.* 45:170.

MHC Class II Polypeptides in Type 1 Diabetes Mellitus (T1D)

[00272] Alleles/isoforms showing increased association with T1D represent suitable sources of MHC II $\alpha 1$, $\alpha 2$, $\beta 1$, and $\beta 2$ polypeptide sequences for incorporation into TMPs directed to the treatment of T1D. T1D is associated with alleles belonging to the HLA-DR3 and HLA-DR4 haplotypes/serotypes, with the strongest risk associated with the HLA-DQ8, (e.g., HLA-DQB1*03:02) and alleles of the HLA-DQ2 serotype. Some high and moderate risk haplotypes and their association with various DR serotypes are shown in Table 5, below, which is adapted from Kantárová and Buc, *Physiol. Res.* 56: 255-266 (2007).

Table 5

High risk T1D haplotypes				
Haplotype	DRB allele	DQ serotype	DQA allele	DQB allele
DR3	DRB1*0301	DQ 2.5	DQA1*0501	DQB1*0201
DR4	DRB1*0401	DQ 8.1	DQA1*0301	DQB1*0302
DR4	DRB1*0402	DQ 8.1	DQA1*0301	DQB1*0302
DR4	DRB1*0405	DQ 8.1	DQA1*0301	DQB1*0302
Moderate risk T1D haplotypes				
DR1	DRB1*01	DQ 5	DQA1*0101	DQB1*0501
DR8	DRB1*0801		DQA1*0401	DQB1*0402
DR9	DRB1*0901		DQA1*0301	DQB1*0303
Recognized associations				
	DPB allele			
	DPB1*02:02			
	DPB1*03:01			

[00273] The stereotypically defined DR3 and DR4 protein isoforms/haplotypes of the DRB1 gene are associated with increased risk that an individual expressing such alleles will develop T1D. The DR3 serotype includes the alleles encoding the DRB1*03:01, *03:02, *03:03, and *03:04 proteins, with the HLA-DRB1*0301 allele often found associated with a predisposition to T1D. The DR4 serotype includes the alleles encoding the DRB1*04:01, *04:02, *04:03, *04:04, *04:05, *04:06, *04:07, *04:08, *04:09, *04:10, *04:11, *04:12, and *04:13 proteins. Certain HLA-DR4 alleles (e.g., HLA-DRB1*0401, HLA-DRB1*0402, and HLA-DRB1*0405) predispose individuals to T1D, whereas HLA-DRB1*04:03

allele/isoform may afford protection. DRB1*16:01 also show an increased frequency in diabetic children relative to healthy controls (Deja, et al., *Mediators of Inflammation* 2006:1-7 (2006)).

[00274] While T1D is associated with DR3 and DR4 alleles as discussed above, among the strongest associated risk factors for T1D, the presence of alleles belonging to the HLA-DQ8 serotype (e.g., the HLA-DQB1*03:02 isoform) and the HLA DQ2 serotype (e.g., HLA-DQB1*0201). HLA-DQ8 T1D susceptible serotypes include the HLA-DQ8.1 serotype (HLA-DQA1*03:01/DQB1* 03:02), The HLA-DQ2 serotype (HLA- DQB1*02) associated with T1D include DQB1*02:01). Jones, et al., *Nat. Rev. Immunol.* 2006, 6: 271-282. By contrast, individuals that carry the HLADQB1* 0602 allele appear to be protected against type 1 diabetes. *Id.* DQ2 is most common in Western Europe, North Africa and East Africa, with the highest frequencies observed in parts of Spain and Ireland.

[00275] The DQB1 locus alone has also been reported to be associated with T1D when position β 57 is a neutral residue such as Ala or Ser. Both the DQ2 and DQ8 serotypes, which are associated with T1D, lack an Asp at the 57 β position, and instead have an Ala in its place (see e.g., Ala 89 in FIGs 19B HLA-DQB1*02:01 and 19C, HLA-DQB1*03:02 respectively) conferred T1D susceptibility. In contrast, DQB1*06:02, which has an Asp at position β 57 of DQB1 (position 89 in **FIG. 11A-11B**) was found to be associated with resistance to T1D. Jones et al, *Nat. Rev. Immunol.* 2006, 6: 271-282. Position β 57 of the molecule forms a critical residue in peptide binding pocket nine (P9) of the DQB1, which is involved in antigen presentation and T cell receptor (TCR) interaction.

[00276] Individuals with the HLA haplotype DQA1*03:01-DRB1*03:02, especially when combined with DQA1*05:01-DRB1*02:01, are highly susceptible (10–20-fold increase) to T1D, see Notkins, A. L., *J. Biol. Chem.*, 2002, 277(46): 43545–48. Among the stereotypically defined groups showing susceptibility to T1D are HLA-DR4.1 (HLA-DRA1*01:01/DRB1*04:01), HLA-DR4.5 (HLA-DRA1*01:01/DRB1*04:05), HLA-DQ2.5 (HLA-DQA1*05:01/ DQB1*02:01), and HLA-DQ8.1 (HLA-DQA1*03:01/DQB1*03:02). (see e.g., Jones et al., *Nat. Rev. Immunol.* 2006, 6: 271-282). The DR β 1*04:05-DQ β 1*04:01/DR β 1*08:02-DQ β 1*03:02 genotype has shown to be associated with acute-onset and slow progressive T1D. Fulminant diabetes has been associated with DR β 1*04:05-DQ β 1*04:01/DR β 1*04:05-DQ β 1*04:01 genotype, in a Japanese population study Kawabata, et al., *Diabetologia* 2009, 52:2513–21.

[00277] Although the HLA-DR associations with T1D are not as strong as those of HLA-DQ, insulin-reactive T cells derived from lymph nodes draining the pancreas of patients with T1D appear to be HLA-DR4.1 restricted rather than HLA-DQ8 or HLA-DQ2 restricted (Kent et al., *Nature* 2005 435: 224–228).

[00278] The above-mentioned alleles associated with an increased risk of T1D represent suitable candidates from which the α 1, α 2, β 1, and/or β 2 polypeptide sequences present in a TMP of the present

disclosure may be taken. In an embodiment, the TMP is DQ2.5-like with the $\alpha 1$ and $\alpha 2$ polypeptides from DQA1*0501, and the $\beta 1$ and $\beta 2$ polypeptides taken from DQB1*0201. In an embodiment, the TMP is DQ8.1-like with the $\alpha 1$ and $\alpha 2$ polypeptides from DQA1*0301, and the $\beta 1$ and $\beta 2$ polypeptides taken from DQB1*0302.

SCAFFOLD POLYPEPTIDES

[00279] A TMP of the present disclosure, whether a heterodimeric TMP or a single-chain TMP, can comprise an immunoglobulin or non-immunoglobulin scaffold. A TMP polypeptide of the present disclosure, whether a heterodimeric TMP or a single-chain TMP, can comprise an Fc polypeptide, or can comprise another suitable scaffold polypeptide.

[00280] Suitable scaffold polypeptides include antibody-based scaffold polypeptides and non-antibody-based scaffolds. Non-antibody-based scaffolds include, e.g., albumin, an XTEN (extended recombinant) polypeptide, transferrin, an Fc receptor polypeptide, an elastin-like polypeptide (see, e.g., Hassouneh et al. (2012) *Methods Enzymol.* 502:215; e.g., a polypeptide comprising a pentapeptide repeat unit of (Val-Pro-Gly-X-Gly; SEQ ID NO:227), where X is any amino acid other than proline), an albumin-binding polypeptide, a silk-like polypeptide (see, e.g., Valluzzi et al. (2002) *Philos Trans R Soc Lond B Biol Sci.* 357:165), a silk-elastin-like polypeptide (SELP; see, e.g., Megeed et al. (2002) *Adv Drug Deliv Rev.* 54:1075), and the like. Suitable XTEN polypeptides include, e.g., those disclosed in WO 2009/023270, WO 2010/091122, WO 2007/103515, US 2010/0189682, and US 2009/0092582; see also Schellenberger et al. (2009) *Nat Biotechnol.* 27:1186). Suitable albumin polypeptides include, e.g., human serum albumin.

[00281] Suitable scaffold polypeptides will in some cases be half-life extending polypeptides. Thus, in some cases, a suitable scaffold polypeptide increases the *in vivo* half-life (e.g., the serum half-life) of the polypeptide (e.g., the TMP), compared to a control polypeptide lacking the scaffold polypeptide. For example, in some cases, a scaffold polypeptide increases the *in vivo* half-life (e.g., the serum half-life) of the polypeptide, compared to a control polypeptide lacking the scaffold polypeptide, by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 50%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, at least about 25-fold, at least about 50-fold, at least about 100-fold, or more than 100-fold. As an example, in some cases, an Fc polypeptide increases the *in vivo* half-life (e.g., the serum half-life) of the polypeptide, compared to a control polypeptide lacking the Fc polypeptide, by at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 50%, at least about 2-fold, at least about 2.5-fold, at least about 5-fold, at least about 10-fold, at least about 25-fold, at least about 50-fold, at least about 100-fold, or more than 100-fold.

Fc Polypeptides

[00282] In some cases, a TMP comprises an Ig Fc polypeptide. An Ig Fc polypeptide is also referred to herein as an “Fc polypeptide.” The Ig Fc polypeptide of a TMP can be a human IgG1 Fc, a human IgG2 Fc, a human IgG3 Fc, a human IgG4 Fc, etc., or a variant of a wild-type Ig Fc polypeptide. Variants include naturally-occurring variants, non-naturally-occurring variants, and combinations thereof. Exemplary Ig Fc polypeptides are discussed below, any of which may further include interspecific binding sequences, if desired.

[00283] In some cases, the Fc polypeptide present in a TMP comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the Fc amino acid sequence depicted in any one of **FIG. 21A-21M**.

[00284] In some cases, the Fc polypeptide present in a TMP is an IgG1 Fc polypeptide, or a variant of an IgG1 Fc polypeptide. For example, in some cases, the Fc polypeptide present in a TMP comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG1 Fc polypeptide depicted in **FIG. 21A**. As another example, in some cases, the Fc polypeptide present in a TMP comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the Fc polypeptide depicted in **FIG. 21B**; where the Ig Fc polypeptide comprises an Ala at position 14 and an Ala at position 15. In any of the above embodiments, the Ig Fc polypeptide can have an N77 substitution; i.e., the Ig Fc polypeptide can have an amino acid other than Asn at position 77, where in some cases, the Ig Fc polypeptide has an Ala at position 77. In some cases, an Fc polypeptide present in a TMP comprises the amino acid sequence depicted in **FIG. 21A**. In some cases, an Fc polypeptide present in a TMP comprises the amino acid sequence depicted in **FIG. 21B**.

[00285] In some cases, the Fc polypeptide present in a TMP is an IgG1 Fc polypeptide, or a variant of an IgG1 Fc polypeptide, where variants include naturally-occurring variants, non-naturally-occurring variants, and combinations thereof. For example, in some cases, the Fc polypeptide present in a TMP comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG1 Fc polypeptide depicted in **FIG. 21C**; where the Ig Fc polypeptide comprises a Glu at position 136 and a Met at position 138. As another example, in some cases, the Fc polypeptide present in a TMP comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%,

at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG1 Fc polypeptide depicted in **FIG. 21D**; where the Ig Fc polypeptide has Ala at positions 14 and 15; and where the Fc polypeptide comprises a Glu at position 136 and a Met at position 138. In any of the above embodiments, the Ig Fc polypeptide can have an N77 substitution; i.e., the Ig Fc polypeptide can have an amino acid other than Asn at position 77, where in some cases, the Ig Fc polypeptide has an Ala at position 77. In some cases, an Fc polypeptide present in a TMP comprises the amino acid sequence depicted in **FIG. 21C**. In some cases, an Fc polypeptide present in a TMP comprises the amino acid sequence depicted in **FIG. 21D**.

[00286] In some cases, the Fc polypeptide present in a TMP comprises the amino acid sequence depicted in **FIG. 21E** (human IgG1 Fc comprising an L234F substitution, an L235E substitution, and a P331S substitution; where L234 corresponds to amino acid 14 of the amino acid sequence depicted in **FIG. 21E**; L235 corresponds to amino acid 15 of the amino acid sequence depicted in **FIG. 21E**; and P331 corresponds to amino acid 111 of the amino acid sequence depicted in **FIG. 21E**). In some cases, the Fc polypeptide present in a TMP comprises the amino acid sequence depicted in **FIG. 21F**, comprising an N279A substitution (N77A of the amino acid sequence depicted in **FIG. 21F**).

[00287] In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG2 Fc polypeptide depicted in **FIG. 21G**; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 99-325 of the human IgG2 Fc polypeptide depicted in **FIG. 21G** (e.g., where the Ig Fc polypeptide has a length of about 227 amino acids). In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG3 Fc polypeptide depicted in **FIG. 21H**; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 19-246 of the human IgG3 Fc polypeptide depicted in **FIG. 21H** (e.g., where the Ig Fc polypeptide has a length of about 228 amino acids). In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgM Fc polypeptide depicted in **FIG. 21J**; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%,

amino acid sequence identity to amino acids 1-276 to the human IgM Fc polypeptide depicted in **FIG. 21J**. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgA Fc polypeptide depicted in **FIG. 21K**; e.g., the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 1-234 to the human IgA Fc polypeptide depicted in **FIG. 21K**.

[00288] In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to the human IgG4 Fc polypeptide depicted in **FIG. 21M**. In some cases, the Fc polypeptide comprises an amino acid sequence having at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100%, amino acid sequence identity to amino acids 100 to 327 of the human IgG4 Fc polypeptide depicted in **FIG. 21M** (e.g., where the Ig Fc polypeptide has a length of about 228 amino acids).

[00289] In some cases, the IgG4 Fc polypeptide comprises the following amino acid sequence: PPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNA KTKPREEQFNSTYRVSVLTVQLHQLDNLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:228).

[00290] In some cases, the Ig Fc employed in a TMP will comprise one or more substitutions of amino acids in the wild-type sequence, such that that Ig Fc that substantially does not induce cell lysis. For example, in some cases the Fc polypeptide present in a TMP comprises the amino acid sequence depicted in **FIG. 21A** (human IgG1 Fc), except for a substitution of L234 (L14 of the amino acid sequence depicted in **FIG. 21A**) with an amino acid other than leucine, or a substitution of L235 (L15 of the amino acid sequence depicted in **FIG. 21A**) with an amino acid other than leucine. Examples include an L234A (L14A) substitution; and an L235A (L15A) substitution.

TGF- β POLYPEPTIDES

[00291] As discussed above, a TMP of the present disclosure comprises at least one TGF- β polypeptide reversibly masked by a polypeptide (a “masking polypeptide”) that binds to the TGF- β polypeptide, which together form a masked TGF- β MOD. The masking polypeptide can be, for instance, a TGF- β receptor polypeptide or an antibody that functions to reversibly mask the TGF- β polypeptide present in the TMP, where the TGF- β polypeptide is otherwise capable of acting as an agonist of a cellular TGF receptor. The masked TGF- β MODs provide active TGF- β polypeptides (e.g., TGF- β

signaling pathway agonists). The TGF- β polypeptides and masking polypeptides (e.g., a TGF- β receptor fragment) interact with each other to reversibly mask the TGF- β polypeptide, thereby permitting the TGF- β polypeptide to interact with its cellular receptor. In addition, the masking sequence competes with cellular receptors that can scavenge TGF- β , such as the non-signaling T β RIII, thereby permitting the TGF- β MOD (and thus the TMP) to effectively deliver active TGF- β agonist to target cells. While the TMP constructs discussed herein permit epitope-specific presentation of a reversibly masked TGF- β to a target T cell, they also provide sites for the presentation of one or more additional MODs. The ability of the TMP construct to include one or more additional MODs thus permits the combined presentation of TGF- β and the additional MOD(s) to direct a target T cell's response in a substantially epitope-specific/selective manner in order to provide modulation of the target T cell. The TMP thereby permits delivery of one or more masked TGF- β MODs in an epitope-selective (e.g., dependent/specific) manner that permits (i) formation of an active immune synapse with a target T cell, such as a CD4+ cell selective for the epitope, and (ii) modulation (e.g., control/regulation) of the target T cell's response to the epitope. Once engaged with the TCR of a T cell, the effect of a masked TGF- β MOD-containing TMP on the T cell will depend on whether any additional MODs are present as part of the TMP and, if so, which additional MOD(s) is/are present.

[00292] Further, although the TMPs of this disclosure may comprise both one or more masked TGF- β MODs and one or more additional MODs such as a wt or variant IL-2, PD-L1 and/or a 4-1BBL MOD (as discussed above), if desired, the TMPs of this disclosure may comprise only one or more masked TGF- β MODs. That is, the one or more additional MODs such as the wt or variant IL-2, PD-L1 and/or a 4-1BBL MOD need not be included in a TMP of this disclosure. The masked TGF- β MOD-containing TMPs of the present disclosure can function as a means of producing TGF- β -driven T cell responses. For example, TGF- β by itself can inhibit the development of effector cell functions of T cells, activate macrophages, and/or promote tissue the repair after local immune and inflammatory actions subside.

[00293] Although masked TGF- β MODs comprise a TGF- β polypeptide that is masked, the TGF- β polypeptide can still act as T β R agonist because the TGF- β polypeptide-mask complex is reversible and “breathes” between an open state where the TGF-beta polypeptide is available to cellular receptors, and a closed state where the mask engages the TGF- β polypeptide. Accordingly, the masking polypeptide functions to bind TGF- β polypeptide and prevent it from entering into tight complexes with, for example, ubiquitous non-signaling T β R3 molecules that can scavenge otherwise free TGF- β . Moreover, because the active forms of TGF- β are dimers that have higher affinity for TBR3, substitutions that limit dimerization (e.g., a C77S substitution of the cysteine at position 77 with a serine) can be incorporated into TGF- β sequences in order to avoid scavenging by that receptor.

[00294] One effect of the masking sequence is to reduce the effective affinity of TGF- β 1, TGF- β 2, and TGF- β 3 polypeptides for T β R β s. At the same time, the affinity of the masking polypeptide for the TGF- β polypeptide can be altered so that it dissociates more readily from the TGF- β polypeptide, making the TGF- β polypeptide more available to cellular T β R proteins. That is, where the affinity of a masking polypeptide for a TGF- β polypeptide is reduced, the masked TGF- β MOD will spend more time in the open state. Although in the open state with the TGF- β polypeptide available for binding to cellular receptors, because the T β R β II protein is generally the first peptide of the heteromeric T β R1/T β R2 signaling complex to interact with TGF- β , control of the affinity of the TGF- β polypeptide for T β R β II effectively controls entry of TGF- β into active signaling complexes. The incorporation of substitution at, for example, one or more, two or more, or all three of Lys 25, Ile 92, and/or Lys 94 of TGF- β 2 (or the corresponding positions of TGF- β 1, TGF- β 3) reduces affinity for T β R β II polypeptides. The reduced affinity permits interactions between the target cell's TCR and the TMPs MHC polypeptides and epitope to effectively control binding and allows for target cell-specific interactions.

[00295] When a T β R β II polypeptide is used as the masking polypeptide, the possibility of direct interactions with cellular T β R β I receptors and off -target signaling can be addressed by appropriate modifications of the masking sequence. Where it is desirable to block/limit signaling by the masked TGF- β polypeptide through T β R β I and/or modify (e.g., reduce) the affinity of a masking T β R β II polypeptide for TGF- β , it is possible to incorporate N-terminal deletions and/or aa substitutions in the masking T β R β II polypeptide. Modifications that can be made include deletions of N-terminal amino acids (e.g., N-terminal Δ 14 or Δ 25 deletions), and/or substitutions at one or more of L27, F30, D32, S49, I50, T51, S52, I53, E55, V77, D118, and/or E119. Some specific T β R β II modifications resulting in a reduction in T β R β I association with T β R β II and reduced affinity for TGF- β include any one or more of L27A, F30A, D32A, D32N, S49A, I50A, T51A, S52A, S52L, I53A, E55A, V77A, D118A, D118R, E119A, and/or E119Q.

[00296] The TGF- β polypeptide present in a TMP is in some cases a variant TGF- β polypeptide, including a variant TGF- β polypeptide that has a lower affinity for at least one class of TGF- β receptors, or is selective for at least one class of TGF- β receptors, compared to a wild-type TGF- β polypeptide.

[00297] While a TGF- β 1 polypeptide, a TGF- β 2 polypeptide, or a TGF- β 3 polypeptide can be incorporated into a TMP as part of a masked TGF- β polypeptide, a variety of factors may influence the choice of the specific TGF- β polypeptide, and the specific sequence and aa substitutions that will be employed. For example, TGF- β 1 and TGF- β 3 polypeptides are subject to “clipping” of their amino acid sequences when expressed in a certain mammalian cell lines (e.g., CHO cells). In addition, dimerized TGF- β (e.g., TGF- β 2) has a higher affinity for the T β R3 (beta glycan receptor) than for the T β R2 receptor, which could lead to off target binding and loss of biologically active masked protein to the large *in vivo* pool of non-signaling T β R3 molecules. To minimize high-affinity off target binding to

TβR3, it may be desirable to substitute the residues leading to dimeric TGF-β molecules, which are joined by a disulfide bond. Accordingly, cysteine 77 (C77) may be substituted by an amino acid other than cysteine (e.g., a serine forming a C77S substitution).

[00298] Amino acid sequences of TGF-β polypeptides are known in the art. In some cases, the TGF-β polypeptide present in a masked TGF-β polypeptide is a TGF-β1 polypeptide. In some cases, the TGF-β polypeptide present in a masked TGF-β polypeptide is a TGF-β2 polypeptide. In some cases, the TGF-β polypeptide present in a masked TGF-β polypeptide is a TGF-β3 polypeptide.

[00299] A suitable TGF-β polypeptide can have a length from about 70 aas to about 125 aas; for example, a suitable TGF-β polypeptide can have a length from about 70 aas to about 80 aas from about 80 aas to about 90 aas; from about 90 aas to about 100 aas; from about 100 aas to about 105 aas, from about 105 aas to about 110 aas, from about 110 aas to about 112 aas, from about 113 aas to about 120 aas, or from about 120 aas to about 125 aas. A suitable TGF-β polypeptide can comprise an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 80, at least 90, at least 100, or at least 110 contiguous aas of the mature form of a human TGF-β1 polypeptide, a human TGF-β2 polypeptide, or a human TGF-β3 polypeptide.

[00300] **FIG. 23A-23G** provide amino acid sequences of TGF-β polypeptides, including: TGF-β1 preproprotein (FIG. 23A), TGF-β2 preproprotein (FIG. 23C), and TGF-β3 preproprotein (FIG. 23E); TGF-β1 mature form (FIG. 23B), TGFβ2 mature form (FIG. 23D), and TGFβ3 mature form (FIG. 23F). The mature form of TGF-β3 with a C77S substitution is provided in FIG. 23G. An alignment of amino acid sequences of *Homo sapiens* TGF-β1, TGF-β2, and TGF-β3 polypeptides is provided in **FIG. 24**.

(i) TGF-β1 polypeptides

[00301] A suitable TGF-β1 polypeptide can comprise an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 112 aas of the following TGF-β1 amino acid sequence: AL DTNYCFSSTE KNCCVRQLYI DF***R***KDLGWKW IHEPKGYHAN FCLGPCPYIW SLDTQYSKVL ALYNQHNPQA SAAP***C***CVPQA LEPLPIVYYYV ***G***RKPKVEQLS NMIVRSCKCS (SEQ ID NO:133; 112 aas in length); where the TGF-β1 polypeptide has a length of about 112 aas. A TGF-β1 preproprotein is provided in **FIG. 23A**. Amino acids R25, C77, V92 and R94 are bolded and italicized in **FIG. 23A**.

[00302] In some cases, a suitable TGF-β1 polypeptide comprises a C77S substitution. Thus, in some cases, a suitable TGF-β1 polypeptide comprises an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 112 aas of the following TGF-β1 amino

acid sequence: AL DTNYCFSSTE KNCCVRQLYI DF***R***KDLGWKW IHEPKGYHAN FCLGPCPYIW SLDTQYSKVL ALYNQHNPQA SAAPSCVPQA LEPLIVYY***V*** ***GR***KPKVEQLS NMIVRSCKCS (SEQ ID NO:229), where amino acid 77 is Ser. Positions 25, 77, 92 and 94 are bolded and italicized.

(ii) **TGF- β 2 polypeptides**

[00303] A suitable TGF- β 2 polypeptide can comprise an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 112 aas of the following TGF- β 2 amino acid sequence: ALDAAYCFR NVQDNCCLRP LYIDF***R***KRDLG WKWIHEPKGY NANFCAGACP YLWSSDTQHS RVLSLYNTIN PEASASPCCV SQDLEPLTIL YY***IG***KTPKIE QLSNMIVKSC KCS (SEQ ID NO:135), where the TGF- β 2 polypeptide has a length of about 112 aas. A TGF- β 2 preproprotein is provided in **FIG. 23C**. Residues Lys 25, Cys 77, Ile 92, and Lys 94 are bolded and italicized in **FIG. 23C**.

[00304] In some cases, a suitable TGF- β 2 polypeptide comprises a C77S substitution. Thus, in some cases, a suitable TGF- β 2 polypeptide comprises an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 112 aas of the following TGF- β 2 amino acid sequence: ALDAAYCFR NVQDNCCLRP LYIDF***R***KRDLG WKWIHEPKGY NANFCAGACP YLWSSDTQHS RVLSLYNTIN PEASASPSCV SQDLEPLTIL YY***IG***KTPKIE QLSNMIVKSC KCS (SEQ ID NO:230), where amino acid 77 is substituted by a Ser. Ser77 is bolded and italicized.

(iii) **TGF- β 3 polypeptides**

[00305] A suitable TGF- β 3 polypeptide can comprise an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 112 aas of the following TGF- β 3 amino acid sequence: ALDTNYCFRN LEENCCVRPL YIDF***R***QDLGW KQVHEPKGY ANFCSGPCPY LRSADTTHST VLGLYNTLNP EASASPCCVP QDLEPLTILY Y***VGR***TPKVEQ LSNMVVKSC CS (SEQ ID NO:137), where the TGF- β 3 polypeptide has a length of about 112 aas. A TGF- β 3 isoform 1 preproprotein is provided in **FIG. 23E**. Positions 25, 92 and 94 are bolded and italicized in **FIG. 23E**.

[00306] In some cases, a suitable TGF- β 3 polypeptide comprises a C77S substitution. In some cases, a suitable TGF- β 3 polypeptide comprises an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 112 aas of the following TGF- β 3 amino acid sequence: ALDTNYCFRN LEENCCVRPL YIDF***R***QDLGW KQVHEPKGY ANFCSGPCPY

LRSADTTHST VLGLYNTLNP EASASPSCVP QDLEPLTILY YVGRTPKVEQ LSNMVVKSCK CS (SEQ ID NO:138), where amino acid 77 is Ser. Positions 25, 92 and 94 are bolded and italicized.

(iv) Additional TGF- β polypeptide sequence variations

[00307] In addition to sequence variations that alter TGF- β dimerization (e.g., cysteine 77 substitutions such as C77S), TGF- β 1, TGF- β 2, and TGF- β 3 polypeptides having sequence variations that affect affinity and other properties may be incorporated into a TGF- β polypeptide. When a variant TGF- β with reduced affinity for the masking polypeptide (e.g., a T β R polypeptide such as a T β RII polypeptide) is present in the TGF- β polypeptide, those components dissociate more readily, making the TGF- β polypeptide more available to cellular T β R proteins. Because the T β RII protein is generally the first peptide of the heteromeric T β R signaling complex to interact with TGF- β , interactions with T β RII effectively controls entry of TGF- β into active signaling complexes. Accordingly, variants controlling the affinity of TGF- β for T β RII may effectively control entry of masked TGF- β MODs into active signaling complexes.

[00308] The present disclosure provides a TMP comprising a variant masking T β R (e.g., T β RII) polypeptide sequence and/or a variant TGF- β polypeptide having altered (e.g., reduced) affinity for each other (relative to an otherwise identical TGF- β polypeptide without the sequence variation(s)). Affinity between a TGF- β polypeptide and a T β R (e.g., T β RII) polypeptide may be determined using (BLI) as described above for MODs and their co-MODs.

(a) Additional TGF- β 2 sequence variants

[00309] The present disclosure provides a TMP comprising either a wild-type (wt) or a variant TGF- β 2 polypeptide; where the variant polypeptide has a reduced affinity for the masking T β R present in the TMP (relative to an otherwise identical wt TGF- β polypeptide without the sequence variations).

[00310] In some cases, a TMP comprises a variant TGF- β 2 polypeptide having greater than 85% (e.g., greater than 90%, 95%, 98% or 99%) sequence identity to at least 100 contiguous aa of the amino acid sequence depicted in **FIG. 23D** and comprising a substitution reducing the affinity of the variant TGF- β 2 polypeptide for the T β RII receptor sequence.

[00311] In some cases, a TMP comprises a variant TGF- β (e.g., TGF- β 2) polypeptide comprising a substitution of one or more, two or more, or all three of Lys 25, Ile 92, and/or Lys 94 (see **FIG. 23D** for the location of the residues, and **FIG. 24** for the corresponding residues in TGF- β 1 and TGF- β 3). Those aa residues have been shown to affect the affinity of TGF- β 2 for T β RII polypeptides (see Crescenzo et al., J. Mol. Biol. 355: 47–62 (2006)). In one instance, a TMP comprises a TGF- β 2 polypeptide having an aa other than Lys or Arg at position 25 (**FIG. 23D**). A TMP may comprise a TGF- β 2 polypeptide having an aa other than Ile or Val at position 92 of the amino acid sequence depicted in **FIG. 23D** (or an aa other than Ile, Val, or Leu at position 92). A TMP may comprise a TGF- β 2 polypeptide having an aa

other than Lys or Arg at position 94 of the amino acid sequence depicted in **FIG. 23D**. A TMP may comprise a TGF- β 2 polypeptide comprising a substitution at one or more, two or more or all three of Lys 25, Ile 92, and/or Lys 94 of the amino acid sequence depicted in **FIG. 23D**.

(b) Additional TGF- β 1 and TGF- β 3 sequence variants

[00312] In some cases, a TMP comprises a variant TGF- β 1 or TGF- β 3 polypeptide comprising a substitution at one or more, two or more or all three aa positions corresponding to Lys 25, Ile 92, and/or Lys 94 in TGF- β 2. In TGF- β 1 or TGF- β 3, the aa that corresponds to: Lys 25 is an Arg 25, Ile 92 is Val 92, and Lys 94 is Arg 94, each of which is a conservative substitution. See e.g., **FIG. 23B** for TGF- β 1 (mature form) and **FIG. 23F** for TGF- β 3 (mature form).

[00313] As an example, in some cases, a TMP comprises a TGF- β 1 or β 3 polypeptide having an aa other than Arg or Lys at position 25. As another example, in some cases, a TMP comprises a TGF- β 1 or β 3 polypeptide having an aa other than Val or Ile at position 92 (or an aa other than Ile, Val, or Leu at position 92). As another example, in some cases, a TMP comprises a TGF- β 2 polypeptide having an aa other than Arg or Lys. As another example, in some cases, a TMP comprises a TGF- β 1 or β 3 polypeptide comprising a substitution at one or more, two or more or all three of Arg 25, Val 92, and/or Arg 94. As another example, in some cases, a TMP comprises a TGF- β 1 or β 3 polypeptide comprising a substitution at one or more, two or more or all three of Arg 25, Val 92, and/or Arg 94.

MASKING POLYPEPTIDES

[00314] As noted above, a TMP of the present disclosure comprises a TGF- β polypeptide and a masking polypeptide. Polypeptides or polypeptide complexes that bind to and mask the TGF- β polypeptide (the “masking polypeptide”) can take a variety of forms, including, e.g., TGF- β RI (“T β RI”), TGF- β RII (“T β RII”), TGF- β RIII (“T β RIII”), and anti-TGF- β antibodies.

TGF- β Receptor Polypeptides

[00315] The masking of TGF- β in masked TGF- β polypeptides may be accomplished by utilizing a TGF- β receptor fragment (e.g., the ectodomain sequences of T β RI, T β RII or T β RIII) that comprises polypeptide sequences sufficient to bind a TGF- β polypeptide (e.g., TGF- β 1, TGF- β 2 or TGF- β 3). In an embodiment, the masking sequence comprises all or part of the T β RI, T β RII, or T β RIII ectodomain. Examples of amino acid sequences of TGF- β receptor polypeptides are provided in **FIG. 25A-25N**. An amino acid sequence of a T β RI ectodomain polypeptide is provided in **FIG. 25B**. Amino acid sequences of T β RII ectodomain polypeptides are provided in **FIG. 25D** and **FIG. 25F-J**.

(1) TGF- β Receptor I (T β RI)

[00316] A masking polypeptide may be derived from a T β RI (e.g., isoform 1; SEQ ID NO:141) and may comprise all or part of the T β RI ectodomain (aas 34-126). A suitable T β RI polypeptide for masking TGF- β may comprise an amino acid sequence having at least 60%, at least 70%, at least 80%, at least

90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, or 103 aas of the following T β RI ectodomain aa sequence: LQCFCHL CTKDNFTCVT DGLCFVSVTE TTDKVIHNSM CIAEIDLIPR DRPFVCAPSS KTGSVTTTTCYCNQDHCNKIE LPTTVKSSPG LGPVEL (SEQ ID NO:142).

(2) **TGF- β Receptor II (T β RII)**

[00317] A masking polypeptide may be derived from a T β RII (e.g., isoform A), and may comprises all or part of the T β RII ectodomain sequence (aas 24 to 177). A suitable T β RII isoform A polypeptide for masking TGF- β may comprise an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, at least 120, at least 130, at least 140, at least 150 or at least 154 aas of the following T β RII isoform A ectodomain aa sequence: IPPHVQK SDVEMEAQKD EIICPSCNRT AHPLRHINND MIVTDNNGAV KFPQLCKFCD VRFSTCDNQK SCMSNCSITS ICEKPQEV CV AVWRKNDENI TLETVCHDPK LPYHDFILED AASPKCIMKE KKKPGETFFM CSCSS***DECND*** NIIFSEE (SEQ ID NO:144). The location of the aspartic acid residue corresponding to D118 in the B isoform is bolded and italicized.

[00318] A masking polypeptide may be derived from T β RII isoform B (SEQ ID NO:145) and may comprises all or part of the T β RII ectodomain sequence (aas 24 to 166). A suitable T β RII isoform B polypeptide for masking TGF- β may comprise an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, at least 120, at least 130, at least 140, or 143 aas of the T β RII isoform B ectodomain aa sequence: IPPHVQKSVN NDMIVTDNNG AVKFPQLCK***FCD***VRFSTCDN QKSCMSNCSI TSIC***E***KPQEV CVAVWRKNDE NITLETVCHD PKLPYHDFIL EDAASPKCIM KEKKKPGETF FMCSCSS***DEC*** NDNIIFSEY NTSNPDLLL V IFQ (SEQ ID NO:146). As discussed below, any one or more of F30, D32, S52, E55, or D118 (italicized and bolded) may be substituted by an amino acid other than the naturally occurring aa at those positions (e.g., alanine). A masking polypeptide can include a D118A or D118R substitution. A masking polypeptide can include a D118A or D118R substitution and one or more of a F30A, D32N, S52L and/or E55A substitution.

[00319] Although T β RII's ectodomain may be utilized as a masking polypeptide, that region of the protein has charged and hydrophobic patches that can lead to an unfavorable pI and can be toxic to cells expressing the polypeptide. In addition, combining a T β RII ectodomain with an active TGF- β polypeptide can result in a complex that could combine with cell surface T β RI and cause activation of that signaling receptor (e.g., signaling through the Smad pathway). Modifying T β RII ectodomain sequences used to mask TGF- β by removing or altering sequences involved in T β RI association can

avoid the unintentional stimulation of cells by the masked TGF- β except through their own cell surface heterodimeric T β RI /T β RII complex. Modifications of T β RII may also alter (e.g., reduce) the affinity of the T β RII for TGF- β (e.g., TGF- β 3), thereby permitting control of TGF- β unmasking and its availability as a signaling molecule. Polypeptides comprising T β R (e.g., T β RII) peptides with the highest affinity for TGF- β (e.g., TGF- β 3) most tightly mask the TGF- β polypeptide and require higher doses to achieve the same effect. In contrast, aa substitutions in T β RII that lower the affinity unmask the TGF- β polypeptide and are biologically effective at lower doses.

[00320] Accordingly, where it is desirable to block/limit signaling by a TGF- β polypeptide through T β RI and/or modify (e.g., reduce) the affinity of a masking T β RII polypeptide for TGF- β , a number of alterations to T β RII may be incorporated into the T β RII polypeptide sequence. Modifications that can be made include the above-mentioned deletions of N-terminal amino acids, such as 14 or 25 N-terminal amino acids (from 1 to 14 aas or from 1 to 25 aas; Δ 14, Δ 25 modifications), and/or substitutions at one or more of L27, F30, D32, S49, I50, T51, S52, I53, E55, V77, D118, and/or E119. Some specific T β RII modifications resulting in a reduction in T β RI association with T β RII and reduced affinity for TGF- β include any one or more of L27A, F30A, D32A, D32N, S49A, I50A, T51A, S52A, S52L, I53A, E55A, V77A, D118A, D118R, E119A, and/or E119Q based on the amino acid numbering of the amino acid sequence depicted in **FIG. 25F**. See e.g., J. Groppe et al. *Mol Cell* 29, 157-168, (2008) and De Crescenzo et al. *JMB* 355, 47-62 (2006) for the effects of those substitutions on TGF- β 3–T β RII and T β RI–T β RII complexes. Modifications of T β RII the including an N-terminal Δ 25 deletion and/or substitutions at F24 (e.g., an F24A substitution) substantially or completely block signal through the canonical SMAD signaling pathway). In one aspect, the aspartic acid at position 118 (D118) of the mature T β RII B isoform (e.g., the amino acid sequence depicted in **FIG. 25F**) is replaced by an amino acid other than Asp or Glu, such as Ala giving rise to a “D118A” substitution or by an Arg giving rise to a D118R substitution. The Asp residues corresponding D118 are indicated with bold and underlining in **FIG. 25F**. N-terminal deletions of from 1 to 25 aa in length (e.g., a Δ 25 deletions) and/or substitutions at F24 (e.g., an F24A substitution) may be combined with D118 substitutions (e.g., D118A or D118R). N-terminal deletions of from 1 to 25 aa in length (e.g., a Δ 25 deletions) and/or substitutions at F24 (e.g., an F24A substitution) may also be combined with substitutions at any of L27, F30, D32, S49, 150, T51, S52, I53, E55, V77, D118, and/or E119 (e.g., D118A) substitutions, and particularly any of the specific substitutions recited for those locations in the amino acid sequence depicted in **FIG. 25F** described above to alter the affinity.

[00321] Deletions of the N-terminus of the T β RII polypeptides may also result in loss of T β RI interactions and prevent masked TGF- β polypeptides comprising a T β RII polypeptide from acting as a constitutively active complex that engages and activates T β RI signaling. A 14 aa deletion (Δ 14) of the T β RII polypeptide substantively reduces the interaction of the protein with T β RI, and a Δ 25 aa deletion

of TβRII appears to completely abrogate the interaction with TβRI. N-terminal deletions also substantially alter the pI of the protein, with the Δ14 TβRII ectodomain mutant displaying a pI of about 4.5-5.0 (e.g., about 4.74). Accordingly, a masking polypeptide may comprise a TβRII ectodomain polypeptide with N-terminal deletions, such as from 14 to 25 aas (e.g., 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 aa). Modified ectodomain sequences, including those that limit interactions with TβRI, that may be utilized to mask TGF-β polypeptides are described in the paragraphs that follow.

[00322] In an embodiment, a masking polypeptide comprises sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, at least 120, at least 130, at least 140, or 142 aas of the TβRII isoform B ectodomain sequence: IPPHVQKSVN NDMIVTDNNG AVKFPQLCK**F** CDVRFSTCDN QKSCMSNCSI TSIC**E**KPQEV CVAVWRKNDE NITLETVCHD PKLPYHDFIL EDAASPKCIM KEKKKPGETF FMCSCSS**D**EC NDNIIFSEE (SEQ ID NO:147). Any one or more of F30, D32, S52, E55, or D118 (italicized and bolded) may be substituted by an amino acid other than the naturally occurring aa at those positions (e.g., alanine). In an embodiment, the masking polypeptide comprises the TβRII isoform B ectodomain bearing a D118A substitution. In an embodiment, the sequence masking TGF-β comprises the TβRII isoform B ectodomain sequence bearing a D118A substitution and one or more of a F30A, D32N, S52L and/or E55A substitution.

[00323] Combinations of N-terminal deletions of TβRII, such as from 14 to 25 aas (e.g., 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 aa), that block inadvertent cell signaling due to the masked TGF-β/TβRII complex interacting with TβRI may be combined with other TβRII ectodomain substitutions, including those at any one or more of F30, D32, S52, E55, and/or D118. The combination of deletions and substitutions ensures the masked TGF-β MOD does not cause cell signaling except through the cell's membrane bound TβRI & TβRII receptors.

[00324] In an embodiment, the masking polypeptide comprises sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 114 aas of the TβRII isoform B ectodomain sequence: TDNNG AVKFPQLCK**F** CDVRFSTCDN QKSCMSNCSI TSIC**E**KPQEV CVAVWRKNDE NITLETVCHD PKLPYHDFIL EDAASPKCIM KEKKKPGETF FMCSCSS**D**EC NDNIIFSEE (SEQ ID NO:231), which has aas 1-14 (Δ14) deleted. Any one or more of F30, D32, S52, E55, or D118 (italicized and bolded) may be substituted by an amino acid other than the naturally occurring aa at those positions (e.g., alanine). In an embodiment, the masking polypeptide comprises the TβRII isoform B ectodomain having a D118A substitution. In an embodiment, the sequence masking TGF-β comprises the amino acid sequence TDNNG AVKFPQLCK**F** CDVRFSTCDN QKSCMSNCSI TSIC**E**KPQEV CVAVWRKNDE NITLETVCHD PKLPYHDFIL EDAASPKCIM KEKKKPGETF

FMSCSS**DEC** NDNIIFSEE (SEQ ID NO:231), and bearing a D118A substitution and one or more of a F30A, D32N, S52L and/or E55A substitution.

[00325] In an embodiment, the masking polypeptide comprises an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, or 104 aas of the sequence: QLCK**F** CDVRFSTCDN QKSCMSNCSI TSIC**E**KPQEV CVAVWRKNDE NITLETVCHD PKLPYHDFIL EDAASPKCIM KEKKKPGETF FMSCSS**DEC** NDNIIFSEE (SEQ ID NO:232), which has aas 1-25 (Δ 25) deleted. Any one or more of F30, D32, S52, E55, or D118 (italicized and bolded) may be substituted by an amino acid other than the naturally occurring aa at those positions (e.g., alanine). In an embodiment, the masking polypeptide has a D118A substitution. In an embodiment, the masking polypeptide has a D118A substitution and one or more of a F30A, D32N, S52L and/or E55A substitution. In an embodiment, the masking polypeptide has D118A and F30A substitutions. In an embodiment, the masking polypeptide has D118A and D32N substitutions. In an embodiment, the masking polypeptide has D118A and S52L substitutions. In an embodiment, the masking polypeptide has D118A and E55A.

(3) TGF- β Receptor III (T β RIII)

[00326] In an embodiment, the masking polypeptide may be derived from a T β RIII and may comprises all or part of a T β RIII ectodomain (aas 27-787 of the A isoform or 27-786 of the B isoform). In some cases, a suitable masking polypeptide comprises an amino acid sequence having at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%, aa sequence identity to at least 70, at least 80, at least 90, at least 100, or 120 aas of a T β RIII A isoform or B isoform ectodomain sequences.

(c) Antibodies

[00327] Although TGF- β receptor polypeptides (e.g., ectodomain sequences) can function to bind and mask TGF- β polypeptides in a TMP, other polypeptides that bind to a TGF- β polypeptide can also be employed as masking polypeptides. Among the suitable polypeptides that can be used to mask TGF- β are antibodies with affinity for TGF- β (e.g., antibodies specific for one or more of TGF- β 1, TGF- β 2, or TGF- β 3) where antibodies include antibody fragments, such as nanobodies with affinity for TGF- β polypeptides, and single chain anti-TGF- β antibodies (e.g., any of which may be humanized). Some antibodies, including scFv antibodies, that bind and neutralize TGF- β have been described. See e.g., US 9,090,685. Throughout the embodiments and/or aspects described in this disclosure, T β R (e.g., T β RII) polypeptides used to mask TGF- β polypeptides may be replaced with a masking antibody (e.g., a scFv or a nanobody) with affinity for the TGF- β polypeptide.

[00328] In some cases, an antibody (e.g., a single chain antibody) may be used as a masking polypeptide and may be limited to the isoform of the TGF- β polypeptide(s) to be masked. By way of example, a single chain antibody based on Metelimumab (CAT192) directed against TGF- β 1 (e.g., Lord et al., mAbs 10(3): 444-452 (2018)) can be used to mask that TGF- β isoform when present in masked TGF- β MODs. In another embodiment, a single chain antibody specific for TGF- β 2 is used to mask that TGF- β isoform. In another embodiment, a single chain antibody specific for TGF- β 3 is used to mask that TGF- β isoform. Single chain antibodies can also be specific for a combination of TGF- β isoforms (e.g., ectodomains selected from the group consisting of: TGF- β 1 & TGF- β 2; TGF- β 1 & TGF- β 3; and TGF- β 2 & TGF- β 3. The single chain antibodies may also be pan-specific for TGF- β 1, TGF- β 2, and TGF- β 3 ectodomain sequences appearing in masked TGF- β MODs See e.g., WO 2014/164709. Antibodies and single chain antibodies that have the desired specificity and affinity for TGF- β isoforms can be prepared by a variety of methods, including screening hybridomas and/or modification (e.g., combinatorial modification) to the variable region sequence of antibodies that have affinity for a target TGF- β polypeptide sequence.

[00329] In an embodiment, a masking polypeptide comprises a single chain antibody to mask a TGF- β (e.g., a TGF- β 3). In one such embodiment the single chain amino acid sequence is specific for the TGF- β 3 comprising a C77S substitution.

LINKERS

[00330] As discussed above, a TMP of the present disclosure can include one or more linker peptides between components of the first and second polypeptides of the TMP, e.g., between a T1D peptide and an MHC polypeptide; between an MHC polypeptide and an Ig Fc polypeptide; between a first MHC polypeptide and a second MHC polypeptide; between an MOD and an MHC polypeptide; etc. As used herein, the phrase “an optional peptide linker between any two of the components of a TMP” refers to a peptide linker between any two adjacent polypeptides within the TMP. For example, as used herein, the phrase “an optional peptide linker between any two of the components of a TMP” refers to a peptide linker between one or more of: i) a peptide and an MHC class II polypeptide; ii) a first MHC class II polypeptide and a second MHC class II polypeptide; iii) an MHC class II polypeptide and an Ig Fc polypeptide; iv) an MHC class II polypeptide and a masking polypeptide; v) an MHC class II polypeptide and a TGF- β polypeptide; vi) an Ig Fc polypeptide and a MOD; vii) an Ig Fc polypeptide and a TGF- β polypeptide; viii) a first MOD and a second MOD; ix) a masking polypeptide and a TGF- β polypeptide; and x) a TGF- β polypeptide and a MOD.

[00331] As also noted above, in some cases, a TMP can include a Cys-containing peptide linker between the T1D peptide and an MHC class II polypeptide, e.g., between the T1D peptide and an MHC class II β chain polypeptide. Generally, a Cys-containing peptide linker will be used in either the first or

second polypeptide of a TMP in order to intentionally facilitate formation of a disulfide bond between the linker and a desired site on the other polypeptide. Where a Cys-containing linker is inserted in one polypeptide of a TMP, the remaining linkers in the TMP will not include a Cys in order to prevent formation of a disulfide bond at an unwanted site in the TMP, with the exception that a Cys-containing linker could be used in each of the first and second polypeptides when it is desired to link the first and second polypeptides through a disulfide bond formed between the linkers. A TMP thus can include: a) a Cys-containing peptide linker between the T1D peptide and an MHC class II polypeptide, e.g., between the T1D peptide and an MHC class II β chain polypeptide; and b) at least one additional peptide linker, where the at least one additional peptide linker does not include a Cys.

[00332] Suitable linkers (also referred to as “spacers”) can be readily selected and can be of any of a number of suitable lengths, such as from 1 amino acid to 25 amino acids, from 3 amino acids to 20 amino acids, from 2 amino acids to 15 amino acids, from 3 amino acids to 12 amino acids, including 4 amino acids to 10 amino acids, 5 amino acids to 9 amino acids, 6 amino acids to 8 amino acids, or 7 amino acids to 8 amino acids. A suitable linker can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids in length. A suitable linker can be from 25 to 35 amino acids in length. A suitable linker can be 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 amino acids in length. A suitable linker can be from 35 to 45 amino acids in length. A suitable linker can be 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, or 45 amino acids in length. A suitable linker can be from 45 to 50 amino acids in length. A suitable linker can be 45, 46, 47, 48, 49, or 50 amino acids in length.

Linkers Containing a Cys

[00333] A peptide linker comprising a Cys can comprise an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10). In some cases, a TMP of the present disclosure comprises a heterodimer comprising a first and a second polypeptide, where the first polypeptide comprises a T1D peptide and an MHC class II polypeptide (e.g., an MHC class II β chain polypeptide), and comprises a linker between the T1D peptide and the MHC class II polypeptide (e.g., the MHC class II β chain polypeptide), where the linker comprises an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10 (e.g., where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10).

Linkers Not Containing a Cys

[00334] Exemplary linkers include glycine polymers (G)_n, glycine-serine polymers (including, for example, (GS)_n, (GSGGS)_n (SEQ ID NO:233) and (GGGS)_n (SEQ ID NO:234), where n is an integer of at least one), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers known in the art. Glycine and glycine-serine polymers can be used; both Gly and Ser are relatively unstructured, and therefore can serve as a neutral tether between components. Glycine polymers can be used; glycine accesses significantly more phi-psi space than even alanine, and is much less restricted than residues with longer side chains (see Scheraga, *Rev. Computational Chem.* 11173-142 (1992)). Exemplary linkers can comprise amino acid sequences including, but not limited to, GGSG (SEQ ID NO:235), GGS GG (SEQ ID NO:236), GSGSG (SEQ ID NO:237), GSGGG (SEQ ID NO:238), GGGSG (SEQ ID NO:239), GSSSG (SEQ ID NO:240), and the like. Exemplary linkers can include, e.g., Gly(Ser₄)_n, (SEQ ID NO:241) where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some cases, a linker comprises the amino acid sequence (GSSSS)_n (SEQ ID NO:242), where n is 4. In some cases, a linker comprises the amino acid sequence (GSSSS)_n (SEQ ID NO:243), where n is 5. Exemplary linkers can include, e.g., (GlyGlyGlyGlySer)_n (SEQ ID NO:244) (also referred to as “G4S” linkers), where n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:245), where n is 1. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:246), where n is 2. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:160), where n is 3. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:171), where n is 4. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:161), where n is 5. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:247), where n is 6. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:248), where n is 7. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:249), where n is 8. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:250), where n is 9. In some cases, a linker comprises the amino acid sequence (GGGGS)_n (SEQ ID NO:259), where n is 10. In some cases, a linker comprises the amino acid sequence AAAGG (SEQ ID NO:184). In some cases, a linker comprises the amino acid sequence GGSAAAGG (SEQ ID NO:162). The AAAGG (SEQ ID NO:184) and GGSAAAGG (SEQ ID NO:162) linkers have been found to be useful, e.g., for linking an MHC class II alpha chain polypeptide (e.g., a DRA class II polypeptide) to an Ig Fc polypeptide.

PEPTIDES PRESENTING T1D-ASSOCIATED EPITOPES (“T1D PEPTIDES”)

[00335] As used herein, a “T1D peptide” is a peptide that, when present in a TMP of this disclosure, presents a T1D-associated epitope capable of being bound by a TCR on the surface of a T cell. A T1D peptide can have a length of from about 4 amino acids to about 25 amino acids, e.g., the

T1D peptide can have a length of from 4 amino acids (aa) to 10 aa, from 8 aa to 12 aa, from 10 aa to 15 aa, from 12 aa to 20 aa, from 15 aa to 20 aa, from 15 aa to 25 aa, or from 20 aa to 25 aa. For example, a T1D peptide present in a TMP can have a length of 4 amino acids (aa), 5 aa, 6 aa, 7, aa, 8 aa, 9 aa, 10 aa, 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, 20 aa, 21 aa, 22 aa, 23 aa, 24 aa, or 25 aa. In some cases, a T1D peptide present in a TMP has a length of from 8 amino acids to 20 amino acids, e.g., 8 aa, 9 aa, 10 aa, 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, or 20 aa.

[00336] Antigens associated with type 1 diabetes (T1D) include, e.g., preproinsulin, proinsulin, insulin, insulin B chain, insulin A chain, 65 kDa isoform of glutamic acid decarboxylase (GAD65), 67 kDa isoform of glutamic acid decarboxylase (GAD67), tyrosine phosphatase (IA-2), heat-shock protein HSP65, islet-specific glucose-6-phosphatase catalytic subunit related protein (IGRP), islet antigen 2 (IA2), and zinc transporter (ZnT8). See, e.g., Mallone et al. (2011) *Clin. Dev. Immunol.* 2011:513210; and U.S. Patent Publication No. 2017/0045529. An antigen “associated with” a particular autoimmune disorder is an antigen that is a target of autoantibodies and/or autoreactive T cells present in individuals with that autoimmune disorder, where such autoantibodies and/or autoreactive T cells mediate a pathological state associated with the autoimmune disorder. A suitable T1D peptide for inclusion in a TMP of the present disclosure can be an epitope-presenting T1D peptide of from 4 amino acids to about 25 amino acids in length of any one of the aforementioned T1D-associated antigens.

[00337] As one non-limiting example, a T1D peptide is proinsulin 73-90 (GAGSLQPLALEGSLQKR; SEQ ID NO:251). As another non-limiting example, a T1D peptide is the following insulin (InsA (1-15) peptide: GIVDQCCTSICSLYQ (SEQ ID NO:252). As another non-limiting example, a T1D peptide is the following insulin (InsA(1-15; D4E) peptide: GIVEQCCTSICSLYQ (SEQ ID NO:253). As another non-limiting example, a T1D peptide is the following GAD65 (555-567) peptide; NFFRMVISNPAAT (SEQ ID NO:177). As another non-limiting example, a T1D peptide is the following GAD65 (555-567; F557I) peptide; NFIRMVISNPAAT (SEQ ID NO:163). As another non-limiting example, a T1D peptide is the following islet antigen 2 (IA2) peptide: SFYLKNVQTQETRTLTFHF (SEQ ID NO:254). As another non-limiting example, a T1D peptide is the following proinsulin peptide: SLQPLALEGSLQSRG (SEQ ID NO:159). As another non-limiting example, a T1D peptide is the following proinsulin peptide GSLQPLALEGSLQSRGIV (SEQ ID NO:255; proIns 75-92(K88S)).

[00338] In some cases, a suitable T1D peptide comprises from 4 to 25 contiguous amino acids of an amino acid sequence having at least 90%, at least 95%, at least 98%, at least 99%, or 100%, amino acid sequence identity to amino acids 25-110 of the following human preproinsulin amino acid sequence (wherein amino acids 1-24 (underlined) is a signal peptide): MALWMRLLPL LALLALWGPD PAAA FVNQHL CGSHLVEALY LVCGERGFFY TPKTRREAED LQVGQVELGG GPGAGSLQPL ALEGLQKRG IVEQCCTSIC SLYQLENYCN (SEQ ID NO:256); where the T1D peptide has a length

of 4 amino acids (aa), 5 aa, 6 aa, 7, aa, 8 aa, 9 aa, 10 aa, 11 aa, 12 aa, 13 aa, 14 aa, 15 aa, 16 aa, 17 aa, 18 aa, 19 aa, 20 aa, 21 aa, 22 aa, 23 aa, 24 aa, or 25 aa. In some cases, the T1D peptide has the amino acid sequence: GAGSLQPLALEGSLQKRG (SEQ ID NO:176) (proIns 73-90). In some cases, the T1D peptide has the amino acid sequence: SLQPLALEGSLQKRG (SEQ ID NO:175) (proIns 76-90). In some cases, the T1D peptide has the amino acid sequence: SLQPLALEGSLQSRG (SEQ ID NO:159) (proIns 76-90; K88S). In some cases, the T1D peptide has the amino acid sequence: QPLALEGSLQKRG (SEQ ID NO:257). In some cases, the T1D peptide has the amino acid sequence: QPLALEGSLQSRG (SEQ ID NO:258).

NUCLEIC ACIDS

[00339] The present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a TMP of the present disclosure. In some cases, where a TMP comprises two different polypeptide chains, the present disclosure provides a single nucleic acid comprising nucleotide sequences encoding both the first polypeptide and the second polypeptide of the TMP. In other cases, where a TMP comprises two different polypeptide chains, the present disclosure provides: a) a first nucleic acid comprising a nucleotide sequence encoding the first polypeptide of a TMP; and b) a second nucleic acid comprising a nucleotide sequence encoding the second polypeptide of a TMP. In other cases, where a TMP is a single-chain TMP, the present disclosure provides a nucleic acid comprising a nucleotide sequence encoding the single-chain TMP. In some cases, the nucleic acid is a recombinant expression vector; thus, the present disclosure provides a recombinant expression vector comprising a nucleotide sequence encoding a TMP.

Separate Nucleic Acids Encoding Individual Polypeptide Chains of a TMP

[00340] The present disclosure provides nucleic acids comprising nucleotide sequences encoding a TMP of the present disclosure. As noted above, in some cases, where a TMP comprises two different polypeptide chains, the individual polypeptide chains of the TMP are encoded in separate nucleic acids. In some cases, nucleotide sequences encoding the separate polypeptide chains of a TMP are operably linked to transcriptional control elements, e.g., promoters, such as promoters that are functional in a eukaryotic cell, where the promoter can be a constitutive promoter or an inducible promoter.

[00341] For example, the present disclosure provides a first nucleic acid and a second nucleic acid, where the first nucleic acid comprises a nucleotide sequence encoding the first polypeptide of a TMP, and where the second nucleic acid comprises a nucleotide sequence encoding the second polypeptide of the TMP. In some cases, the nucleotide sequences encoding the first and the second polypeptides are operably linked to transcriptional control elements. In some cases, the transcriptional

control element is a promoter that is functional in a eukaryotic cell. In some cases, the nucleic acids are present in separate expression vectors.

Single Nucleic Acid Encoding Two Or More Polypeptides Present in a TMP

[00342] The present disclosure provides a nucleic acid comprising nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMP. In some cases, the nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMP includes a proteolytically cleavable linker interposed between the nucleotide sequence encoding the first polypeptide and the nucleotide sequence encoding the second polypeptide. In some cases, the nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMP includes an internal ribosome entry site (IRES) interposed between the nucleotide sequence encoding the first polypeptide and the nucleotide sequence encoding the second polypeptide. In some cases, the nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMP includes a ribosome skipping signal (or *cis*-acting hydrolase element, CHYSEL) interposed between the nucleotide sequence encoding the first polypeptide and the nucleotide sequence encoding the second polypeptide. Examples of nucleic acids are described below, where a proteolytically cleavable linker is provided between nucleotide sequences encoding the first polypeptide and the second polypeptide of a TMP; in any of these embodiments, an IRES or a ribosome skipping signal can be used in place of the nucleotide sequence encoding the proteolytically cleavable linker.

[00343] In some cases, a first nucleic acid (e.g., a recombinant expression vector, an mRNA, a viral RNA, etc.) comprises a nucleotide sequence encoding a first polypeptide chain of a TMP; and a second nucleic acid (e.g., a recombinant expression vector, an mRNA, a viral RNA, etc.) comprises a nucleotide sequence encoding a second polypeptide chain of a TMP. In some cases, the nucleotide sequence encoding the first polypeptide, and the second nucleotide sequence encoding the second polypeptide, are each operably linked to transcriptional control elements, e.g., promoters, such as promoters that are functional in a eukaryotic cell, where the promoter can be a constitutive promoter or an inducible promoter.

Nucleic Acid Encoding a Single-Chain TMP

[00344] The present disclosure provides a nucleic acid comprising a nucleotide sequence encoding a single-chain TMP described herein. In some cases, the nucleotide sequence encoding the single-chain TMP is operably linked to one or more transcriptional control elements. In some cases, the transcriptional control element is a promoter that is functional in a eukaryotic cell.

RECOMBINANT EXPRESSION VECTORS

[00345] The present disclosure provides recombinant expression vectors comprising nucleic acids of the present disclosure. In some cases, the recombinant expression vector is a non-viral vector. In some cases, the recombinant expression vector is a viral construct, e.g., a recombinant adeno-associated virus construct (see, e.g., U.S. Patent No. 7,078,387), a recombinant adenoviral construct, a recombinant lentiviral construct, a recombinant retroviral construct, a non-integrating viral vector, etc.

[00346] Suitable expression vectors include, but are not limited to, viral vectors (e.g. viral vectors based on vaccinia virus; poliovirus; adenovirus (see, e.g., Li et al., *Invest Ophthalmol Vis Sci* 35:2543-2549, 1994; Borrás et al., *Gene Ther* 6:515-524, 1999; Li and Davidson, *PNAS* 92:7700-7704, 1995; Sakamoto et al., *Hum Gene Ther* 5:1088-1097, 1999; WO 94/12649, WO 93/03769; WO 93/19191; WO 94/28938; WO 95/11984 and WO 95/00655); adeno-associated virus (see, e.g., Ali et al., *Hum Gene Ther* 9:81-86, 1998; Flannery et al., *PNAS* 94:6916-6921, 1997; Bennett et al., *Invest Ophthalmol Vis Sci* 38:2857-2863, 1997; Jomary et al., *Gene Ther* 4:683-690, 1997; Rolling et al., *Hum Gene Ther* 10:641-648, 1999; Ali et al., *Hum Mol Genet* 5:591-594, 1996; Srivastava in WO 93/09239, Samulski et al., *J. Vir.* (1989) 63:3822-3828; Mendelson et al., *Virol.* (1988) 166:154-165; and Flotte et al., *PNAS* (1993) 90:10613-10617); SV40; herpes simplex virus; human immunodeficiency virus (see, e.g., Miyoshi et al., *PNAS* 94:10319-23, 1997; Takahashi et al., *J Virol* 73:7812-7816, 1999); a retroviral vector (e.g., Murine Leukemia Virus, spleen necrosis virus, and vectors derived from retroviruses such as Rous Sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, a lentivirus, human immunodeficiency virus, myeloproliferative sarcoma virus, and mammary tumor virus); and the like. Numerous suitable expression vectors are known to those of skill in the art, and many are commercially available.

[00347] Depending on the host/vector system utilized, any of a number of suitable transcription and translation control elements, including constitutive and inducible promoters, transcription enhancer elements, transcription terminators, etc. may be used in the expression vector (see e.g., Bitter et al. (1987) *Methods in Enzymology*, 153:516-544).

[00348] In some cases, a nucleotide sequence encoding a TMP is operably linked to a control element, e.g., a transcriptional control element, such as a promoter. The transcriptional control element may be functional in either a eukaryotic cell, e.g., a mammalian cell; or a prokaryotic cell (e.g., bacterial or archaeal cell). In some cases, a nucleotide sequence encoding TMP is operably linked to multiple control elements that allow expression of the nucleotide sequence in both prokaryotic and eukaryotic cells.

[00349] Non-limiting examples of suitable eukaryotic promoters (promoters functional in a eukaryotic cell) include those from cytomegalovirus (CMV) immediate early, herpes simplex virus (HSV) thymidine kinase, early and late SV40, long terminal repeats (LTRs) from retrovirus, and mouse

metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. The expression vector may also contain a ribosome binding site for translation initiation and a transcription terminator. The expression vector may also include appropriate sequences for amplifying expression.

GENETICALLY MODIFIED HOST CELLS

[00350] The present disclosure provides a genetically modified host cell, where the host cell is genetically modified with a nucleic acid(s) of the present disclosure. The present disclosure provides a genetically modified host cell, where the host cell is genetically modified with a recombinant expression vector of the present disclosure.

[00351] Suitable host cells include eukaryotic cells, such as yeast cells, insect cells, and mammalian cells. In some cases, the host cell is a cell of a mammalian cell line. Suitable mammalian cell lines include human cell lines, non-human primate cell lines, rodent (e.g., mouse, rat) cell lines, and the like. Suitable mammalian cell lines include, but are not limited to, HeLa cells (e.g., American Type Culture Collection (ATCC) No. CCL-2), CHO cells (e.g., ATCC Nos. CRL9618, CCL61, CRL9096), 293 cells (e.g., ATCC No. CRL-1573), Vero cells, NIH 3T3 cells (e.g., ATCC No. CRL-1658), Huh-7 cells, BHK cells (e.g., ATCC No. CCL10), PC12 cells (ATCC No. CRL1721), COS cells, COS-7 cells (ATCC No. CRL1651), RAT1 cells, mouse L cells (ATCC No. CCL1.3), human embryonic kidney (HEK) cells (ATCC No. CRL1573), HLHepG2 cells, and the like.

[00352] Genetically modified host cells can be used to produce a TMP. An expression vector(s) comprising nucleotide sequence(s) encoding the polypeptide(s) is/are introduced into a host cell, generating a genetically modified host cell, which genetically modified host cell produces the polypeptide(s). For example, the genetically modified host cell is cultured in a suitable culture medium under conditions such that the TMP is synthesized by the genetically modified host cell. The TMP can then be obtained from the culture medium and/or a lysate of the genetically modified host cell. The TMP can be purified from the cell culture medium and/or the cell lysate.

METHODS OF PRODUCING A TMP

[00353] The present disclosure provides methods of producing a TMP of the present disclosure. The methods generally involve culturing, in a culture medium, a host cell (e.g., a genetically modified host cell of the present disclosure) that is genetically modified with a recombinant expression vector(s) comprising a nucleotide sequence(s) encoding the TMP; and isolating the TMP from the genetically modified host cell and/or the culture medium. As noted above, in some cases, the individual polypeptide chains of a TMP are encoded in separate recombinant expression vectors. In some cases, all polypeptide chains of a TMP are encoded in a single recombinant expression vector. Where a TMP is a single-chain TMP, a single recombinant expression vector encodes the single-chain TMP.

[00354] Isolation of the TMP from the expression host cell (e.g., from a lysate of the genetically modified host cell) and/or the culture medium in which the host cell is cultured, can be carried out using standard methods of protein purification.

[00355] For example, a lysate may be prepared of the expression host and the lysate purified using high performance liquid chromatography (HPLC), exclusion chromatography (e.g., size exclusion chromatography), gel electrophoresis, affinity chromatography, or other purification technique.

Alternatively, where the TMP is secreted from the expression host cell into the culture medium, the TMP can be purified from the culture medium using HPLC, exclusion chromatography, gel electrophoresis, affinity chromatography, or other purification technique. In some cases, the TMP is purified, e.g., a composition is generated that comprises at least 80% by weight, at least about 85% by weight, at least about 95% by weight, or at least about 99.5% by weight, of the TMP in relation to contaminants related to the method of preparation of the product and its purification. The percentages can be based upon total protein.

[00356] In some cases, e.g., where the TMP comprises an affinity tag, the TMP can be purified using an immobilized binding partner of the affinity tag. For example, where a TMP comprises an Ig Fc polypeptide, the TMP can be isolated from genetically modified mammalian host cell and/or from culture medium in which the mammalian cells are cultured, where isolation of the TMP or APP can be carried out by affinity chromatography, e.g., on a Protein A column, a Protein G column, or the like. An example of a suitable mammalian cell is a CHO cell; e.g., an Expi-CHO-S™ cell (e.g., ThermoFisher Scientific, Catalog #A29127).

[00357] In some cases, the first and second polypeptides of a TMP will self-assemble into heterodimers by spontaneously forming disulfide bonds between the above-discussed Cys residues in the first and second polypeptides. As also noted above, when both heterodimers include Ig Fc polypeptides, disulfide bonds will spontaneously form between the respective Ig Fc polypeptides to covalently link the two heterodimers to one another.

COMPOSITIONS

[00358] The present disclosure provides compositions, including pharmaceutical compositions, comprising a TMP of the present disclosure. The present disclosure provides compositions, including pharmaceutical compositions, comprising a nucleic acid or a recombinant expression vector of the present disclosure.

Compositions Comprising a TMP

[00359] A composition of the present disclosure can comprise, in addition to a TMP, one or more pharmaceutically acceptable components/excipients such as: a salt, e.g., NaCl, MgCl₂, KCl, MgSO₄, etc.; a buffering agent, e.g., a Tris buffer, N-(2-Hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid) (HEPES),

2-(N-Morpholino)ethanesulfonic acid (MES), 2-(N-Morpholino)ethanesulfonic acid sodium salt (MES), 3-(N-Morpholino)propanesulfonic acid (MOPS), N-tris[Hydroxymethyl]methyl-3-aminopropanesulfonic acid (TAPS), etc.; a solubilizing agent; a detergent, e.g., a non-ionic detergent such as Tween-20, etc.; a protease inhibitor; glycerol; and the like. Pharmaceutically acceptable excipients have been amply described in a variety of publications, including, for example, "Remington: The Science and Practice of Pharmacy", 19th Ed. (1995), or latest edition, Mack Publishing Co; A. Gennaro (2000) "Remington: The Science and Practice of Pharmacy", 20th edition, Lippincott, Williams, & Wilkins; Pharmaceutical Dosage Forms and Drug Delivery Systems (1999) H.C. Ansel et al., eds 7th ed., Lippincott, Williams, & Wilkins; and Handbook of Pharmaceutical Excipients (2000) A.H. Kibbe et al., eds., 3rd ed. Amer. Pharmaceutical Assoc.

[00360] A pharmaceutical composition can comprise: i) a TMP of the present disclosure; and ii) a pharmaceutically acceptable excipient. In some cases, a subject pharmaceutical composition will be suitable for administration to a subject, e.g., will be sterile. For example, in some cases, a subject pharmaceutical composition will be suitable for administration to a human subject, e.g., where the composition is sterile and is free of detectable pyrogens and/or other toxins, or the amount of detectable pyrogens and/or other toxins are below a permissible limit.

[00361] For example, compositions may include aqueous solution, powder form, granules, tablets, pills, suppositories, capsules, suspensions, sprays, and the like. The composition may be formulated according to the various routes of administration described below.

[00362] Where a TMP is administered as an injectable (e.g. subcutaneously, intraperitoneally, intramuscularly, intralymphatically, and/or intravenously) directly into a tissue, a formulation can be provided as a ready-to-use dosage form, or as non-aqueous form (e.g. a reconstitutible storage-stable powder) or aqueous form, such as liquid composed of pharmaceutically acceptable carriers and excipients. The protein-containing formulations may also be provided so as to enhance serum half-life of the subject protein following administration. For example, the protein may be provided in a liposome formulation, prepared as a colloid, or other conventional techniques for extending serum half-life. A variety of methods are available for preparing liposomes, as described in, e.g., Szoka et al. 1980 *Ann. Rev. Biophys. Bioeng.* 9:467, U.S. Pat. Nos. 4,235,871, 4,501,728 and 4,837,028. The preparations may also be provided in controlled release or slow-release forms.

[00363] In some cases, a composition of the present disclosure comprises: a) a TMP; and b) saline (e.g., 0.9% NaCl). In some cases, the composition is sterile. In some cases, the composition is suitable for administration to a human subject, e.g., where the composition is sterile and is free of detectable pyrogens and/or other toxins. Thus, the present disclosure provides a composition comprising: a) a TMP of the present disclosure; and b) saline (e.g., 0.9% NaCl), where the composition is sterile and

is free of detectable pyrogens and/or other toxins, or where the detectable pyrogens and/or other toxins are below a permissible limit.

[00364] The concentration of a TMP in a formulation can vary widely (e.g., from less than about 0.1%, usually at or at least about 2% to as much as 20% to 50% or more by weight) and will usually be selected primarily based on fluid volumes, viscosities, and patient-based factors in accordance with the particular mode of administration selected and the patient's needs.

[00365] The present disclosure provides a container comprising a composition of the present disclosure, e.g., a liquid composition. The container can be, e.g., a syringe, an ampoule, and the like. In some cases, the container is sterile. In some cases, both the container and the composition are sterile.

Compositions Comprising a Nucleic Acid or a Recombinant Expression Vector

[00366] The present disclosure provides compositions, e.g., pharmaceutical compositions, comprising a nucleic acid or a recombinant expression vector of the present disclosure. A wide variety of pharmaceutically acceptable excipients is known in the art and need not be discussed in detail herein. Pharmaceutically acceptable excipients have been amply described in a variety of publications, including, for example, A. Gennaro (2000) "Remington: The Science and Practice of Pharmacy", 20th edition, Lippincott, Williams, & Wilkins; Pharmaceutical Dosage Forms and Drug Delivery Systems (1999) H. C. Ansel et al., eds 7th ed., Lippincott, Williams, & Wilkins; and Handbook of Pharmaceutical Excipients (2000) A. H. Kibbe et al., eds., 3rd ed. Amer. Pharmaceutical Assoc.

[00367] A pharmaceutical formulation of the present disclosure can include a nucleic acid or recombinant expression vector in an amount of from about 0.001% to about 90% (w/w). In the description of formulations, below, "subject nucleic acid or recombinant expression vector" will be understood to include a nucleic acid or recombinant expression vector. For example, in some cases, a subject formulation comprises a nucleic acid or recombinant expression vector.

[00368] A subject nucleic acid or recombinant expression vector can be admixed, encapsulated, conjugated or otherwise associated with other compounds or mixtures of compounds; such compounds can include, e.g., liposomes or receptor-targeted molecules. A subject nucleic acid or recombinant expression vector can be combined in a formulation with one or more components that assist in uptake, distribution and/or absorption.

METHODS

[00369] A TMP of the present disclosure is useful for modulating an activity of a T cell. Thus, the present disclosure provides methods of modulating an activity of a T cell, the methods generally involving contacting a target T cell with a TMP of the present disclosure.

[00370] The present disclosure provides a method of selectively modulating the activity of an epitope-specific T cell, the method comprising contacting the T cell with a TMP, where contacting the T

cell with a TMP selectively modulates the activity of the epitope-specific T cell. In some cases, the contacting occurs *in vivo*. In some cases, the contacting occurs *in vitro*.

[00371] The present disclosure thus also provides a method of selectively delivering a TGF- β polypeptide to an epitope-specific target T cell, the method comprising contacting the T cell with a TMP comprising a masked TGF- β MOD, where contacting the epitope-specific T cell with a TMP comprising a masked TGF- β MOD selectively provides TGF- β modulation to the epitope-specific T cell. In some cases, the contacting occurs *in vivo*. In some cases, the contacting occurs *in vitro*. As used herein, the phrases “selectively delivers” and “selectively provides” means that the majority of T cells for which the TMP provides TGF- β modulation comprise a TCR that specifically or preferentially binds the epitope of the TMP.

[00372] In some cases, a TMP reduces activity of an autoreactive T cell and/or an autoreactive B cell. In some cases, a TMP increases the number and/or activity of a regulator T cell (Treg), resulting in reduced activity of an autoreactive T cell and/or an autoreactive B cell.

[00373] In some cases, the T cell being contacted with a TMP is a regulatory T cell (Treg). Tregs are CD4⁺, FOXP3⁺, and CD25⁺. Tregs can suppress autoreactive T cells. In some cases, a method of the present disclosure activates Tregs, thereby reducing autoreactive T cell activity.

[00374] The present disclosure provides a method of increasing proliferation of Tregs, the method comprising contacting Tregs with a TMP, where the contacting increases proliferation of Tregs. The present disclosure provides a method of increasing the number of Tregs in an individual, the method comprising administering to the individual a TMP, where the administering results in an increase in the number of Tregs in the individual. For example, the number of Tregs can be increased by at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 2-fold, at least 2.5-fold, at least 5-fold, at least 10-fold, or more than 10-fold.

TREATMENT METHODS

[00375] The present disclosure provides treatment methods, the methods comprising administering to the individual an amount of a TMP of the present disclosure, or one or more nucleic acids or expression vectors encoding the TMP effective to selectively modulate the activity of an epitope-specific (e.g., T1D peptide-specific) T cell in an individual and to treat the individual. In some cases, a treatment method of the present disclosure comprises administering to an individual in need thereof one or more recombinant expression vectors comprising nucleotide sequences encoding a TMP. In some cases, a treatment method comprises administering to an individual in need thereof one or more mRNA molecules comprising nucleotide sequences encoding a TMP. In some cases, a treatment method

of the present disclosure comprises administering to an individual in need thereof a TMP e. A TMP is useful for treating type 1 diabetes (T1D).

[00376] The present disclosure provides a method of selectively modulating the activity of an epitope-specific T cell in an individual, the method comprising administering to the individual an effective amount of a TMP, or one or more nucleic acids (e.g., expression vectors; mRNA; etc.) comprising nucleotide sequences encoding the TMP, where the TMP selectively modulates the activity of the epitope-specific T cell in the individual. Selectively modulating the activity of an epitope-specific T cell can treat a disease or disorder in the individual. Thus, the present disclosure provides a treatment method comprising administering to an individual in need thereof an effective amount of a TMP. A treatment method of the present disclosure, comprising administering an effective amount of a TMP, is suitable for treating T1D.

[00377] The present disclosure provides a method of treating T1D in an individual, the method comprising administering to the individual an effective amount of a TMP, or one or more nucleic acids comprising nucleotide sequences encoding the TMP, where the TMP comprises a T1D peptide (as described above). In some cases, an “effective amount” of a TMP is an amount that, when administered in one or more doses to an individual in need thereof, reduces the number of self-reactive (i.e., reactive with a T1D-associated antigen) CD4⁺ and/or CD8⁺ T cells by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or at least 95%, compared to number of self-reactive T cells in the individual before administration of the TMP, or in the absence of administration with the TMP. In some cases, an “effective amount” of a TMP is an amount that, when administered in one or more doses to an individual in need thereof, reduces production of Th2 cytokines in the individual. In some cases, an “effective amount” of a TMP is an amount that, when administered in one or more doses to an individual in need thereof, ameliorates one or more symptoms associated with T1D in the individual. In some instances, the TMP reduces the number of CD4⁺ self-reactive T cells (i.e., the number of CD4⁺ T cells reactive with a T1D-associated antigen), which in turn leads to a reduction in CD8⁺ self-reactive T cells. In some instances, the TMP increases the number of CD4⁺ Tregs, which in turn reduces the number of CD4⁺ self-reactive T cells and/or CD8⁺ T self-reactive T cells.

[00378] As noted above, in some cases, in carrying out a subject treatment method, a TMP is administered to an individual in need thereof, as the polypeptide *per se*. In other instances, in carrying out a subject treatment method, one or more nucleic acids comprising nucleotide sequences encoding a TMP is/are administering to an individual in need thereof. Thus, in other instances, one or more nucleic acids of the present disclosure, e.g., one or more recombinant expression vectors of the present disclosure, is/are administered to an individual in need thereof.

Dosages

[00379] A suitable dosage can be determined by an attending physician or other qualified medical personnel, based on various clinical factors. As is well known in the medical arts, dosages for any one patient depend upon many factors, including the patient's size, body surface area, age, the particular polypeptide or nucleic acid to be administered, sex of the patient, time, and route of administration, general health, and other drugs being administered concurrently. A TMP (as a single heterodimer; as a homodimer comprising two heterodimers linked together; as a heterodimer comprising two heterodimers linked together; as a single-chain TMP; as a homodimer comprising two single-chain TMPs linked together; or as a heterodimer comprising two single-chain TMPs linked together) may be administered in amounts between 1 ng/kg body weight and 20 mg/kg body weight per dose, e.g. between 0.1 mg/kg body weight to 10 mg/kg body weight, e.g. from 0.1 mg/kg body weight to 0.5 mg/kg body weight, from 0.5 mg/kg body weight to 1 mg/kg body weight, from 1.0 mg/kg body weight to 5 mg/kg body weight, from 5 mg/kg body weight to 10 mg/kg body weight, from 10 mg/kg body weight to 15 mg/kg body weight, and from 15 mg/kg body weight to 20 mg/kg body weight; however, doses below 0.1 mg/kg body weight or above 20 mg/kg are envisioned, especially considering the aforementioned factors. Amounts thus include from about 0.1 mg/kg body weight to about 0.5 mg/kg body weight, from about 0.5 mg/kg body weight to about 1 mg/kg body weight, from about 1.0 mg/kg body weight to about 5 mg/kg body weight, from about 5 mg/kg body weight to about 10 mg/kg body weight, from about 10 mg/kg body weight to about 15 mg/kg body weight, from about 15 mg/kg body weight to about 20 mg/kg body weight, from about 20 mg/kg body weight to about 25 mg/kg body weight, from about 25 mg/kg body weight to about 30 mg/kg body weight, from about 30 mg/kg body weight to about 35 mg/kg body weight, from about 35 mg/kg body weight to about 40 mg/kg body weight, or from about 40 mg/kg body weight to about 50 mg/kg body weight. If the regimen is a continuous infusion, it can also be in the range of 1 μ g to 10 mg per kilogram of body weight per minute.

[00380] Persons of ordinary skill in the art can easily estimate repetition rates for dosing based on measured residence times and concentrations of the administered agent in bodily fluids or tissues. Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the T1D disease state, wherein a TMP is administered in maintenance doses, ranging from those recited above, i.e., 0.1 mg/kg body weight to about 0.5 mg/kg body weight, from about 0.5 mg/kg body weight to about 1 mg/kg body weight, from about 1.0 mg/kg body weight to about 5 mg/kg body weight, from about 5 mg/kg body weight to about 10 mg/kg body weight, from about 10 mg/kg body weight to about 15 mg/kg body weight, from about 15 mg/kg body weight to about 20 mg/kg body weight, from about 20 mg/kg body weight to about 25 mg/kg body weight, from about 25 mg/kg body weight to about 30 mg/kg body weight, from about 30 mg/kg body weight to about 35

mg/kg body weight, from about 35 mg/kg body weight to about 40 mg/kg body weight, or from about 40 mg/kg body weight to about 50 mg/kg body weight.

[00381] Those of skill will readily appreciate that dose levels can vary as a function of the specific TMP, the severity of the symptoms and the susceptibility of the subject to side effects. Preferred dosages for a given compound are readily determinable by those of skill in the art by a variety of means.

[00382] In some cases, multiple doses of a TMP, a nucleic acid, or a recombinant expression vector are administered. The frequency of administration of a TMP, a nucleic acid, or a recombinant expression vector can vary depending on any of a variety of factors, e.g., severity of the symptoms, patient response, etc. For example, in some cases, a TMP, a nucleic acid, or a recombinant expression vector is administered less frequently than once per month, e.g., once every two, three, four, six or twelve months, once per month, twice per month, three times per month, every other week (qow), one every three weeks, once every four weeks, once per week (qw), twice per week (biw), three times per week (tiw), four times per week, five times per week, six times per week, every other day (qod), daily (qd), twice a day (qid), or three times a day (tid).

[00383] The duration of administration of a TMP, a nucleic acid, or a recombinant expression vector, e.g., the period of time over which a TMP, a nucleic acid, or a recombinant expression vector is administered, can vary, depending on any of a variety of factors, e.g., patient response, etc. For example, TMP, a nucleic acid, or a recombinant expression vector can be administered over a period of time ranging from about one day to about one week, from about two weeks to about four weeks, from about one month to about two months, from about two months to about four months, from about four months to about six months, from about six months to about eight months, from about eight months to about 1 year, from about 1 year to about 2 years, or from about 2 years to about 4 years, or more, including continued administration for the patient's life.

[00384] Where treatment is of a finite duration, following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the T1D disease state, wherein a TMP is administered in maintenance doses, ranging from those recited above, i.e., 0.1 mg/kg body weight to about 0.5 mg/kg body weight, from about 0.5 mg/kg body weight to about 1 mg/kg body weight, from about 1.0 mg/kg body weight to about 5 mg/kg body weight, from about 5 mg/kg body weight to about 10 mg/kg body weight, from about 10 mg/kg body weight to about 15 mg/kg body weight, from about 15 mg/kg body weight to about 20 mg/kg body weight, from about 20 mg/kg body weight to about 25 mg/kg body weight, from about 25 mg/kg body weight to about 30 mg/kg body weight, from about 30 mg/kg body weight to about 35 mg/kg body weight, from about 35 mg/kg body weight to about 40 mg/kg body weight, or from about 40 mg/kg body weight to about 50 mg/kg body weight.

Routes of administration

[00385] An active agent (a TMP, a nucleic acid, or a recombinant expression vector) is administered to an individual using any available method and route suitable for drug delivery, including *in vivo* and *in vitro* methods, as well as systemic and localized routes of administration. A TMP, a nucleic acid, or a recombinant expression vector can be administered to a host using any available conventional methods and routes suitable for delivery of conventional drugs, including systemic or localized routes. In general, routes of administration contemplated for use in a method of the present disclosure include, but are not necessarily limited to, enteral, parenteral, and inhalational routes.

[00386] Conventional and pharmaceutically acceptable routes of administration include intramuscular, intratracheal, intralymphatic, subcutaneous, intradermal, topical application, intravenous, intraarterial, rectal, nasal, oral, and other enteral and parenteral routes of administration. Of these, intravenous, intramuscular and subcutaneous may be more commonly employed. Routes of administration may be combined, if desired, or adjusted depending upon the TMP and/or the desired effect. A TMP, or a nucleic acid or recombinant expression vector, can be administered in a single dose or in multiple doses.

[00387] In some cases, a TMP, a nucleic acid, or a recombinant expression vector is administered intravenously. In some cases, a TMP, a nucleic acid, or a recombinant expression vector is administered intramuscularly. In some cases, a TMP, a nucleic acid of the present disclosure, or a recombinant expression vector is administered intralymphatically. In some cases, a TMP, a nucleic acid of the present disclosure, or a recombinant expression vector is administered subcutaneously.

Subjects suitable for treatment

[00388] Subjects suitable for treatment with a method of the present disclosure include individuals who have T1D, including individuals who have been diagnosed as having T1D, and individuals who have been treated for T1D but who failed to respond to the treatment. Suitable subjects also may include individuals who have been diagnosed as being likely to develop T1D or who have symptoms indicating the imminent onset of T1D.

Examples of Non-Limiting Aspects of the Disclosure**ASPECTS SET A**

[00389] Aspects, including embodiments, of the present subject matter described above may be beneficial alone or in combination, with one or more other aspects or embodiments. Without limiting the foregoing description, certain non-limiting aspects of the disclosure are provided below. As will be apparent to those of skill in the art upon reading this disclosure, each of the individually numbered aspects may be used or combined with any of the preceding or following individually numbered aspects.

This is intended to provide support for all such combinations of aspects and is not limited to combinations of aspects explicitly provided below:

[00390] Aspect 1. A T-cell modulatory polypeptide (TMP) comprising:

- a) a peptide that displays a Type 1 Diabetes-associated epitope capable of being bound by a T-cell receptor (a “T1D peptide”);
- b) a TGF- β polypeptide;
- c) a masking polypeptide, optionally wherein the masking polypeptide comprises a TGF- β receptor polypeptide or an anti-TGF- β polypeptide;
- d) an MHC class II α chain polypeptide;
- e) an MHC class II β chain polypeptide; and
- f) one or more immunomodulatory polypeptides (MOD),

wherein optionally the TMP comprises a scaffold polypeptide, and

wherein optionally the TMP comprises one or more independently selected linker polypeptides.

[00391] Aspect 2. The TMP of aspect 1, wherein at least one of the one or more MODs is selected from the group consisting of an IL-2 polypeptide, PD-L1 polypeptide, a 4-1BBL polypeptide, and combinations thereof.

[00392] Aspect 3. The TMP of aspect 1 or 2, wherein at least one of the one or more MODs is a PD-L1 polypeptide, optionally wherein the PD-L1 polypeptide comprises a PD-L1 polypeptide extracellular domain.

[00393] Aspect 4. The TMP of aspect 3, wherein the PD-L1 polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to the PD-L1 amino acid sequence depicted in FIG. 22D and has a length of from about 215 amino acids to about 220 amino acids.

[00394] Aspect 5. The TMP of aspect 1 or aspect 2, wherein at least one of the one or more MODs is a 4-1BBL polypeptide.

[00395] Aspect 6. The TMP of aspect 5, wherein the 4-1BBL polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to the 4-1BBL amino acid sequence depicted in FIG. 22E, and has a length of from about 160 amino acids to about 170 amino acids.

[00396] Aspect 7. The TMP of any one of aspects 1-5, wherein at least one of the one or more MODs is a variant IL-2 polypeptide, optionally wherein the one or more variant IL-2 polypeptides exhibit a binding affinity for an IL-2 receptor, and wherein the binding affinity of such one or more variant IL-2 polypeptides is less than the binding affinity of a wild-type human IL-2 polypeptide for the same IL-2 receptor, when assayed under the same conditions in a bio-layer interferometry (BLI) assay.

[00397] Aspect 8. The TMP of aspect 7, wherein the at least one variant IL-2 polypeptide exhibits reduced binding to the α chain of IL-2 receptor and/or the β chain of IL-2 receptor, and

optionally wherein the at least one variant IL-2 polypeptide exhibits reduced binding to both the α chain of IL-2 receptor and the β chain of IL-2 receptor.

[00398] Aspect 9. The TMP of aspect 8, comprising two variant IL-2 polypeptides that exhibits reduced binding to the α chain of IL-2 receptor and the β chain of IL-2 receptor.

[00399] Aspect 10. The TMP of aspect 8 or 9, wherein the variant IL-2 polypeptide comprises: i) an H16A substitution and an F42A substitution; or ii) an H16T substitution and an F42A substitution.

[00400] Aspect 11. The TMP of aspect 1, wherein at least one of the one or more MODs is a 4-1BBL polypeptide.

[00401] Aspect 12. The TMP of any one of aspects 1-11, wherein the T1D peptide has a length of from about 4 amino acids to about 25 amino acids, or from about 8 amino acids to about 20 amino acids, and comprises a proinsulin peptide or a glutamic acid decarboxylase (GAD) peptide.

[00402] Aspect 13. The TMP of aspect 12, wherein the T1D peptide is:

a) a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90); or

b) a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).

[00403] Aspect 14. The TMP of aspect 13, wherein the T1D peptide comprises the amino acid sequence SLQPLALEGSLQSRG (SEQ ID NO:159).

[00404] Aspect 15. The TMP of any one of aspects 1-14, wherein the masking polypeptide comprises a TGF- β receptor ("T β R") polypeptide.

[00405] Aspect 16. The TMP of aspect 15, wherein the masking polypeptide comprises at least a portion of a type I T β R (T β RI) polypeptide, a type II T β R (T β RII) polypeptide, or a type III T β R (T β RIII) polypeptide.

[00406] Aspect 17. The TMP of aspect 16, wherein the masking polypeptide comprises at least a portion of an ectodomain of a T β RI polypeptide, a T β RII polypeptide, or a T β RIII polypeptide.

[00407] Aspect 18. The TMP of aspect 17, optionally wherein the masking polypeptide comprises at least a portion of the ectodomain of a T β RII isoform A polypeptide or the ectodomain of a T β RII isoform B polypeptide.

[00408] Aspect 19. The TMP of any one of aspects 15-18, wherein the T β R polypeptide comprises one or more sequence variations relative to the corresponding wild type T β R polypeptide, and wherein the T β R polypeptide exhibits reduced affinity for the TGF- β polypeptide relative to the corresponding wild type T β R polypeptide.

- [00409]** Aspect 20. The TMP of aspect 19, wherein the one or more sequence variations are selected from the group consisting of deletions, insertions, substitutions, and combinations thereof.
- [00410]** Aspect 21. The TMP of any one of aspects 15-20, wherein the TGF- β polypeptide comprises at least a portion of a TGF- β 1 polypeptide, a TGF- β 2 polypeptide or a TGF- β 3 polypeptide.
- [00411]** Aspect 22. The TMP of aspect 21, wherein the TGF- β polypeptide comprises at least a portion of a TGF- β 3 polypeptide.
- [00412]** Aspect 23. The TMP of aspect 18 or aspect 19, wherein the T β R polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence depicted in any one of FIG. 25B, 25D, and 25F-25J.
- [00413]** Aspect 24. The TMP of aspect 22, wherein the TGF- β 3 polypeptide comprises an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence depicted in FIG. 23F.
- [00414]** Aspect 25. The TMP of any one of aspects 1-24, wherein the scaffold polypeptide comprises an immunoglobulin (Ig) Fc polypeptide.
- [00415]** Aspect 26. The TMP of aspect 25, wherein the Ig Fc polypeptide is a variant Ig Fc polypeptide comprising one or more sequence variations relative to the wild type polypeptide, wherein the ability of the Ig Fc polypeptide to induce cell lysis through complement-dependent cytotoxicity (CDC) and/or antibody-dependent cellular cytotoxicity (ADCC) is reduced or substantially eliminated.
- [00416]** Aspect 27. The TMP of aspect 26, wherein the Ig Fc polypeptide is a variant human IgG1 Fc polypeptide comprising an L234A and/or L235A substitutions (L14 and L15 in the amino acid sequence depicted in FIG. 21A).
- [00417]** Aspect 28. The TMP of any one of aspects 25-27, wherein the Ig Fc polypeptide is a variant Ig Fc polypeptide comprising at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to least 125 contiguous aas (at least 150, at least 175, at least 200, or at least 220 contiguous aas) of wt. IgG1 Fc comprising the amino acid sequence depicted in FIG. 21A.
- [00418]** Aspect 29. The TMP of aspect 25, wherein the Ig Fc polypeptide is an Ig Fc polypeptide comprising at least about 90%, at least about 95%, at least about 98%, at least about 99%, or 100% aa sequence identity to the amino acid sequence depicted in any one of FIG. 21A-21M.
- [00419]** Aspect 30. The TMP of any one of aspects 1-29, wherein the MHC class II α polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to a DRA1*01:01 polypeptide; and the MHC class II β polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to a DRB1*04:01 polypeptide.

[00420] Aspect 31. The TMP of any one of aspects 1-30, wherein the TMP comprises at least one heterodimer, wherein each heterodimer comprises:

- a) a first polypeptide comprising:
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide; and
 - iv) a first scaffold polypeptide comprising a first interspecific binding sequence,

and

- b) a second polypeptide comprising:
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide; and
 - iv) a second scaffold polypeptide comprising a counterpart interspecific binding sequence to the interspecific binding sequence of the first polypeptide, wherein the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other in the heterodimer, and wherein, the first and/or the second polypeptide comprises the one or more MODs, the first or the second polypeptide comprises the TGF- β polypeptide, and the first or the second polypeptide comprises the masking polypeptide, and the components of the first polypeptide and/or the components of the second polypeptide optionally may be joined by one or more independently selected linkers.

[00421] Aspect 32. The TMP of aspect 31, wherein:

[00422] a) the TGF- β polypeptide is on the first polypeptide and the masking polypeptide is on the second polypeptide; or

[00423] b) the masking polypeptide is on the first polypeptide and the TGF- β polypeptide is on the second polypeptide.

[00424] Aspect 33. The TMP of aspect 32, wherein:

[00425] the one or more MODs and the TGF- β polypeptide are both on the same polypeptide, or

[00426] the one or more MODs and the masking polypeptide are both on the same polypeptide.

[00427] Aspect 34. The TMP of aspect 31, wherein the TGF- β polypeptide and the masking polypeptide are both on the same polypeptide.

[00428] Aspect 35. The TMP of aspect 34, wherein the one or more MODs are on the same polypeptide as the TGF- β polypeptide and masking polypeptide.

[00429] Aspect 36. The TMP of aspect 34, wherein:

[00430] a) the one or more MODs are on the first polypeptide and the TGF- β polypeptide and the masking polypeptide are on the second polypeptide; or

[00431] b) the TGF- β polypeptide and the masking polypeptide are on the first polypeptide and the one or more MODs are on the second polypeptide.

[00432] Aspect 37. The TMP of any one of aspects 31-36, wherein the interspecific binding sequence and the counterpart interspecific binding sequence comprise knob-in-hole sequences.

[00433] Aspect 38. The TMP of any one of aspects 1-30, wherein the TMP comprises at least one heterodimer, wherein each heterodimer comprises:

a) a first polypeptide comprising:

i) the T1D peptide; and

ii) an MHC class II α chain polypeptide or an MHC class II β chain polypeptide;

and

iii) optionally a linker that links the T1D peptide to the first MHC class II polypeptide; and

b) a second polypeptide comprising i) an MHC class II α chain polypeptide if the first polypeptide comprises an MHC class II β chain polypeptide, or ii) an MHC class II β chain polypeptide if the first polypeptide comprises an MHC class II α chain polypeptide wherein the first and/or the second polypeptide comprises the one or more MODs, the first or the second polypeptide comprises the TGF- β polypeptide, and the first or the second polypeptide comprises the masking polypeptide, and optionally wherein the first polypeptide and the second polypeptide of the heterodimer are covalently linked to one another via at least one disulfide bond.

[00434] Aspect 39. The TMP of aspect 38, wherein the first polypeptide comprises an MHC class II β chain polypeptide.

[00435] Aspect 40. The TMP of aspect 38, wherein

a1) the first polypeptide comprises:

i) the T1D peptide;

ii) an MHC class II β polypeptide; and

b1) the second polypeptide comprises:

i) an MHC class II α polypeptide;

ii) the TGF- β polypeptide;

iii) the masking polypeptide;

iv) the one or more MODs; and

v) an Ig Fc polypeptide, or

a2) the first polypeptide comprises:

- i) the T1D peptide;
- ii) an MHC class II β polypeptide; and
- iii) the TGF- β polypeptide or the masking polypeptide, and

b2) the second polypeptide comprises:

- i) an MHC class II α polypeptide;
- ii) the masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or the TGF- β polypeptide if the first polypeptide comprises the masking polypeptide;
- iii) the one or more MODs; and
- iv) an Ig Fc polypeptide, or

a3) the first polypeptide comprises:

- i) the T1D peptide;
- ii) an MHC class II β polypeptide;
- iii) the TGF- β polypeptide or the masking polypeptide; and
- iv) an Ig Fc polypeptide, and

b3) the second polypeptide comprises:

- i) an MHC class II α polypeptide;
- ii) the masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or the TGF- β polypeptide if the first polypeptide comprises the masking polypeptide;
- iii) the one or more MODs, or

a4) the first polypeptide comprises:

- i) the T1D peptide;
- ii) an MHC class II β polypeptide;
- iii) the TGF- β polypeptide or the masking polypeptide; and
- iv) the one or more MODs, and

b4) the second polypeptide comprises:

- i) an MHC class II α polypeptide;
- ii) the masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or the TGF- β polypeptide if the first polypeptide comprises the masking polypeptide;
- iii) an Ig Fc polypeptide, or

a5) the first polypeptide comprises:

- i) the T1D peptide;

- ii) an MHC class II β polypeptide;
- iii) the TGF- β polypeptide or the masking polypeptide; and
- iv) the one or more MODs; and
- v) an Ig Fc polypeptide

b5) the second polypeptide comprises:

- i) an MHC class II α polypeptide; and
- ii) the masking polypeptide if the first polypeptide comprises the TGF- β polypeptide, or the TGF- β polypeptide if the first polypeptide comprises the masking polypeptide, or

a6) the first polypeptide comprises:

- i) the T1D peptide;
- ii) an MHC class II β polypeptide;
- iii) the TGF- β polypeptide;
- iv) the masking polypeptide;
- v) the one or more MODs; and
- vi) an Ig Fc polypeptide

b6) the second polypeptide comprises:

- i) an MHC class II α polypeptide,

wherein, in any of the above TMPs, the components of the first polypeptide optionally may be joined by one or more independently selected linkers, and where the second polypeptide comprises more than one component, the components of the second polypeptide optionally may be joined by one or more independently selected linkers.

[00436] Aspect 41. The TMP of aspect 39 or 40, wherein the TMP comprises a Cys-containing linker between the T1D peptide and the MHC Class II β chain polypeptide, and a disulfide bond is formed between the Cys in the linker and a Cys in the MHC class II α chain polypeptide.

[00437] Aspect 42. The TMP of aspect 41, wherein the linker comprises an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10.

[00438] Aspect 43. The TMP of any one of aspects 38-42, wherein the MHC class II α chain polypeptide is a variant MHC class II α chain polypeptide that comprises a non-naturally occurring Cys residue.

[00439] Aspect 44. The TMP of aspect 43, wherein the variant MHC class II α chain polypeptide is a variant of a DRA MHC class II polypeptide.

[00440] Aspect 45. The TMP of aspect 43 or 44, wherein the non-naturally occurring Cys residue is located at an amino acid residue from amino acids 55 to 110 of the MHC class II α chain polypeptide.

[00441] Aspect 46. The TMP of aspect 43 or 44, wherein the MHC class II α chain polypeptide is a variant DRA MHC class II polypeptide comprising a Cys at position 72 or 75 based on the amino acid numbering depicted in FIG. 19A.

[00442] Aspect 47. The TMP of aspect 46, wherein the variant DRA MHC class II polypeptide comprises a K75C substitution.

[00443] Aspect 48. The TMP of aspect 46, wherein the variant DRA MHC class II polypeptide comprises an I72C substitution.

[00444] Aspect 49. The TMP of any one of aspects 38-40, wherein a disulfide bond is formed between a Cys in the MHC class II α chain polypeptide and a Cys in the MHC class II β chain polypeptide.

[00445] Aspect 50. The TMP of aspect 49, wherein the MHC class II α chain polypeptide is a variant MHC class II polypeptide that comprises a non-naturally occurring Cys residue, and the MHC class II β chain polypeptide is a variant MHC class II polypeptide that comprises a non-naturally occurring Cys residue.

[00446] Aspect 51. The TMP of aspect 49 or 50, wherein the MHC class II β chain polypeptide is a variant DRB MHC class II polypeptide that comprises an amino acid substitution selected from the group consisting of P5C, F7C, Q10C, N19C, G20C, H33C, G151C, D152C, and W153C.

[00447] Aspect 52. The TMP of any one of aspects 49-51, wherein the MHC class II α chain polypeptide is a variant DRA MHC class II polypeptide that comprises an amino acid substitution selected from E3C, E4C, F12C, G28C, D29C, I72C, K75C, T80C, P81C, I82C, T93C, N94C, and S95C.

[00448] Aspect 53. The TMP of aspect 52, wherein:

- a) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;
- b) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C;
- c) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is H33C;
- d) the amino acid substitution in the DRA MHC class II polypeptide is E4C; and the amino acid substitution in the DRB MHC class II polypeptide is N19C;
- e) the amino acid substitution in the DRA MHC class II polypeptide is E4C; and the amino acid substitution in the DRB MHC class II polypeptide is G20C;

- f) the amino acid substitution in the DRA MHC class II polypeptide is T93C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C;
- g) the amino acid substitution in the DRA MHC class II polypeptide is T93C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C;
- h) the amino acid substitution in the DRA MHC class II polypeptide is F12C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;
- i) the amino acid substitution in the DRA MHC class II polypeptide is F12C; and the amino acid substitution in the DRB MHC class II polypeptide is Q10C;
- j) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;
- k) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C;
- l) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is I82C;
- m) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;
- n) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C;
- o) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is H33C;
- p) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is G151C;
- q) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is D152C;
- r) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C;
- s) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is G151C;
- t) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is D152C;
- u) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C;
- v) the amino acid substitution in the DRA MHC class II polypeptide is N94C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C;

w) the amino acid substitution in the DRA MHC class II polypeptide is N94C; and the amino acid substitution in the DRB MHC class II polypeptide is N120C;

y) the amino acid substitution in the DRA MHC class II polypeptide is S95C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C;

z) the amino acid substitution in the DRA MHC class II polypeptide is S95C; and the amino acid substitution in the DRB MHC class II polypeptide is N120C;

aa) the amino acid substitution in the DRA MHC class II polypeptide is E3C; and the amino acid substitution in the DRB MHC class II polypeptide is N19C; or

bb) the amino acid substitution in the DRA MHC class II polypeptide is E3C; and the amino acid substitution in the DRB MHC class II polypeptide is G20C.

[00449] Aspect 54. A TMP comprising a homodimer of two heterodimeric TMPs according to any one of aspects 38-53.

[00450] Aspect 55. The TMP of any one of aspects 1-30, wherein the TMP comprises a single polypeptide chain.

[00451] Aspect 56. The TMP of aspect 55, wherein the single polypeptide chain comprises one or more intrachain disulfide bonds, and wherein the components optionally may be joined by one or more independently selected linkers.

[00452] Aspect 57. The TMP of aspect 55 or 56, wherein the single polypeptide chain comprises, from N-terminus to C-terminus:

a)

- i) the T1D peptide;
- ii) an MHC class II β polypeptide;
- iii) an MHC class II α polypeptide;
- iv) the TGF- β polypeptide or the masking polypeptide;
- v) the masking polypeptide or the TGF- β polypeptide;
- vi) an Ig Fc polypeptide; and
- vii) the one or more MODs; or

b)

- i) the T1D peptide;
- ii) an MHC class II β polypeptide;
- iii) an MHC class II α polypeptide;
- iv) the TGF- β polypeptide or the masking polypeptide;
- v) the masking polypeptide or the TGF- β polypeptide;
- vi) the one or more MODs; and
- vii) an Ig Fc polypeptide; or

- c)
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide;
 - iv) the one or more MODs;
 - v) the TGF- β polypeptide or the masking polypeptide;
 - vi) the masking polypeptide or the TGF- β polypeptide; and
 - vii) an Ig Fc polypeptide; or
- d)
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide;
 - iv) the one or more MODs;
 - v) an Ig Fc polypeptide;
 - vi) the TGF- β polypeptide or the masking polypeptide; and
 - vii) the masking polypeptide or the TGF- β polypeptide; or
- e)
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide;
 - iv) an Ig Fc polypeptide;
 - v) the one or more MODs;
 - vi) the TGF- β polypeptide or the masking polypeptide; and
 - vii) the masking polypeptide or the TGF- β polypeptide; or
- f)
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide;
 - iv) the one or more MODs;
 - v) the TGF- β polypeptide or the masking polypeptide;
 - vi) the masking polypeptide or the TGF- β polypeptide; and
 - vii) an Ig Fc polypeptide; or
- g)
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;

- iii) an MHC class II α polypeptide;
- iv) an Ig Fc polypeptide;
- v) the TGF- β polypeptide or the masking polypeptide;
- vi) the masking polypeptide or the TGF- β polypeptide; and
- vii) the one or more MODs.

[00453] Aspect 58. A TMP comprising a homodimer of two single-chain TMPs according to any one of aspects 55-57.

[00454] Aspect 59. A nucleic acid comprising a nucleotide sequence encoding the first and/or the second polypeptide of any one of aspects 31-54.

[00455] Aspect 60. A nucleic acid comprising a nucleotide sequence encoding the single-chain TMP according to any one of aspects 55-57.

[00456] Aspect 61. An expression vector comprising the nucleic acid of aspect 59.

[00457] Aspect 62. An expression vector comprising the nucleic acid of aspect 60.

[00458] Aspect 63. A genetically modified host cell, wherein the host cell is genetically modified with a nucleic acid of aspect 59, or an expression vector of aspect 61.

[00459] Aspect 64. A genetically modified host cell, wherein the host cell is genetically modified with a nucleic acid of aspect 60, or an expression vector of aspect 62.

[00460] Aspect 65. A method of making a TMP, the method comprising culturing the genetically modified host cell of aspect 63 in vitro in a culture medium under conditions such that the host cell synthesizes the TMP.

[00461] Aspect 66. A method of making a TMP, the method comprising culturing the genetically modified host cell of aspect 64 in vitro in a culture medium under conditions such that the host cell synthesizes the TMP.

[00462] Aspect 67. A pharmaceutical composition comprising the TMP of any one of aspects 1-58.

[00463] Aspect 68. A method of increasing the number of regulatory T cells (Tregs) in an individual, the method comprising administering to the individual an effective amount of the TMP of any one of aspects 1-58, or the pharmaceutical composition of aspect 67.

[00464] Aspect 69. A method of treating type I diabetes in an individual, the method comprising administering to the individual an effective amount of the TMP of the TMP of any one of aspects 1-58, or the pharmaceutical composition of aspect 67.

[00465] Aspect 70. The TMP of any one of aspects 31-37, wherein the interspecific binding sequence and the counterpart interspecific binding sequence are a pair of interspecific binding sequence

and counterpart interspecific binding sequence selected from the group consisting of KiH, KiHs-s, HA-TF, ZW-1, 7.8.60, DD-KK, EW-RVT, EW-RVTs-s, and A107 sequence pairs as depicted in Table 1.

[00466] Aspect 71. The TMP of aspect 70, wherein one of the first polypeptide and the second polypeptide comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising a T366Y substitution, and the other of the first polypeptide and the second polypeptide comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising a Y407T substitution, or corresponding substitutions in other interspecific Ig Fc polypeptides (e.g., IgA, IgD, IgE, IgG2, IgG3, or IgG4 Fc polypeptide comprising interspecific binding sequences).

[00467] Aspect 72. The TMP of aspect 70, wherein one of the first polypeptide and the second polypeptides comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising a T366W substitution, and the other of the first polypeptide and the second polypeptide comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising T366S, L368A and Y407V substitutions, or corresponding substitutions in other interspecific Ig Fc polypeptides (e.g., IgA, IgD, IgE, IgG2, IgG3, or IgG4 Fc polypeptide comprising interspecific binding sequences).

[00468] Aspect 73. The TMP of aspect 70, wherein one of the first polypeptide and the second polypeptides comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising Y349C, T366S, L368A, and Y407V substitutions, and the other of the first polypeptide and the second polypeptide comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising S354C and T366W substitutions or corresponding substitutions in other interspecific Ig Fc polypeptides (e.g., IgA, IgD, IgE, IgG2, IgG3, or IgG4 Fc polypeptide comprising interspecific binding sequences).

[00469] Aspect 74. The TMP of aspect 70, wherein one of the first polypeptide and the second polypeptides comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising a T146W substitution, and the other of the first polypeptide and the second polypeptide comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid

sequence depicted in FIG. 21A) comprising T146S, L148A, and Y187V substitutions, or corresponding substitutions in other interspecific Ig Fc polypeptides (e.g., IgA, IgD, IgE, IgG2, IgG3, or IgG4 Fc polypeptide comprising interspecific binding sequences).

[00470] Aspect 75. The TMP of aspect 70, wherein one of the first polypeptide and the second polypeptides comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising T146W and S134C substitutions, and the other of the first polypeptide and the second polypeptide comprises an interspecific IgG1 Fc polypeptide (e.g., a polypeptide having at least 90%, at least 95%, at least 98%, or at least 99%, amino acid sequence identity to the amino acid sequence depicted in FIG. 21A) comprising T146S, L148A, Y187V and Y129C substitutions, or corresponding substitutions in other interspecific Ig Fc polypeptides (e.g., IgA, IgD, IgE, IgG2, IgG3, or IgG4 Fc polypeptide comprising interspecific binding sequences).

[00471] Aspect 76. The TMP of aspect 70, wherein:

- i) the first polypeptide comprises an Ig Fc polypeptide having S144H and F185A substitutions, and the second polypeptide comprises an Ig Fc polypeptide having Y129T and T174F substitutions; or
- ii) the first polypeptide comprises an Ig Fc polypeptide having T130V, L131Y, F185A, and Y187V substitutions, and the second polypeptide comprises an Ig Fc polypeptide having 130V, T146L, K172L, and T174W substitutions; or
- iii) the first polypeptide comprises an Ig Fc polypeptide having K140D, D179M, and Y187A substitutions, and the second polypeptide comprises an Ig Fc polypeptide having E125R, Q127R, T146V, and K189V substitutions; or
- iv) the first polypeptide comprises an Ig Fc polypeptide having K189D, and K172D substitutions, and the second polypeptide comprises an Ig Fc polypeptide having D179K and E136K substitutions; or
- v) the first polypeptide comprises an Ig Fc polypeptide having K140E and K189W substitutions, and the second polypeptide comprises an Ig Fc polypeptide having Q127R, D179V, and F185T substitutions; or
- vi) the first polypeptide comprises an Ig Fc polypeptide having K140E, K189W, and Y129C substitutions, and the second polypeptide comprises an Ig Fc polypeptide having Q127R, D179V, F185T, and S134C substitutions; or
- vii) the first polypeptide comprises an Ig Fc polypeptide having K150E and K189W substitutions, and the second polypeptide comprises an Ig Fc polypeptide having E137N, D179V, and F185T substitutions; wherein the Ig Fc polypeptide comprise an amino acid sequence having at least 80%, 90%, 95%, 98%, 99%, or 100% sequence identity to at least 170 (e.g., at least 180, at least 190, at least 200, at least 210, at least 220, or all 227) contiguous aas of the IgG1 Fc amino acid sequence depicted in FIG. 21A.

[00472] Aspect 77. The TMP of any one of aspects 70-76, with none, one, or both of the Ig Fc polypeptides comprise L14 and L15 substitutions and/or an N77 substitution (based on the amino acid numbering of the Ig Fc polypeptide depicted in FIG. 21A).

[00473] Aspect 78. The TMP of any one of aspects 1-58 and 70-76, wherein the masking polypeptide is a TGF- β receptor ("T β R") polypeptide that comprises an ectodomain fragment of a type I (T β RI), a type II (T β RII) or a type III (T β RIII) T β R.

[00474] Aspect 79. The TMP of aspect 78, wherein the masking polypeptide is a T β RII ectodomain polypeptide comprising an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to at least 90 (e.g., at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, or 154) contiguous amino acids of the T β RII isoform A ectodomain amino acid sequence depicted in **FIG. 25D**.

[00475] Aspect 80. The TMP of aspect 78, wherein the masking polypeptide is a T β RII ectodomain polypeptide comprising an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to at least 90 (e.g., at least 100, at least 110, at least 120, at least 130, at least 140, at least 150, or 154) contiguous amino acids of the T β RII isoform B ectodomain amino acid sequence depicted in **FIG. 25F**.

[00476] Aspect 81. The TMP of aspect 78, wherein the masking polypeptide is a T β RII ectodomain polypeptide comprising an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to at least 90 (e.g., at least 100, at least 110, at least 120, at least 130, at least 140, or 143) contiguous amino acids of the T β RII isoform B ectodomain amino acid sequence depicted in **FIG. 25G**.

[00477] Aspect 82. The TMP of aspect 78, wherein the masking polypeptide is a T β RII ectodomain polypeptide comprising an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to at least 70, at least 80, at least 90, at least 100, at least 110, or 118) contiguous amino acid sequences of: i) the T β RII isoform B ectodomain polypeptide Δ 14(delta 14) amino acid sequence depicted in **FIG. 25H**; or ii) the T β RII isoform B ectodomain polypeptide Δ 25(delta 25) amino acid sequence depicted in **FIG. 25I**; or iii) the T β RII isoform B ectodomain polypeptide Δ 25(delta 25) amino acid sequence depicted in **FIG. 25J**.

[00478] Aspect 83. The TMP of any one of aspects 79-82, wherein the T β RII ectodomain polypeptide comprises a substitution of one, two, three, four, or five substitutions selected from the group consisting of F30, D32, S52, E55, and D118 (e.g., with alanine or arginine).

[00479] Aspect 84. The TMP of aspect 83, wherein the T β RII ectodomain polypeptide comprises: i) a D118A or a D118R substitution; or ii) a D118A or D118R substitution and one, two, three, or four substitutions selected from the group consisting of F30A, D32N, S52L and E55A.

[00480] Aspect 85. The TMP of aspect 83 or 84, wherein the T β RII ectodomain polypeptide comprises an N-terminal deletion up to 14 aas (a Δ 14 aa deletion) of the amino acid sequence depicted in **FIG. 25F** or **FIG. 25G** (see e.g., **FIG. 25H**) and a D118 substitution (e.g., D118A or D118R); or an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) aa sequence identity to at least 70 (e.g., at least 80, at least 90, at least 100, at least 110, or 118) amino acids of any of those T β RII polypeptides.

[00481] Aspect 86. The TMP of aspect 85, further comprising one, two, three, or four substitutions selected from the group consisting of F30A, D32N, S52L and E55A.

[00482] Aspect 87. The TMP of any one of aspects 83-86, wherein the T β RII ectodomain polypeptide comprises an N-terminal deletion up to 25 aas (a Δ 25 aa deletion) of the amino acid sequence depicted in **FIG. 25F** or **FIG. 25G** and a D118 substitution (e.g., D118A or D118R, see SEQ ID NO:148); or a sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) aa sequence identity to at least 70 (e.g., at least 80, at least 90, or at least 100) contiguous amino acids of any of those T β RII polypeptides.

[00483] Aspect 88. The TMP of aspect 87, further comprising one, two, three, or four substitutions selected from the group consisting of F30A, D32N, S52L and E55A.

[00484] Aspect 89. The TMP of aspect 78, wherein the masking polypeptide is a T β RI ectodomain polypeptide.

[00485] Aspect 90. The TMP of aspect 89, wherein the T β RI ectodomain polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to at least 70 (e.g., at least 80, at least 90, or 93) contiguous amino acids of the amino acid sequence depicted in **FIG. 25B**.

[00486] Aspect 91. The TMP of aspect 78, wherein the masking polypeptide is a T β RIII ectodomain polypeptide.

[00487] Aspect 92. The TMP of aspect 91, wherein the T β RI III ectodomain polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to at least 70 (e.g., at least 80, 90, 100, 150, 200, 250, 300, 400, 500 or 600) contiguous amino acids of the A isoform amino acid sequence depicted in **FIG. 25L** or the B isoform amino acid sequence depicted in **FIG. 25N**.

[00488] Aspect 93. The TMP of any one of aspects 1-58 and 70-92, wherein the TGF- β polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at

least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) aa sequence identity to a polypeptide comprising at least 70 (e.g., at least 80, at least 90, at least 100, or at least 110) contiguous amino acids of the mature form of a human TGF- β 1 polypeptide (e.g., **FIG. 23B**), a human TGF- β 2 polypeptide (e.g., **FIG. 23D**), or a human TGF- β 3 polypeptide (e.g., **FIG. 23F**).

[00489] Aspect 94. The TMP of aspect 93, wherein the TGF- β polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to a polypeptide comprising at least 70 (e.g., at least 80, at least 90, at least 100, at least 110, or 112) contiguous amino acids of the amino acid sequence depicted in **FIG. 23B** (TGF β 1 mature form).

[00490] Aspect 95. The TMP of aspect 93, wherein the TGF- β polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99%) amino acid sequence identity to a polypeptide comprising at least 70 (e.g., at least 80, at least 90, at least 100, at least 110, or 112) contiguous amino acids of the amino acid sequence depicted in **FIG. 23B** and comprises a C77S substitution (i.e., the TGF- β polypeptide comprises a Ser at position 77).

[00491] Aspect 96. The TMP of aspect 93, wherein the TGF- β polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to a polypeptide comprising at least 70 (e.g., at least 80, at least 90, at least 100, at least 110, or 112) contiguous amino acids of the amino acid sequence depicted in **FIG. 23D** (TGF β 2 mature form).

[00492] Aspect 97. The TMP of aspect 93, wherein the TGF- β polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99%) amino acid sequence identity to a polypeptide comprising at least 70 (e.g., at least 80, at least 90, at least 100, at least 110, or 112) contiguous amino acids of the amino acid sequence depicted in **FIG. 23D** and comprises a C77S substitution (i.e., the TGF- β polypeptide comprises a Ser at position 77).

[00493] Aspect 98. The TMP of aspect 93, wherein the TGF- β polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or 100%) amino acid sequence identity to a polypeptide comprising at least 70 (e.g., at least 80, at least 90, at least 100, at least 110, or 112) contiguous amino acids of the amino acid sequence depicted in **FIG. 23F** (TGF β 3 mature form).

[00494] Aspect 99. The TMP of aspect 93, wherein the TGF- β polypeptide comprises an amino acid sequence having at least 60% (e.g., at least 70%, at least 80%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99%) amino acid sequence identity to a polypeptide

comprising at least 70 (e.g., at least 80, at least 90, at least 100, at least 110, or 112) contiguous amino acids of the amino acid sequence depicted in **FIG. 23F** and comprises a C77S substitution (i.e., the TGF- β polypeptide comprises a Ser at position 77).

[00495] Aspect 100. The TMP of any one of aspects 93-99, wherein the TGF- β polypeptide comprises a substitution at one or more of positions 25, 92 and/or 94 of the mature TGF- β polypeptide (e.g., an amino acid sequence depicted in **FIG. 23B**, **FIG. 23D**, or **FIG. 23F**).

[00496] Aspect 101. The TMP of aspect 100, wherein the TGF- β polypeptide comprises:

- (i) an amino acid other than Lys or Arg at position 25
- (ii) an amino acid other than Ile or Val at position 92; and/or
- (iii) an amino acid other than Lys or Arg at position 94 (e.g., based on the amino acid sequence depicted in **FIG. 23B**, **FIG. 23D**, or **FIG. 23F**).

ASPECTS SET B

[00497] Aspects, including embodiments, of the present subject matter described above may be beneficial alone or in combination, with one or more other aspects or embodiments. Without limiting the foregoing description, certain non-limiting aspects of the disclosure are provided below. As will be apparent to those of skill in the art upon reading this disclosure, each of the individually numbered aspects may be used or combined with any of the preceding or following individually numbered aspects. This is intended to provide support for all such combinations of aspects and is not limited to combinations of aspects explicitly provided below:

[00498] Aspect 1. A T-cell modulatory polypeptide (TMP) comprising: a) a peptide that displays a Type 1 Diabetes-associated epitope capable of being bound by a T-cell receptor (a "T1D peptide"); b) a TGF- β polypeptide; c) a masking polypeptide, optionally wherein the masking polypeptide comprises a TGF- β receptor polypeptide or an anti-TGF- β polypeptide; d) an MHC class II α chain polypeptide; e) an MHC class II β chain polypeptide; and f) one or more immunomodulatory polypeptides (MOD), wherein optionally the TMP comprises a scaffold polypeptide, wherein optionally the TMP comprises one or more independently selected linker polypeptides, and optionally wherein the T1D peptide has a length of from about 8 amino acids to about 20 amino acids, and comprises a proinsulin peptide or a glutamic acid decarboxylase (GAD) peptide.

[00499] Aspect 2. The TMP of aspect 1, wherein at least one of the one or more MODs is a variant IL-2 polypeptide, optionally wherein the one or more variant IL-2 polypeptides exhibit a binding affinity for an IL-2 receptor, and wherein the binding affinity of such one or more variant IL-2 polypeptides is less than the binding affinity of a wild-type human IL-2 polypeptide for the same IL-2 receptor, when assayed under the same conditions in a bio-layer interferometry (BLI) assay, optionally

wherein the at least one variant IL-2 polypeptide exhibits reduced binding to both the α chain of IL-2 receptor and the β chain of IL-2 receptor.

[00500] Aspect 3. The TMP of aspect 1, wherein the T1D peptide is: a) a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90); or b) a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).

[00501] Aspect 4. The TMP of aspect 1, wherein the masking polypeptide comprises a TGF- β receptor ("T β R") polypeptide, optionally wherein the masking polypeptide comprises at least a portion of an ectodomain of a type I T β R (T β RI) polypeptide, a type II T β R (T β RII) polypeptide, or a type III T β R (T β RIII) polypeptide.

[00502] Aspect 5. The TMP of aspect 4, wherein the T β R polypeptide comprises one or more sequence variations relative to the corresponding wild type T β R polypeptide, and wherein the T β R polypeptide exhibits reduced affinity for the TGF- β polypeptide relative to the corresponding wild type T β R polypeptide.

[00503] Aspect 6. The TMP of aspect 1, wherein the TMP comprises a scaffold polypeptide that is an immunoglobulin (Ig) Fc polypeptide, optionally wherein the Ig Fc polypeptide is a variant Ig Fc polypeptide comprising one or more sequence variations relative to the wild type polypeptide, and wherein the ability of the Ig Fc polypeptide to induce cell lysis through complement-dependent cytotoxicity (CDC) and/or antibody-dependent cellular cytotoxicity (ADCC) is reduced or substantially eliminated.

[00504] Aspect 7. The TMP of aspect 1, wherein the MHC class II α polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to a DRA1*01:01 polypeptide; and the MHC class II β polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to a DRB1*04:01 polypeptide.

[00505] Aspect 8. The TMP of aspect 1, wherein the TMP comprises at least one heterodimer, wherein each heterodimer comprises: a) a first polypeptide comprising: i) the T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; and iv) a first scaffold polypeptide comprising a first interspecific binding sequence, and b) a second polypeptide comprising: i) the T1D peptide; ii) an MHC class II β polypeptide; iii) an MHC class II α polypeptide; and iv) a second scaffold polypeptide comprising a counterpart interspecific binding sequence to the interspecific binding sequence of the first polypeptide, wherein the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other in the heterodimer, and wherein, the first and/or the second polypeptide

comprises the one or more MODs, the first or the second polypeptide comprises the TGF- β polypeptide, and the first or the second polypeptide comprises the masking polypeptide, and the components of the first polypeptide and/or the components of the second polypeptide optionally may be joined by one or more independently selected linkers.

[00506] Aspect 9. The TMP of aspect 1, wherein the TMP comprises at least one heterodimer, wherein each heterodimer comprises: a) a first polypeptide comprising: i) the T1D peptide; and ii) an MHC class II α chain polypeptide or an MHC class II β chain polypeptide; and iii) optionally a linker that links the T1D peptide to the first MHC class II polypeptide; and b) a second polypeptide comprising i) an MHC class II α chain polypeptide if the first polypeptide comprises an MHC class II β chain polypeptide, or ii) an MHC class II β chain polypeptide if the first polypeptide comprises an MHC class II α chain polypeptide wherein the first and/or the second polypeptide comprises the one or more MODs, the first or the second polypeptide comprises the TGF- β polypeptide, and the first or the second polypeptide comprises the masking polypeptide, and optionally wherein the first polypeptide and the second polypeptide of the heterodimer are covalently linked to one another via at least one disulfide bond.

[00507] Aspect 10. The TMP of aspect 8 or 9, wherein the TMP comprises a Cys-containing linker between the T1D peptide and the MHC Class II β chain polypeptide, and a disulfide bond is formed between the Cys in the linker and a Cys in the MHC class II α chain polypeptide, optionally wherein the linker comprises an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10.

[00508] Aspect 11. The TMP of aspect 1, wherein the MHC class II β chain polypeptide is a variant DRB MHC class II polypeptide that comprises an amino acid substitution selected from the group consisting of P5C, F7C, Q10C, N19C, G20C, H33C, G151C, D152C, and W153C, and/or wherein the MHC class II α chain polypeptide is a variant DRA MHC class II polypeptide that comprises an amino acid substitution selected from E3C, E4C, F12C, G28C, D29C, I72C, K75C, T80C, P81C, I82C, T93C, N94C, and S95C.

[00509] Aspect 12. The TMP of aspect 11, wherein: a) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C; b) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C; c) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is H33C; d) the amino acid substitution in the DRA MHC class II polypeptide is E4C; and the amino acid substitution in the DRB MHC class II polypeptide is N19C; e) the amino acid substitution in the

DRA MHC class II polypeptide is E4C; and the amino acid substitution in the DRB MHC class II polypeptide is G20C; f) the amino acid substitution in the DRA MHC class II polypeptide is T93C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C; g) the amino acid substitution in the DRA MHC class II polypeptide is T93C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C; h) the amino acid substitution in the DRA MHC class II polypeptide is F12C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C; i) the amino acid substitution in the DRA MHC class II polypeptide is F12C; and the amino acid substitution in the DRB MHC class II polypeptide is Q10C; j) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C; k) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C; l) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is I82C; m) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C; n) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C; o) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is H33C; p) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is G151C; q) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is D152C; r) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C; s) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is G151C; t) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is D152C; u) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C; v) the amino acid substitution in the DRA MHC class II polypeptide is N94C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C; w) the amino acid substitution in the DRA MHC class II polypeptide is N94C; and the amino acid substitution in the DRB MHC class II polypeptide is N120C; y) the amino acid substitution in the DRA MHC class II polypeptide is S95C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C; z) the amino acid substitution in the DRA MHC class II polypeptide is S95C; and the amino acid substitution in the DRB MHC class II polypeptide is N120C; aa) the amino acid substitution in the DRA MHC class II polypeptide is E3C; and the amino acid substitution in the DRB MHC class II polypeptide

is N19C; or bb) the amino acid substitution in the DRA MHC class II polypeptide is E3C; and the amino acid substitution in the DRB MHC class II polypeptide is G20C.

[00510] Aspect 13. A TMP comprising a homodimer of two TMPs according to aspect 8 or 9.

[00511] Aspect 14. One or more nucleic acids comprising one or more nucleotide sequences encoding the first and/or the second polypeptide of a TMP according to aspect 8 or 9.

[00512] Aspect 15. An expression vector comprising the one or more nucleic acids of aspect 14.

[00513] Aspect 16. A genetically modified host cell, wherein the host cell is genetically modified with the one or more nucleic acids of aspect 14, or an expression vector of aspect 15.

[00514] Aspect 17. A method of making a TMP, the method comprising culturing the genetically modified host cell of aspect 16 *in vitro* in a culture medium under conditions such that the host cell synthesizes the TMP.

[00515] Aspect 18. A pharmaceutical composition comprising the TMP of any one of aspects 1-9.

[00516] Aspect 19. A method of increasing the number of regulatory T cells (Tregs) in an individual, the method comprising administering to the individual an effective amount of the pharmaceutical composition of aspect 18.

[00517] Aspect 20. A method of treating type I diabetes in an individual, the method comprising administering to the individual an effective amount of the pharmaceutical composition of aspect 18.

EXAMPLES

[00518] The following examples are put forth so as to provide those of ordinary skill in the art with a disclosure and description of how to make and use aspects of the present disclosure, and are not intended to limit the scope of the disclosure nor are they intended to represent that the experiments below are all or the only experiments performed. Efforts have been made to ensure accuracy with respect to numbers used (e.g., amounts, temperature, etc.) but some experimental errors and deviations should be accounted for. Unless indicated otherwise, parts are parts by weight, molecular weight is weight average molecular weight, temperature is in degrees Celsius, and pressure is at or near atmospheric. Standard abbreviations may be used, e.g., bp, base pair(s); kb, kilobase(s); pl, picoliter(s); s or sec, second(s); min, minute(s); h or hr, hour(s); aa, amino acid(s); kb, kilobase(s); bp, base pair(s); nt, nucleotide(s); i.m., intramuscular(ly); i.p., intraperitoneal(ly); s.c., subcutaneous(ly); and the like.

Example 1:

[00519] The following TMPs were synthesized:

- [00520] (1) 3858-3859 (FIG. 31A-31B);
 [00521] (2) 3858-3869 (FIG. 32A-32B);
 [00522] (3) 3870-3871 (FIG. 33A-33B);
 [00523] (4) 4415-4416 (FIG. 29A-29B);
 [00524] (5) 4415-4417 (FIG. 26A-26B);
 [00525] (6) 4418-4419 (FIG. 30A-30B);
 [00526] (7) 4418-4420 (FIG. 27A-27B).

Constructs (1) – (3)

- [00527] Constructs (1) – (3) are depicted schematically in FIG. 34A. The construct properties are shown in Table 6, below.

Table 6

	3858-3859	3858-3869	3870-3871
Peptide	proIns (76-90; K88S)	proIns (76-90; K88S)	proIns (76-90; K88S)
MHC	DR4 single chain	DR4 single chain	DR4 single chain (L158F)
TGF- β /TGF- β R; MOD	TGF β 3:T β RII (no MOD)	TGF β 3:T β RII IL-2	TGF β 3:T β RII IL-2
Harvest Titer (mg/L)	11.9	16.2	12.6
Yield (mg/L)	4.5	6.8	10.2
aSEC (% monomer)	>95	>95	>95

- [00528] The constructs were produced in a mammalian cell line and harvested. The constructs were analyzed on sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE), under both reducing and non-reducing conditions. The data in Table 6 indicate that TMPs (1) – (3) could be produced in a mammalian cell line. The data shown in FIG. 34B indicate that the constructs, including those containing IL-2, were intact.

- [00529] The effect of construct (1) – (3) on induction of FoxP3-positive cell proliferation was tested. As shown in FIG. 35, constructs (2) and (3) induced proliferation of FoxP3-positive cell.

Constructs (4) – (7)

- [00530] The structure of constructs (5) and (7), which include IL-2 as the MOD), is depicted schematically in FIG. 28. Constructs (4) and (6) have a similar structure, but do not include IL-2.

- [00531] Constructs (4) – (7) were also produced in a mammalian cell line. Properties of constructs (5) and (7) are provided in Table 7, below.

Table 7

Lane	construct	epitope	TGFβ	IL-2	Fc-DS	RT	% monomer	MW kD
1	4415-4416	proIns	+	-	+	7.473	79.1	89/88
2	4415-4417	proIns	+	+	+	7.255	77.8	89/105
3	4418-4419	GAD	+	-	+	7.478	81.2	89/88
4	4418-4420	GAD	+	+	+	7.28	90	89/105

[00532] The lane numbers in Table 7 refer to the lanes of the SDS-PAGE results depicted in FIG.

36. “Fc-DS” refers to disulfide-linked Fc. MW refers to the molecular weight of the chains as confirmed by SDS-PAGE. The constructs were analyzed by reducing SDS-PAGE. The results are shown in FIG. 36.

[00533] While the present disclosure has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the disclosure. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present disclosure. All such modifications are intended to be within the scope of the claims appended hereto.

CLAIMS

What is claimed is:

1. A T-cell modulatory polypeptide (TMP) comprising:
 - a) a peptide that displays a Type 1 Diabetes-associated epitope capable of being bound by a T-cell receptor (a “T1D peptide”);
 - b) a TGF- β polypeptide;
 - c) a masking polypeptide, optionally wherein the masking polypeptide comprises a TGF- β receptor polypeptide or an anti-TGF- β polypeptide;
 - d) an MHC class II α chain polypeptide;
 - e) an MHC class II β chain polypeptide; and
 - f) one or more immunomodulatory polypeptides (MOD),wherein optionally the TMP comprises a scaffold polypeptide, wherein optionally the TMP comprises one or more independently selected linker polypeptides, and optionally wherein the T1D peptide has a length of from about 8 amino acids to about 20 amino acids, and comprises a proinsulin peptide or a glutamic acid decarboxylase (GAD) peptide.
2. The TMP of claim 1, wherein at least one of the one or more MODs is a variant IL-2 polypeptide, optionally wherein the one or more variant IL-2 polypeptides exhibit a binding affinity for an IL-2 receptor, and wherein the binding affinity of such one or more variant IL-2 polypeptides is less than the binding affinity of a wild-type human IL-2 polypeptide for the same IL-2 receptor, when assayed under the same conditions in a bio-layer interferometry (BLI) assay, optionally wherein the at least one variant IL-2 polypeptide exhibits reduced binding to both the α chain of IL-2 receptor and the β chain of IL-2 receptor.
3. The TMP of claim 1, wherein the T1D peptide is:
 - a) a proinsulin peptide selected from SLQPLALEGSLQKRG (SEQ ID NO:175; proIns 76-90), SLQPLALEGSLQSRG (SEQ ID NO:159; proIns 76-90; K88S), and GAGSLQPLALEGSLQKRG (SEQ ID NO:176; proIns 73-90); or
 - b) a GAD peptide selected from NFFRMVISNPAAT (SEQ ID NO:177; GAD65 555-567) and NFIRMVISNPAAT (SEQ ID NO:163; GAD65 555-567; F557I).
4. The TMP of claim 1, wherein the masking polypeptide comprises a TGF- β receptor (“T β R”) polypeptide,

optionally wherein the masking polypeptide comprises at least a portion of an ectodomain of a type I T β R (T β RI) polypeptide, a type II T β R (T β RII) polypeptide, or a type III T β R (T β RIII) polypeptide.

5. The TMP of claim 4, wherein the T β R polypeptide comprises one or more sequence variations relative to the corresponding wild type T β R polypeptide, and wherein the T β R polypeptide exhibits reduced affinity for the TGF- β polypeptide relative to the corresponding wild type T β R polypeptide.

6. The TMP of claim 1, wherein the TMP comprises a scaffold polypeptide that is an immunoglobulin (Ig) Fc polypeptide, optionally wherein the Ig Fc polypeptide is a variant Ig Fc polypeptide comprising one or more sequence variations relative to the wild type polypeptide, and wherein the ability of the Ig Fc polypeptide to induce cell lysis through complement-dependent cytotoxicity (CDC) and/or antibody-dependent cellular cytotoxicity (ADCC) is reduced or substantially eliminated.

7. The TMP of claim 1, wherein the MHC class II α polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to a DRA1*01:01 polypeptide; and the MHC class II β polypeptide comprises an amino acid sequence having at least 95% amino acid sequence identity to a DRB1*04:01 polypeptide.

8. The TMP of claim 1, wherein the TMP comprises at least one heterodimer, wherein each heterodimer comprises:

- a) a first polypeptide comprising:
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide; and
 - iv) a first scaffold polypeptide comprising a first interspecific binding sequence, and
- b) a second polypeptide comprising:
 - i) the T1D peptide;
 - ii) an MHC class II β polypeptide;
 - iii) an MHC class II α polypeptide; and
 - iv) a second scaffold polypeptide comprising a counterpart interspecific binding sequence to the interspecific binding sequence of the first polypeptide, wherein

the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other in the heterodimer,

and wherein,

the first and/or the second polypeptide comprises the one or more MODs,
the first or the second polypeptide comprises the TGF- β polypeptide, and
the first or the second polypeptide comprises the masking polypeptide, and
the components of the first polypeptide and/or the components of the second polypeptide optionally may be joined by one or more independently selected linkers.

9. The TMP of claim 1, wherein the TMP comprises at least one heterodimer, wherein each heterodimer comprises:

a) a first polypeptide comprising:

- i) the T1D peptide; and
- ii) an MHC class II α chain polypeptide or an MHC class II β chain polypeptide; and
- iii) optionally a linker that links the T1D peptide to the first MHC class II polypeptide; and

b) a second polypeptide comprising i) an MHC class II α chain polypeptide if the first polypeptide comprises an MHC class II β chain polypeptide, or ii) an MHC class II β chain polypeptide if the first polypeptide comprises an MHC class II α chain polypeptide

wherein

the first and/or the second polypeptide comprises the one or more MODs,
the first or the second polypeptide comprises the TGF- β polypeptide, and
the first or the second polypeptide comprises the masking polypeptide, and
optionally wherein the first polypeptide and the second polypeptide of the heterodimer are covalently linked to one another via at least one disulfide bond.

10. The TMP of claim 8 or 9, wherein

the TMP comprises a Cys-containing linker between the T1D peptide and the MHC Class II β chain polypeptide, and

a disulfide bond is formed between the Cys in the linker and a Cys in the MHC class II α chain polypeptide,

optionally wherein the linker comprises an amino acid sequence selected from (CGGGS)(GGGGS)_n (SEQ ID NO:178), (GCGGS)(GGGGS)_n (SEQ ID NO:179), (GGCGS)(GGGGS)_n (SEQ ID NO:180), (GGGCS)(GGGGS)_n (SEQ ID NO:181), and (GGGGC)(GGGGS)_n (SEQ ID NO:182), where n is an integer from 1 to 10.

11. The TMP of claim 1, wherein the MHC class II β chain polypeptide is a variant DRB MHC class II polypeptide that comprises an amino acid substitution selected from the group consisting of P5C, F7C, Q10C, N19C, G20C, H33C, G151C, D152C, and W153C, and/or

wherein the MHC class II α chain polypeptide is a variant DRA MHC class II polypeptide that comprises an amino acid substitution selected from E3C, E4C, F12C, G28C, D29C, I72C, K75C, T80C, P81C, I82C, T93C, N94C, and S95C.

12. The TMP of claim 11, wherein:

a) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;

b) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C;

c) the amino acid substitution in the DRA MHC class II polypeptide is P81C; and the amino acid substitution in the DRB MHC class II polypeptide is H33C;

d) the amino acid substitution in the DRA MHC class II polypeptide is E4C; and the amino acid substitution in the DRB MHC class II polypeptide is N19C;

e) the amino acid substitution in the DRA MHC class II polypeptide is E4C; and the amino acid substitution in the DRB MHC class II polypeptide is G20C;

f) the amino acid substitution in the DRA MHC class II polypeptide is T93C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C;

g) the amino acid substitution in the DRA MHC class II polypeptide is T93C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C;

h) the amino acid substitution in the DRA MHC class II polypeptide is F12C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;

i) the amino acid substitution in the DRA MHC class II polypeptide is F12C; and the amino acid substitution in the DRB MHC class II polypeptide is Q10C;

j) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;

k) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C;

l) the amino acid substitution in the DRA MHC class II polypeptide is T80C; and the amino acid substitution in the DRB MHC class II polypeptide is I82C;

m) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is F7C;

- n) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is P5C;
- o) the amino acid substitution in the DRA MHC class II polypeptide is I82C; and the amino acid substitution in the DRB MHC class II polypeptide is H33C;
- p) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is G151C;
- q) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is D152C;
- r) the amino acid substitution in the DRA MHC class II polypeptide is G28C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C;
- s) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is G151C;
- t) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is D152C;
- u) the amino acid substitution in the DRA MHC class II polypeptide is D29C; and the amino acid substitution in the DRB MHC class II polypeptide is W153C;
- v) the amino acid substitution in the DRA MHC class II polypeptide is N94C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C;
- w) the amino acid substitution in the DRA MHC class II polypeptide is N94C; and the amino acid substitution in the DRB MHC class II polypeptide is N120C;
- y) the amino acid substitution in the DRA MHC class II polypeptide is S95C; and the amino acid substitution in the DRB MHC class II polypeptide is Q156C;
- z) the amino acid substitution in the DRA MHC class II polypeptide is S95C; and the amino acid substitution in the DRB MHC class II polypeptide is N120C;
- aa) the amino acid substitution in the DRA MHC class II polypeptide is E3C; and the amino acid substitution in the DRB MHC class II polypeptide is N19C; or
- bb) the amino acid substitution in the DRA MHC class II polypeptide is E3C; and the amino acid substitution in the DRB MHC class II polypeptide is G20C.

- 13. A TMP comprising a homodimer of two TMPs according to claim 8 or 9.
- 14. One or more nucleic acids comprising one or more nucleotide sequences encoding the first and/or the second polypeptide of a TMP according to claim 8 or 9.
- 15. An expression vector comprising the one or more nucleic acids of claim 14.

16. A genetically modified host cell, wherein the host cell is genetically modified with the one or more nucleic acids of claim 14, or an expression vector of claim 15.

17. A method of making a TMP, the method comprising culturing the genetically modified host cell of claim 16 *in vitro* in a culture medium under conditions such that the host cell synthesizes the TMP.

18. A pharmaceutical composition comprising the TMP of any one of claims 1-9.

19. A method of increasing the number of regulatory T cells (Tregs) in an individual, the method comprising administering to the individual an effective amount of the pharmaceutical composition of claim 18.

20. A method of treating type I diabetes in an individual, the method comprising administering to the individual an effective amount of the pharmaceutical composition of claim 18.

FIG. 1A

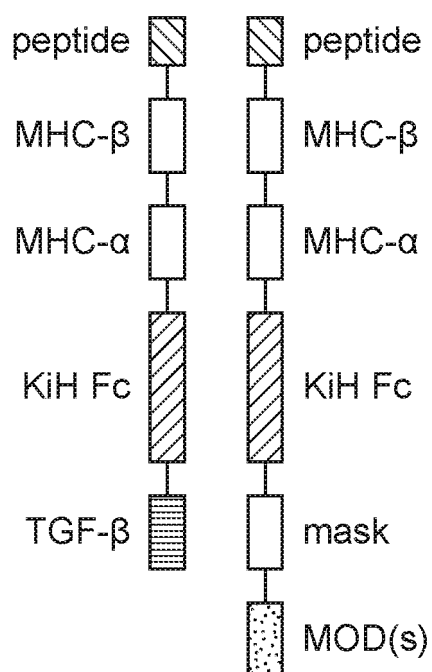


FIG. 1B

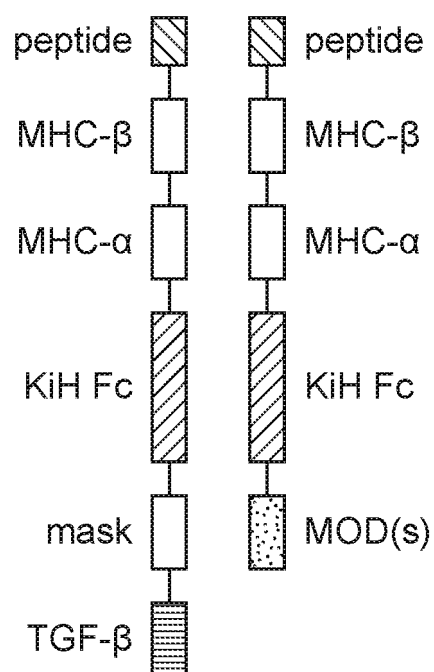


FIG. 1C

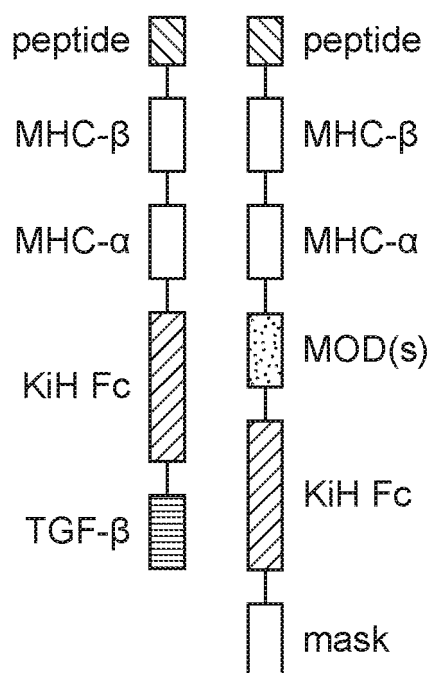


FIG. 1D

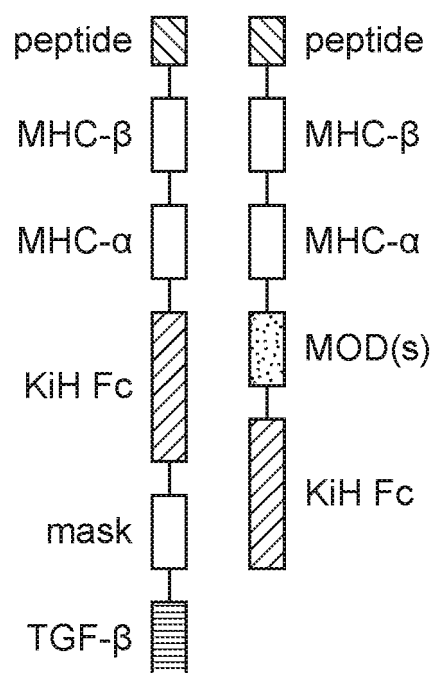


FIG. 1E

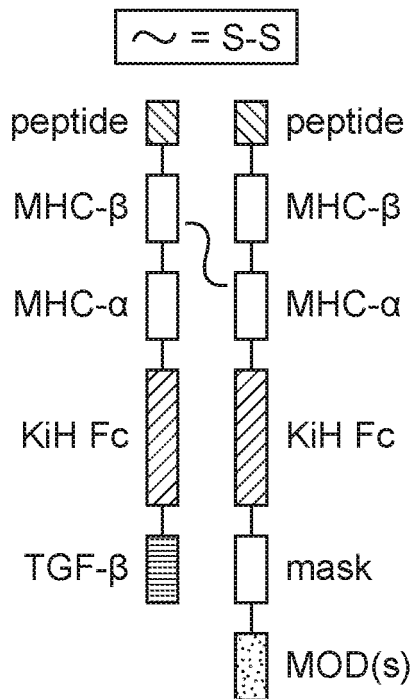


FIG. 1F

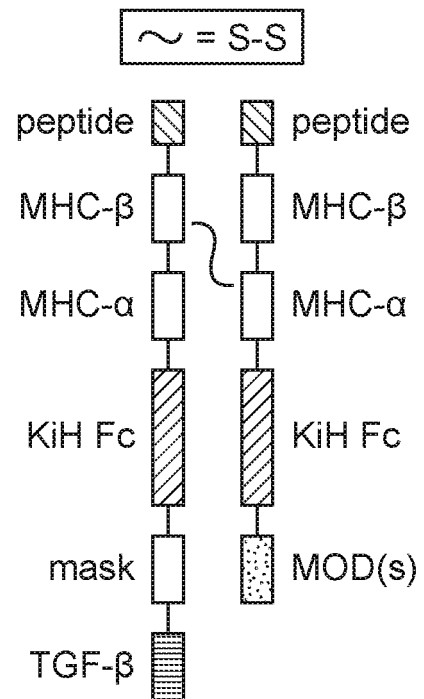


FIG. 1G

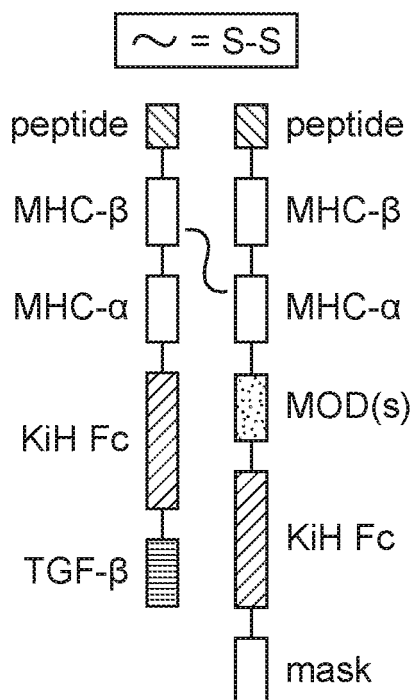


FIG. 1H

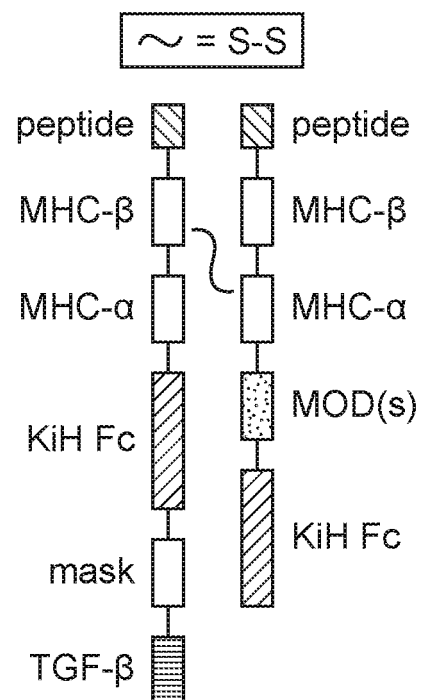


FIG. 2A

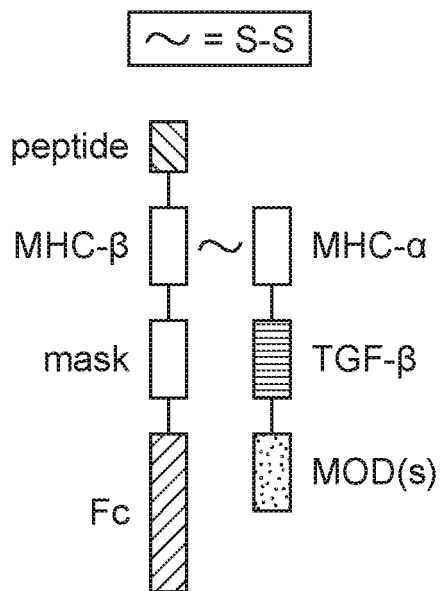


FIG. 2B

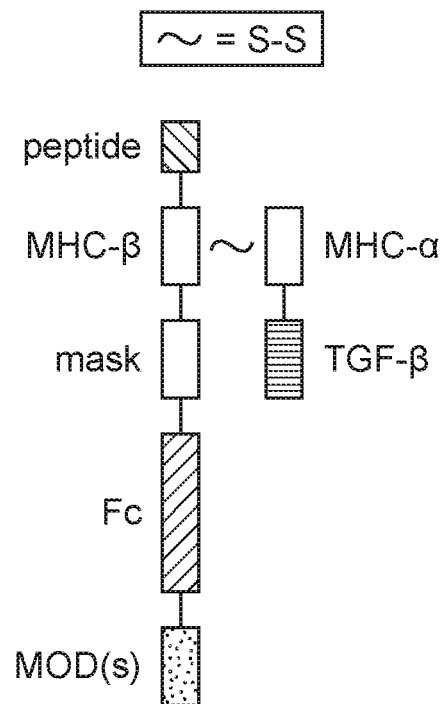


FIG. 2C

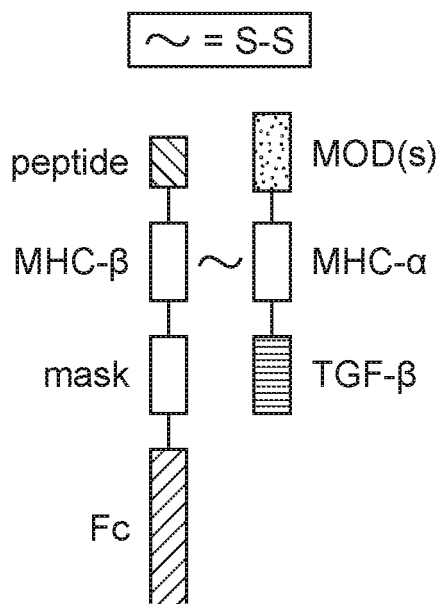


FIG. 2D

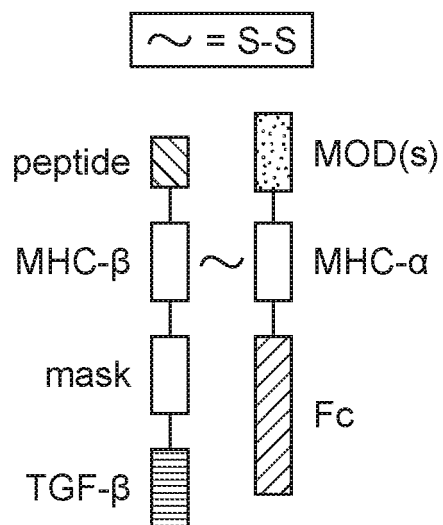




FIG. 4**MHC Class II DRA alpha chain***Homo sapiens*

GenBank NP_061984 MHC Class II DRA(DRA*01:02) alpha chain

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1  MAISGVPVLG FFIIAVLMSA QESWAIKEEH VIIQAEFYLN PDQSGEFMFD FDGDEIFHVD
61 MAKKETVWRL EEFGRFASFE AQGALANIAV DKANLEIMTK RSNYTPITNV PPEVTVLTNS
121 PVELREPNVL ICFIDKFTTP VVNVTWLRNG KPVTTGVSET VFLPREDHLF RKFHLYLPFLP
181 STEDVYDCRV EHWGLDEPLL KHWEFDAPSP LPETTENVVC ALGLTVGLVG IIIGTIFIIK
241 GLRKSNAAER RGPL (SEQ ID NO:1)

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Amino acids 1-25 = signal peptide

Amino acids 26-109 = α 1Amino acids 110-203 = α 2

Amino acids 204-216 = connecting peptide

Amino acids 217-239 = TM

* DRA*01:01 contains a Val residue at position 242 in place of the Leu in DRA*01:02

DRB1*01:01	MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQKLFECHEFFNGTERVRLLERCI	60
DRB1*01:02	MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQKLFECHEFFNGTERVRLLERCI	60
DRB1*01:03	MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQKLFECHEFFNGTERVRLLERCI	60
DRB1*03:01	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRYLDRYF	60
DRB1*03:02	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLERYF	60
DRB1*03:04	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRYLDRYF	60
DRB1*04:01	MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTERVRFLDRYF	60
DRB1*04:02	MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTERVRFLDRYF	60
DRB1*04:03	MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTERVRFLDRYF	60
DRB1*04:04	MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTERVRFLDRYF	60
DRB1*04:05	MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTERVRFLDRYF	60
DRB1*04:06	MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTERVRFLDRYF	60
DRB1*04:08	MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTERVRFLDRYF	60
DRB1*07:01	MVCLKLPGGSCMAALTVTLMVLSSPLALAGDTQPRFLWQGKYKCHFFNGTERVQFLERLF	60
DRB1*08:01	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTGECYFFNGTERVRFLDRYF	60
DRB1*08:02	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTGECYFFNGTERVRFLDRYF	60
DRB1*08:03	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTGECYFFNGTERVRFLDRYF	60
DRB1*09:01	MVCLKLPGGSCMAALTVTLMVLSSPLALAGDTQPRFLKQDKFECHEFFNGTERVRYLHRGI	60
DRB1*10:01	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEEVKFECHFFNGTERVRLERRV	60
DRB1*11:01	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF	60
DRB1*11:03	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF	60
DRB1*11:04	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF	60
DRB1*12:01	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTGECYFFNGTERVRLLERHF	60
DRB1*13:01	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF	60
DRB1*13:03	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF	60
DRB1*14:01	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLDRYF	60
DRB1*14:02	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLERYF	60
DRB1*14:05	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECQFFNGTERVRFLDRYF	60
DRB1*14:06	MVCLRLPGGSCMAVLTVTLMVLSSPLALAGDTRPRFLEYSTSECHFFNGTERVRFLERYF	60
DRB1*15:01	MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRYF	60
DRB1*15:02	MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRYF	60
DRB1*15:03	MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFDRHF	60
DRB1*15:04	MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRYF	60
DRB1*15:05	MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRYF	60
DRB1*15:06	MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRYF	60
DRB1*15:07	MVCLKLPGGSCMTALTVTLMVLSSPLALSGDTRPRFLWQPKRECHFFNGTERVRFLDRYF	60
DRB1*16:01	MVCLKLPGGSCMTALTVTLMVLSSPLALAGDTRPRFLWQPKRECHFFNGTERVRFLDRYF	60
****.:*****.:*****:***:*** .:* *****:*. *		
DRB1*01:01	YNQEESVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQRRAAVD TYCRHNYGVGESFTV	120
DRB1*01:02	YNQEESVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQRRAAVD TYCRHNYGAVESFTV	120
DRB1*01:03	YNQEESVRFSDVGEYRAVTELGPRDAEYWN SQKD ILEDERAAVD TYCRHNYGVGESFTV	120
DRB1*03:01	HNQEENVRFDSDVGEFRAVTELGPRDAEYWN SQKD LLEQKRGRVDNYCRHNYGVVESFTV	120
DRB1*03:02	HNQEENVRFDSDVGEYRAVTELGPRDAEYWN SQKD LLEQKRGRVDNYCRHNYGVGESFTV	120
DRB1*03:04	HNQEESVRFSDVGEFRAVTELGPRDAEYWN SQKD LLEQKRGRVDNYCRHNYGVVESFTV	120
DRB1*04:01	YHQEEYVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQKRAAVD TYCRHNYGVGESFTV	120
DRB1*04:02	YHQEEYVRFSDVGEYRAVTELGPRDAEYWN SQKD ILEDERAAVD TYCRHNYGVVESFTV	120
DRB1*04:03	YHQEEYVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQRRAEVD TYCRHNYGVVESFTV	120
DRB1*04:04	YHQEEYVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQRRAAVD TYCRHNYGVVESFTV	120
DRB1*04:05	YHQEEYVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQRRAAVD TYCRHNYGVGESFTV	120
DRB1*04:06	YHQEESVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQRRAEVD TYCRHNYGVVESFTV	120
DRB1*04:08	YHQEEYVRFSDVGEYRAVTELGPRDAEYWN SQKD LLEQRRAAVD TYCRHNYGVGESFTV	120

FIG. 5 (continued)

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DRB1*07:01 YNQEEFVRFDSDVGEYRAVTELGPRVAESWNSQKDILEDRRGQVDTVCRHNYGVGESFTV 120
DRB1*08:01 YNQEYVRFDSDVGEYRAVTELGPRSAEYWNSQKDFLEDRRALVDITYCRHNYGVGESFTV 120
DRB1*08:02 YNQEYVRFDSDVGEYRAVTELGPRDAEYWNSQKDFLEDRRALVDITYCRHNYGVGESFTV 120
DRB1*08:03 YNQEYVRFDSDVGEYRAVTELGPRSAEYWNSQKDILEDRRALVDITYCRHNYGVGESFTV 120
DRB1*09:01 YNQEENVRFDSDVGEYRAVTELGPRVAESWNSQKDFLERRRAEVDITYCRHNYGVGESFTV 120
DRB1*10:01 HNQEYARYDSVGEYRAVTELGPRDAEYWNSQKDLLERRRAAVDITYCRHNYGVGESFTV 120
DRB1*11:01 YNQEYVRFDSDVGEFRAVTELGPRDEEYWNSQKDFLEDRAAVIDITYCRHNYGVGESFTV 120
DRB1*11:03 YNQEYVRFDSDVGEFRAVTELGPRDEEYWNSQKDFLEDRAAVIDITYCRHNYGVGESFTV 120
DRB1*11:04 YNQEYVRFDSDVGEFRAVTELGPRDEEYWNSQKDFLEDRAAVIDITYCRHNYGVGESFTV 120
DRB1*12:01 HNQEELLRFDSVGEFRAVTELGPRVAESWNSQKDILEDRAAVIDITYCRHNYGAVESFTV 120
DRB1*13:01 HNQEENVRFDSDVGEFRAVTELGPRDAEYWNSQKDILEDRAAVIDITYCRHNYGVGESFTV 120
DRB1*13:03 YNQEYVRFDSDVGEYRAVTELGPRSAEYWNSQKDILEDKRAAVDITYCRHNYGVGESFTV 120
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DRB1*15:02 YNQEESVRFDSDVGEFRAVTELGPRDAEYWNSQKDILEQARAVIDITYCRHNYGVGESFTV 120
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DRB1*15:05 YNQEESVRFDSDVGEFRAVTELGPRDAEYWNSQKDILEQARAVIDITYCRHNYGVGESFTV 120
DRB1*15:06 YNQEESVRFDSDVGEFRAVTELGPRDAEYWNSQKDILEQARAVIDITYCRHNYGVGESFTV 120
DRB1*15:07 YNQEESVRFDSDVGEYRAVTELGPRDAEYWNSQKDILEQARAVIDITYCRHNYGVGESFTV 120
DRB1*16:01 YNQEESVRFDSDVGEYRAVTELGPRDAEYWNSQKDFLEDRAAVIDITYCRHNYGVGESFTV 120
:: *** *:*****:***** * *****: ** *. *. *****. *****

DRB1*01:01 QRRVEPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*01:02 QRRVEPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*01:03 QRRVEPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*03:01 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*03:02 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*03:04 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
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DRB1*04:05 QRRVPEVTVYP AKTQPLQHHNLLVCSVNGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*04:06 QRRVPEVTVYP AKTQPLQHHNLLVCSVNGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
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DRB1*08:01 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
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DRB1*08:03 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*09:01 QRRVHPKVTVYP AKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*10:01 QRRVQPKVTVYP SKTQPLQHHNLLVCSVNGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*11:01 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*11:03 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*11:04 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*12:01 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*13:01 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*13:03 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180
DRB1*14:01 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIHNG 180

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FIG. 5 (continued)

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DRB1*14:02 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTG VVSTGLIHNG 180
DRB1*14:05 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTG VVSTGLIHNG 180
DRB1*14:06 QRRVHPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTG VVSTGLIHNG 180
DRB1*15:01 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
DRB1*15:02 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
DRB1*15:03 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
DRB1*15:04 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
DRB1*15:05 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
DRB1*15:06 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
DRB1*15:07 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
DRB1*16:01 QRRVQPKVTVYP SKTQPLQHHNLLVCSVSGFYPGSIEVRWFLNGQEEKAGMVSTGLIQNG 180
      **** *:*****:*****:*****.***** *****:*:*****:**

DRB1*01:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*01:02 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*01:03 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*03:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*03:02 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*03:04 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*04:01 DWTFTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*04:02 DWTFTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*04:03 DWTFTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*04:04 DWTFTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*04:05 DWTFTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*04:06 DWTFTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*04:08 DWTFTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*07:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVMSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*08:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWSARSESAQSKMLSGVGGFVLGLL 240
DRB1*08:02 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWSARSESAQSKMLSGVGGFVLGLL 240
DRB1*08:03 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWSARSESAQSKMLSGVGGFVLGLL 240
DRB1*09:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVMSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*10:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVMSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*11:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*11:03 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*11:04 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*12:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*13:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*13:03 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*14:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*14:02 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*14:05 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*14:06 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*15:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*15:02 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*15:03 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*15:04 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*15:05 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*15:06 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*15:07 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
DRB1*16:01 DWTFTLVMLETVPRSGEVYTCQVEHPSVTSPLTVEWRARSESAQSKMLSGVGGFVLGLL 240
      *****:*****: ***** *****

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FIG. 5 (continued)

DRB1*01:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:2)
DRB1*01:02	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:3)
DRB1*01:03	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:4)
DRB1*03:01	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:5)
DRB1*03:02	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:6)
DRB1*03:04	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:7)
DRB1*04:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:8)
DRB1*04:02	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:9)
DRB1*04:03	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:10)
DRB1*04:04	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:11)
DRB1*04:05	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:12)
DRB1*04:06	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:13)
DRB1*04:08	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:14)
DRB1*07:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:15)
DRB1*08:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:16)
DRB1*08:02	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:17)
DRB1*08:03	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:18)
DRB1*09:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:19)
DRB1*10:01	FLGAGLFIYFRNQKGHSGLPPTGFLS	266 (SEQ ID NO:20)
DRB1*11:01	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:21)
DRB1*11:03	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:22)
DRB1*11:04	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:23)
DRB1*12:01	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:24)
DRB1*13:01	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:25)
DRB1*13:03	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:26)
DRB1*14:01	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:27)
DRB1*14:02	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:28)
DRB1*14:05	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:29)
DRB1*14:06	FLGAGLFIYFRNQKGHSGLQPRGFLS	266 (SEQ ID NO:30)
DRB1*15:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:31)
DRB1*15:02	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:32)
DRB1*15:03	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:33)
DRB1*15:04	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:34)
DRB1*15:05	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:31)
DRB1*15:06	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:31)
DRB1*15:07	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:35)
DRB1*16:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:36)
***** * *****		

Amino acids 1-29 = signal peptide

Amino acids 30-124 = β 1Amino acids 125-227 = β 2

Amino acids 228-250 = TM (transmembrane)

DRB3*01:01	<u>MVCLKLPGGSSLAALTVTLMVLSSRLAFAGDTRPRFLELRKSECHFFNGT</u> <u>ERVRYLDRYF</u>	60
DRB3-EAX03632	<u>MVCLKLPGGSSLAALTVTLMVLSSRLAFAGDTRPRFLELRKSECHFFNGT</u> <u>ERVRYLDRYF</u>	60
DRB3*02:01	<u>MVCLKLPGGSSLAALTVTLMVLSSRLAFAGDTRPRFLELLKSECHFFNGT</u> <u>ERVRLERHF</u>	60
DRB3*03:01	<u>MVCLKLPGGSSLAALTVTLMVLSSRLAFAGDTRPRFLELLKSECHFFNGT</u> <u>ERVRLFERYF</u>	60
	*****:****:	
DRB3*01:01	<u>HNQEEFLRFDS</u> <u>SDVGEYRAVTELGRPVAESWNSQKDLLEQKRGRVDNYCRHNYGVGESFTV</u>	120
DRB3-EAX03632	<u>HNQEEFLRFDS</u> <u>SDVGEYRAVTELGRPVAESWNSQKDLLEQKRQVDNYCRHNYGVVESFTV</u>	120
DRB3*02:01	<u>HNQEEYARFDS</u> <u>SDVGEYRAVRELGRPDAEYWSNSQKDLLEQKRQVDNYCRHNYGVVESFTV</u>	120
DRB3*03:01	<u>HNQEEFVRFDS</u> <u>SDVGEYRAVTELGRPVAESWNSQKDLLEQKRQVDNYCRHNYGVVESFTV</u>	120
	*****:*****:*****	
DRB3*01:01	<u>QRRVHPQVTVP</u> <u>AKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIQNG</u>	180
DRB3-EAX03632	<u>QRRVHPQVTVP</u> <u>AKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIQNG</u>	180
DRB3*02:01	<u>QRRVHPQVTVP</u> <u>AKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKAGVVSTGLIQNG</u>	180
DRB3*03:01	<u>QRRVHPQVTVP</u> <u>AKTQPLQHHNLLVCSVSGFYPGSIEVRWFRNGQEEKTGVVSTGLIHNG</u>	180
	*****:*****:*****	
DRB3*01:01	<u>DWTFQTLVMLET</u> <u>VP</u> <u>RSGEVYTCQVEHPSVTSALTVEWRARSESAQSK</u> <u>M</u> <u>LSGVGGFVLGLL</u>	240
DRB3-EAX03632	<u>DWTFQTLVMLET</u> <u>VP</u> <u>RSGEVYTCQVEHPSVTSALTVEWRARSESAQSK</u> <u>M</u> <u>LSGVGGFVLGLL</u>	240
DRB3*02:01	<u>DWTFQTLVMLET</u> <u>F</u> <u>PRSGEVYTCQVEHPSVTSPLTVEWSARSESAQSK</u> <u>M</u> <u>LSGVGGFVLGLL</u>	240
DRB3*03:01	<u>DWTFQTLVMLET</u> <u>VP</u> <u>RSGEVYTCQVEHPSVTSPLTVEWRARSESAQSK</u> <u>M</u> <u>LSGVGGFVLGLL</u>	240
	*****:*****:*****	
DRB3*01:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:37)
DRB3-EAX03632	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:38)
DRB3*02:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:39)
DRB3*03:01	FLGAGLFIYFRNQKGHSGLQPTGFLS	266 (SEQ ID NO:40)

Amino acids 1-29 = signal peptide
Amino acids 30-124 = β 1
Amino acids 125-227 = β 2

1	MVCLKLPGGS	CMAALTVTLT	VLSSPLALAG	DTQPRFLEQA	KCECHFNGT	ERVWNLIIRYI
61	YNQEEYARYN	SDLGEYQAVT	ELGRPDAEYW	NSQKDLLERR	RAEVDTYCRY	NYGVVESFTV
121	QRRVQPKVTV	YPSKTQPLQH	HNLLVCSVNG	FYPGSIEVRW	FRNSQEEKAG	VVSTGLIQNG
181	DWTFQTLVML	ETVPRSGEVY	TCQVEHPSMM	SPLTVQWSAR	SESAQSKMLS	GVGGFVLGLL
241	FLGTGLEFIYF	RNOKGHSGLO	PTGLLS	(SEQ ID NO:41)		

FIG. 7 MHC Class II DRB4 beta chain (continued)

GenBank NP_068818.4 & ImMunoGeneTics ("IMGT")/HLA Acc No: HLA00908 (DRB4*01:03)

```

1  MVCLKLPGGG CMAALTVTLT VLSSPLALAG DTQPRFLEQA KCECHFLNGT ERVWNLIRYI
61 YNQEEYARYN SDLGEYQAVT ELGRPDAEYW NSQKDLLERR RAEVDTYCRY NYGVVESFTV
121 QRRVQPKVTV YPSKTQPLQH HNLLVCSVNG FYPGSIEVRW FRNGQEEKAG VVSTGLIQNG
181 DWTFQTLVML ETVPRSGEVY TCQVEHPSMM SPLTVQWSAR SESAQSKMLS GVGGEVLGLL
241 FLGTGLFIYF RNQKGHSGLQ PTGLLS (SEQ ID NO:42)

```

Amino acids 1-29 = signal peptide

Amino acids 30-124 = β 1Amino acids 125-227 = β 2**FIG. 8****MHC Class II DRB5 beta chain (*Homo sapiens*)**

GenBank NP_002116.2 and IMGT/HLA Acc No: HLA00915 (DRB5*01:01)

```

1  MVCLKLPGGG YMAKLTVTLM VLSSPLALAG DTRPRFLQOD KYECHFFNGT ERVRFLLHRDI
61 YNQEEDLRFD SDVGEYRAVT ELGRPDAEYW NSQKDFLEDR RAAVDTYCRH NYGVGESFTV
121 QRRVEPKVTV YPARTQTLQH HNLLVCSVNG FYPGSIEVRW FRNSQEEKAG VVSTGLIQNG
181 DWTFQTLVML ETVPRSGEVY TCQVEHPSVT SPLTVEWRAQ SESAQSKMLS GVGGEVLGLL
241 FLGAGLFIYF KNQKGHSGLH PTGLVS (SEQ ID NO:43)

```

Amino acids 1-29 = signal peptide

Amino acids 30-124 = β 1Amino acids 125-227 = β 2**FIG. 9****MHC Class II DMA alpha chain (*Homo sapiens*)**

GenBank NP_006111.2 and IMGT/HLA Acc No: HLA00485 MHC Class II DMA(DMA*01:01)alpha chain

```

1  MGHEQNQGAA LLQMLPLLWL LPHSWAVPEA PTPMWPDDLQ NHTFLHTVYC QDGSPSVGLS
61 EAYDEDQLFF FDFSQNTVRP RLPEFADWAQ EQGDAPAILF DKEFCEWMIQ QIGPKLDGKI
121 PVSRGFP IAE VFTLKPLEFG KPNTLVCFVS NLFPMLTVN WQHHSVPVEG FGPTFVSAVD
181 GLSFQAFSYL NTFPEPSDIF SCIVTHEIDR YTAIAYWVPR NALPSDLLEN VLCGVAFGLG
241 VLGIIVGIVL IIYFRKPCSG D (SEQ ID NO:44)

```

Amino acids 1-26 = signal peptide

Amino acids 27-124 = α 1Amino acids 125-217 = α 2

FIG. 10**MHC Class II DMB beta chain (*Homo sapiens*)**

GenBank NP_002109.2 and IMGT/HLA Acc No: HLA00489 (DMB*01:03)

1 MITFLPLLLG LSLGCTGAGG FVAHVESTCL LDDAGTPKDF TYCISFNKDL LTCWDPEENK
61 MAPCEFGVLN SLANVLSQHL NQKDTLMQRL RNGLQNCATH TQPFWGSLTN RTRPSPVQVA
121 KTTFPNTREP VMLACYVWGF YPAEVTITWR KNGKLVMPHS SAHKTAQPNG DWTYQTLSHL
181 ALTPSYGDTY TCVVEHTGAP EPILRDWTPG LSPMQTLKVS VSAVTLGLGL IIFSLGVISW
241 RRAGHSSYTP LPGSNYSEGW HIS (SEQ ID NO:45)

Amino acids 1-18 = signal peptide

Amino acids 19-112 = β 1Amino acids 113-207 = β 2**FIG. 11****MHC Class II DOA alpha chain (*Homo sapiens*)**

GenBank NP_002110.1 and 2 and IMGT/HLA Acc No: HLA00494 MHC Class II DOA (DOA*01:01) alpha chain

1 MALRAGLVLG FHTLMTLLSP QEAGATKADH MGSYGPAFYQ SYGASGQFTH EFDEEQLFVS
61 DLKKSEAVWR LPEFGDFARF DPQGGLAGIA AIKAHLDILV ERSNRSRAIN VPPRVTVLPK
121 SRVELGQPNL LICIVDNIFP PVINITWLRN GQTVTEGVAQ TSFYSQPDHL FRKFHYLPFV
181 PSAEDVYDCQ VEHWGLDAPL LRHWELQVPI PPPDAMETLV CALGLAIGLV GFLVGTVLII
241 MGTYVSSVPR (SEQ ID NO:46)

Amino acids 1-25 = signal peptide

Amino acids 26-110 = α 1Amino acids 111-204 = α 2**FIG. 12****MHC Class II DOB beta chain (*Homo sapiens*)**

GenBank NP_002111.1 and IMGT/HLA Acc No:HLA01098 MHC Class II DOB (DOB*01:01) beta chain

1 MGSGWVPWV ALLVNLTRLD SSMTQGTDSP EDFVIQAKAD CYFTNGTEKV QFVVRFIFNL
61 EEYVRFDSDV GMFVALTKLG QPDAEQWNSR LDLLERSRQA VDGVCRHNYR LGAPFTVGRK
121 VQPEVTVYPE RTPLLHQHNL LHCSVTGFYP GDIKIKWFLN GQEERAGVMS TGPIRNGDWT
181 FQTVVMLEMT PELGHVYTCL VDHSSLLSPV SVEWRAQSEY SWRKMLSGIA AFLGLIFLL
241 VGIVIQLRQA KGYVRTQMSG NEVSRAVLLP QSC (SEQ ID NO:47)

Amino acids 1-26 = signal peptide

Amino acids 27-120 = β 1Amino acids 121-214 = β 2

FIG. 13**MHC Class II DPA1 alpha chains (*Homo sapiens*)**

GenBank NP_001229453.1 and IMGT/HLA Acc No: HLA00499 MHC Class II DPA1(DPA1*01:03) alpha chain

```

1   MRPEDRMFHI RAVILRALSL AFLLSLRGAG AIKADHVSTY AAFVQTHRPT GEFMFEFDED
61  EMFYVDLDDK ETVWHLEEFQ QAFSFEAQGG LANIAILNNN LNTLIQRSNH TQATNDPPEV
121 TVFPKEPVEL GQNTLICH I DKFFPPVLNV TWLCNGELVT EGVAESLFLP RTDYSFHKFH
181 YLTFVPSAED FYDCRVEHWG LDQPLLKHWE AQEPIQMPET TETVLCALGL VLGLVGIIVG
241 TVLIIKSLRS GHDPRAQGTL (SEQ ID NO:48)

```

IMGT/HLA Acc No: HLA00504 MHC Class II DPA1:02(DPA1*02:01) alpha chain

```

1   MRPEDRMFHI RAVILRALSL AFLLSLRGAG AIKADHVSTY AAFVQTHRPT GEFMFEFDED
61  EQFYVDLDDK ETVWHLEEFQ RAFSFEAQGG LANIAILNNN LNTLIQRSNH TQAANDPPEV
121 TVFPKEPVEL GQNTLICH I DRFFPPVLNV TWLCNGEPVT EGVAESLFLP RTDYSFHKFH
181 YLTFVPSAED VYDCRVEHWG LDQPLLKHWE AQEPIQMPET TETVLCALGL VLGLVGIIVG
241 TVLIIKSLRS GHDPRAQGPL (SEQ ID NO:49)

```

Amino acids 1-28 = signal peptide

Amino acids 29-115 = $\alpha 1$

Amino acids 116-209 = $\alpha 2$

FIG. 14

MHC Class II DPB1 beta chain (*Homo sapiens*)

```
DPB1*01:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVYQGRQECYAFNGTQRFLERYIYN  60
DPB1*02:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYLFQGRQECYAFNGTQRFLERYIYN  60
DPB1*03:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVYQLRQECYAFNGTQRFLERYIYN  60
DPB1*04:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYLFQGRQECYAFNGTQRFLERYIYN  60
DPB1*06:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVYQLRQECYAFNGTQRFLERYIYN  60
DPB1*09:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVHQLRQECYAFNGTQRFLERYIYN  60
DPB1*11:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVYQLRQECYAFNGTQRFLERYIYN  60
DPB1*13:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVYQLRQECYAFNGTQRFLERYIYN  60
DPB1*35:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVHQLRQECYAFNGTQRFLERYIYN  60
DPB1*71:01  MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYLFQGRQECYAFNGTQRFLERYIYN  60
DPB1*104:01 MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYVYQLRQECYAFNGTQRFLERYIYN  60
DPB1*141:01 MMVLQVSAAPRTVALTALLMVLLTSVVQGRATPENYLFQGRQECYAFNGTQRFLERYIYN  60
*****:.******

DPB1*01:01  REEYARFSDSDVGEFRAVTELGRPAAEYWNSQKDILEEKRAVPDRVCRHNYELDEAVTLQR  120
DPB1*02:01  REEFVRFSDSDVGEFRAVTELGRPDEEYWNSQKDILEEERAVPDRMCRHNYELGGPMTLQR  120
DPB1*03:01  REEFVRFSDSDVGEFRAVTELGRPDEDYWNSQKDLLEEKRAVPDRVCRHNYELDEAVTLQR  120
DPB1*04:01  REEFARFSDSDVGEFRAVTELGRPAAEYWNSQKDILEEKRAVPDRMCRHNYELGGPMTLQR  120
DPB1*06:01  REEFVRFSDSDVGEFRAVTELGRPDEDYWNSQKDLLEEERAVPDRMCRHNYELDEAVTLQR  120
DPB1*09:01  REEFVRFSDSDVGEFRAVTELGRPDEDYWNSQKDILEEERAVPDRVCRHNYELDEAVTLQR  120
DPB1*11:01  RQEYARFSDSDVGEFRAVTELGRPAAEYWNSQKDLLEERAVPDRMCRHNYELDEAVTLQR  120
DPB1*13:01  REEYARFSDSDVGEFRAVTELGRPAAEYWNSQKDILEEERAVPDRICRHNLYELDEAVTLQR  120
DPB1*35:01  REEFVRFSDSDVGEFRAVTELGRPDEDYWNSQKDILEEKRAVPDRVCRHNYELDEAVTLQR  120
DPB1*71:01  REEFVRFSDSDVGEFRAVTELGRPAAEYWNSQKDILEEERAVPDRMCRHNYELGGPMTLQR  120
DPB1*104:01 REEFVRFSDSDVGEFRAVTELGRPDEDYWNSQKDLLEEKRAVPDRVCRHNYELDEAVTLQR  120
DPB1*141:01 REEFVRFSDSDVGEFRAVTELGRPDEEYWNSQKDILEEERAVPDRMCRHNYELGGPMTLQR  120
*:.:.******:*****:***.*****:*****.:****

DPB1*01:01  RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*02:01  RVQPRVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*03:01  RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*04:01  RVQPRVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*06:01  RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*09:01  RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*11:01  RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*13:01  RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*35:01  RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*71:01  RVQPRVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*104:01 RVQPKVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVRWFLNGQEETAGVVSTNLIRNGDW  180
DPB1*141:01 RVQPRVNVSPSKKGPLQHHNLLVCHVTDFYPGSIQVQWFLNGQEETAGVVSTNLIRNGDW  180
****.******:*****:*****:*****:*****:*****:*****:*****
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FIG. 14 (continued)

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DPB1*01:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSAQSKTLTGAGGFVLGLIIC  240
DPB1*02:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*03:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*04:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*06:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*09:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*11:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*13:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*35:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*71:01  TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*104:01 TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
DPB1*141:01 TFQILVMLEMTPOQGDVYICQVEHTSLDSPVTVEWKAQSDSARSKTLTGAGGFVLGLIIC  240
*****:*****:*****

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DPB1*01:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:50)
DPB1*02:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:51)
DPB1*03:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:52)
DPB1*04:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:53)
DPB1*06:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:54)
DPB1*09:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:55)
DPB1*11:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:56)
DPB1*13:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:57)
DPB1*35:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:58)
DPB1*71:01  GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:59)
DPB1*104:01 GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:60)
DPB1*141:01 GVGIFMHRRSKKVQRGSA  258  (SEQ ID NO:61)
*****

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Amino acids 1-29 = signal peptide

Amino acids 30-121 = β 1

Amino acids 122-215 = β 2

FIG. 15**MHC Class II DQA1 alpha chain (*Homo sapiens*)**

```

DQA1*01:01  MILNKALLLGALALTTVMSPCGGEDIVADHVASCGVNLYQFYGPSGQYTHEFDGDEEFYV  60
DQA1*01:02  MILNKALLLGALALTTVMSPCGGEDIVADHVASCGVNLYQFYGPSGQYTHEFDGDEQFYV  60
DQA1*01:03  MILNKALLLGALALTTVMSPCGGEDIVADHVASCGVNLYQFYGPSGQYTHEFDGDEQFYV  60
DQA1*01:04  MILNKALLLGALALTTVMSPCGGEDIVADHVASCGVNLYQFYGPSGQYTHEFDGDEEFYV  60
DQA1*02:01  MILNKALMLGALALTTVMSPCGGEDIVADHVASGVNLYQSYGPSGQYTHEFDGDEEFYV  60
DQA1*03:01  MILNKALMLGALALTTVMSPCGGEDIVADHVASGVNLYQSYGPSGQYSHEFDGDEEFYV  60
DQA1*03:02  MILNKALMLGALALTTVTSPCGGEDIVADHVASGVNLYQSYGPSGQYSHEFDGDEEFYV  60
DQA1*04:01  MILNKALLLGALALTTVMSPCGGEDIVADHVASGVNLYQSYGPSGQYTHEFDGDEQFYV  60
DQA1*05:01  MILNKALMLGALALTTVMSPCGGEDIVADHVASGVNLYQSYGPSGQYTHEFDGDEQFYV  60
DQA1*05:05  MILNKALMLGTLALTTVMSPCGGEDIVADHVASGVNLYQSYGPSGQYTHEFDGDEQFYV  60
DQA1*06:01  MILNKALLLGALALTTVMSPCGGEDIVADHVASGVNLYQSYGPSGQYTHEFDGDEQFYV  60
*****:*****:*****

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FIG. 15 (continued)

```

DQA1*01:01  DLERKETAWRWPEFSKFGGFDPPQALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK 120
DQA1*01:02  DLERKETAWRWPEFSKFGGFDPPQALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK 120
DQA1*01:03  DLEKKETAWRWPEFSKFGGFDPPQALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK 120
DQA1*01:04  DLERKETAWRWPEFSKFGGFDPPQALRNMAVAKHNLNIMIKRYNSTAATNEVPEVTVFSK 120
DQA1*02:01  DLERKETVWKLPLFHRL-RFDPQFALTNI AVLKHNLNILIKRSNSTAATNEVPEVTVFSK 119
DQA1*03:01  DLERKETVWQLPLFRRFRFRFDPQFALTNI AVLKHNLNIVIKRSNSTAATNEVPEVTVFSK 120
DQA1*03:02  DLERKETVWQLPLFRRFRFRFDPQFALTNI AVLKHNLNIVIKRSNSTAATNEVPEVTVFSK 120
DQA1*04:01  DLGRKETVWCLPVLRQF-RFDPQFALTNI AVLTKHNLNILIKRSNSTAATNEVPEVTVFSK 119
DQA1*05:01  DLGRKETVWCLPVLRQF-RFDPQFALTNI AVLKHNLNLSLIKRSNSTAATNEVPEVTVFSK 119
DQA1*05:05  DLGRKETVWCLPVLRQF-RFDPQFALTNI AVLKHNLNLSLIKRSNSTAATNEVPEVTVFSK 119
DQA1*06:01  DLGRKETVWCLPVLRQF-RFDPQFALTNI AVLTKHNLNILIKRSNSTAATNEVPEVTVFSK 119
              ** :***.* * : :: ***** ** *:* ** ***** :*** *****
              :

DQA1*01:01  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGQSVTEGVSETSFLSKSDHSFFKISYLTFL 180
DQA1*01:02  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGQSVTEGVSETSFLSKSDHSFFKISYLTFL 180
DQA1*01:03  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHAVTEGVSETSFLSKSDHSFFKISYLTFL 180
DQA1*01:04  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGQSVTEGVSETSFLSKSDHSFFKISYLTFL 180
DQA1*02:01  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTFL 179
DQA1*03:01  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHSVTEGVTS-TSFLSKSDHSFFKISYLTFL 179
DQA1*03:02  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTFL 180
DQA1*04:01  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTFL 179
DQA1*05:01  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTLL 179
DQA1*05:05  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTLL 179
DQA1*06:01  SPVTLGQPNTLICLVDNIFPPVVNITWLSNGHSVTEGVSETSFLSKSDHSFFKISYLTFL 179
              ***** *****:***** *****
              :

DQA1*01:01  PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII 240
DQA1*01:02  PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLMGIVVGTVFII 240
DQA1*01:03  PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII 240
DQA1*01:04  PSADEIYDCKVEHWGLDQPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII 240
DQA1*02:01  PSADEIYDCKVEHWGLDEPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVLI 239
DQA1*03:01  PSADEIYDCKVEHWGLDEPLLKHWEPEIPTPMSELTETVVCALGLSVGLVGIVVGTVLI 239
DQA1*03:02  PSDDEIYDCKVEHWGLDEPLLKHWEPEIPTPMSELTETVVCALGLSVGLVGIVVGTVLI 240
DQA1*04:01  PSADEIYDCKVEHWGLDEPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII 239
DQA1*05:01  PSAEESYDCKVEHWGLDKPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII 239
DQA1*05:05  PSAEESYDCKVEHWGLDKPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII 239
DQA1*06:01  PSADEIYDCKVEHWGLDEPLLKHWEPEIPAPMSELTETVVCALGLSVGLVGIVVGTVFII 239
              ** :* *****:*****:*****:*****:*****:*****:
              :

DQA1*01:01  QGLRSVGASRHQGPL 255 (SEQ ID NO:62)
DQA1*01:02  QGLRSVGASRHQGPL 255 (SEQ ID NO:63)
DQA1*01:03  QGLRSVGASRHQGPL 255 (SEQ ID NO:64)
DQA1*01:04  QGLRSVGASRHQGPL 255 (SEQ ID NO:65)
DQA1*02:01  RGLRSVGASRHQGPL 254 (SEQ ID NO:66)
DQA1*03:01  RGLRSVGASRHQGPL 254 (SEQ ID NO:67)
DQA1*03:02  RGLRSVGASRHQGPL 254 (SEQ ID NO:68)
DQA1*04:01  RGLRSVGASRHQGPL 254 (SEQ ID NO:69)
DQA1*05:01  RGLRSVGASRHQGPL 254 (SEQ ID NO:70)
DQA1*05:05  RGLRSVGASRHQGPL 254 (SEQ ID NO:71)
DQA1*06:01  RGLRSVGASRHQGPL 254 (SEQ ID NO:72)
              :*****

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Amino acids 1-23 = signal peptide

Amino acids 24-110 = $\alpha 1$

Amino acids 111-204 = $\alpha 2$

FIG. 16**MHC Class II DQA2 alpha chain** (*Homo sapiens*)

GenBank NP_064440.1

```
1  MILNKALLLG ALALTAVMSP CGGEDIVADH VASYGVNIFYQ SHGPSGQYTH EFDGDEEFYV
61  DLETKETVWQ LPMFSKFISF DPQSALRNMA VGKHTLEFMM RQSNSTAATN EVPEVTVFSK
121 FPVTLGQPNT LICLDVNIFP PVVNITWLSN GHSVTEGVSE TSFLSKSDHS FFKISYLTFL
181 PSADEIYDCK VEHWGLDEPL LKHWEPEIPA PMSELTETLV CALGLSVGLM GIVVGTVFII
241 QGLRSVGASR HQGLL (SEQ ID NO:73)
```

Amino acids 1-23 = signal peptide

Amino acids 24-110 = α 1Amino acids 111-204 = α 2

DQB1*02:01	MSWKKALRIPGGLRAATVTLMLSMLSTPVAEGRDSPEDFVYQFKGMCYFTNGTERVRLVS	60
DQB1*02:02	MSWKKALRIPGGLRAATVTLMLSMLSTPVAEGRDSPEDFVYQFKGMCYFTNGTERVRLVS	60
DQB1*03:01	MSWKKALRIPGGLRAATVTLMLAMLSTPVAEGRDSPEDFVYQFKAMCYFTNGTERVRYVT	60
DQB1*03:02	MSWKKALRIPGGLRVATVTLMLAMLSTPVAEGRDSPEDFVYQFKGMCYFTNGTERVRLVT	60
DQB1*03:03	MSWKKALRIPGGLRVATVTLMLAMLSTPVAEGRDSPEDFVYQFKGMCYFTNGTERVRLVT	60
DQB1*03:04	MSWKKALRIPGGLRAATVTLMLAMLSTPVAEGRDSPEDFVYQFKAMCYFTNGTERVRYVT	60
DQB1*04:01	MSWKKALRIPGGLRVATVTLMLAMLSTPVAEGRDSPEDFVYQFKGMCYFTNGTELVRGVT	60
DQB1*04:02	MSWKKALRIPGGLRVATVTLMLAMLSTPVAEGRDSPEDFVYQFKGMCYFTNGTERVRGVT	60
DQB1*05:01	MSWKKSLRIPGDLRVATVTLMLAILSSSLAEGRDSPEDFVYQFKGLCYFTNGTERVRGVT	60
DQB1*05:03	MSWKKSLRIPGDLRVATVTLMLAILSSSLAEGRDSPEDFVYQFKGLCYFTNGTERVRGVT	60
DQB1*06:01	MSWKKALRIPGGLRAPVTLMLAMLSTPVAEGRDPPEDFVLQFKAMCYFTNGTERVRYVT	60
DQB1*06:02	MSWKKALRIPGDLRVATVTLMLAMLSSSLAEGRDSPEDFVYQFKGMCYFTNGTERVRLVT	60
	*****:*****.**. *****:***: :***** ***** ***.:***** ** *	
DQB1*02:01	RSIYNREEIVRFDSVGEFRAVTLGLPAAEYWNSSQKDI LERKRAAVDRVCRHNYQLELR	120
DQB1*02:02	RSIYNREEIVRFDSVGEFRAVTLGLPAAEYWNSSQKDI LERKRAAVDRVCRHNYQLELR	120
DQB1*03:01	RYIYNREEYARFDSVGEVYRAVTPLGPPDAEYWNSSQKEVLERTRAE LDTVCRHNYQLELR	120
DQB1*03:02	RYIYNREEYARFDSVGVYRAVTPLGPPDAEYWNSSQKEVLERTRAE LDTVCRHNYQLELR	120
DQB1*03:03	RYIYNREEYARFDSVGVYRAVTPLGPPDAEYWNSSQKEVLERTRAE LDTVCRHNYQLELR	120
DQB1*03:04	RYIYNREEYARFDSVGEVYRAVTPLGPPDAEYWNSSQKEVLERTRAE LDTVCRHNYQLELR	120
DQB1*04:01	RYIYNREEYARFDSVGVYRAVTPLGRLDAEYWNSSQKDI LEE DRASVDTVCRHNYQLELR	120
DQB1*04:02	RYIYNREEYARFDSVGVYRAVTPLGRLDAEYWNSSQKDI LEE DRASVDTVCRHNYQLELR	120
DQB1*05:01	RHIYNREEYVRFDSVGVYRAVTPQGRPVAEYWNSSQKEVLE GARASVDRVCRHNYEVA YR	120
DQB1*05:03	RHIYNREEYVRFDSVGVYRAVTPQGRPDAEYWNSSQKEVLE GARASVDRVCRHNYEVA YR	120
DQB1*06:01	RYIYNREEDVRFDSVGVYRAVTPQGRPDAEYWNSSQKDI LERTRAE LDTVCRHNYEVA FR	120
DQB1*06:02	RYIYNREEYARFDSVGVYRAVTPQGRPDAEYWNSSQKEVLE GTRAE LDTVCRHNYEVA FR	120
	* ***** . ***** : **** * *****:*** ** *: * *****: : *	
DQB1*02:01	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETAGV VSTPLI	180
DQB1*02:02	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETAGV VSTPLI	180
DQB1*03:01	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETTGV VSTPLI	180
DQB1*03:02	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETTGV VSTPLI	180
DQB1*03:03	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETTGV VSTPLI	180
DQB1*03:04	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETTGV VSTPLI	180
DQB1*04:01	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETTGV VSTPLI	180
DQB1*04:02	TTLQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPAQIKVRWFRNDQEETTGV VSTPLI	180
DQB1*05:01	GILQRRVEPTVTI SPSRTEALNHHNLLICSVTD FYPSQIKVRWFRNDQEETAGV VSTPLI	180
DQB1*05:03	GILQRRVEPTVTI SPSRTEALNHHNLLICSVTD FYPSQIKVRWFRNDQEETAGV VSTPLI	180
DQB1*06:01	GILQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPGQIKVRWFRNDQEETAGV VSTPLI	180
DQB1*06:02	GILQRRVEPTVTI SPSRTEALNHHNLLVCSVTD FYPGQIKVRWFRNDQEETAGV VSTPLI	180
	*****:*****.*****.*****.***.:*****	
DQB1*02:01	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQSPITVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*02:02	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQSPITVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*03:01	RNGDWTFFQILVMLEMPQHGDVYTCHVEHPSLQNPITVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*03:02	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQNP IIVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*03:03	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQNP IIVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*03:04	RNGDWTFFQILVMLEMPQHGDVYTCHVEHPSLQNPITVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*04:01	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQNP IIVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*04:02	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQNP IIVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*05:01	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQSPITVEWRAQSESAQSKMLSGVGGFVL	240
DQB1*05:03	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQSPITVEWRAQSESAQSKMLSGVGGFVL	240
DQB1*06:01	RNGDWTFFQILVMLEMPQHGDVYTCHVEHPSLQSPITVEWRAQSESAQSKMLSGIGGFVL	240
DQB1*06:02	RNGDWTFFQILVMLEMPQRGDVYTCHVEHPSLQSPITVEWRAQSESAQSKMLSGVGGFVL	240
	*****:*****.*****.*****.***.:*****	

FIG. 17 (continued)

DQB1*02:01 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:74)
 DQB1*02:02 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:75)
 DQB1*03:01 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:76)
 DQB1*03:02 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:77)
 DQB1*03:03 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:78)
 DQB1*03:04 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:79)
 DQB1*04:01 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:80)
 DQB1*04:02 GLIFLGLGLIIHHRSQKGLLH----- 261 (SEQ ID NO:81)
 DQB1*05:01 GLIFLGLGLIIRQRSRKGLLH----- 261 (SEQ ID NO:82)
 DQB1*05:03 GLIFLGLGLIIRQRSRKGPQGPPAGLLH 269 (SEQ ID NO:83)
 DQB1*06:01 GLIFLGLGLIIRQRSQKGPQGPPAGLLH 269 (SEQ ID NO:84)
 DQB1*06:02 GLIFLGLGLIIRQRSQKGPQGPPAGLLH 269 (SEQ ID NO:85)
 *****:***:

Amino acids 1-32 = signal peptide

Amino acids 33-126 = β 1

Amino acids 127-220 = β 2

FIG. 18A**MHC Class II DQB2 beta chain (*Homo sapiens*)**

GenBank NP_001185787.1 MHC Class II DQB2 beta chain Isoform 2

1 MALQIPGGFW AAVTVMLVM LSTPVAEARD FPKDFLVQFK GMCYFTNGTE RVRGVARYIY
 61 NREEYGRFDS DVGEFQAVTE LGRSIEDWNN YKDFLEQERA AVDKVCRHNY EAELRTTLQR
 121 QVEPTVTISP SRTEALNHHN LLVCSVTDFY PAQIKVRWFR NDQEETAGVV STSLIRNGDW
 181 TFQILVMLEI TPQRGDIYTC QVEHPSLQSP ITVEWRPRGP PPAGLLH (SEQ ID NO:86)

Amino acids 1-32 = signal peptide

Amino acids 33-126 = β 1

Amino acids 127-215 = β 2

FIG. 18B (*Homo sapiens*)

GenBank NP_001287719 MHC Class II DQB2 beta chain Isoform 1

1 MALQIPGGFW AAVTVMLVM LSTPVAEARD FPKDFLVQFK GMCYFTNGTE RVRGVARYIY
 61 NREEYGRFDS DVGEFQAVTE LGRSIEDWNN YKDFLEQERA AVDKVCRHNY EAELRTTLQR
 121 QVEPTVTISP SRTEALNHHN LLVCSVTDFY PAQIKVRWFR NDQEETAGVV STSLIRNGDW
 181 TFQILVMLEI TPQRGDIYTC QVEHPSLQSP ITVEWRAQSE SAQSKMLSGI GGFVLGLIFL
 241 GLGLIIRHRG QKGPRGPPPA GLLH (SEQ ID NO:87)

Amino acids 1-32 = signal peptide

Amino acids 33-126 = β 1

Amino acids 127-215 =

FIG. 19A

DRA*0101 (wild-type)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:88)

FIG. 19B

DRA*0101 (E3C)

IKCEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:89)

FIG. 19C

DRA*0101 (E4C)

IKECHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:90)

FIG. 19D

DRA*0101 (F12C)

IKEEHVIIQAECYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:91)

FIG. 19E

DRA*0101 (G28C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDCDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:92)

FIG. 19F

DRA*0101 (D29C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGCEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:93)

FIG. 19G

DRA*0101 (I72C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLECMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:94)

FIG. 19H

DRA*0101 (K75C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTCRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:95)

FIG. 19I

DRA*0101 (T80C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYCPITNVPPEVTVLTNSPVELREPNVLCFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:96)

FIG. 19J

DRA*0101 (P81C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTCITNVPPEVTVLTNSPVELREPNVLCFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:97)

FIG. 19K

DRA*0101 (I82C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPCTNVPPEVTVLTNSPVELREPNVLCFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:98)

FIG. 19L

DRA*0101 (T93C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLCNSPVELREPNVLCFIDK
FTPPVVNVTWLRNGKPVTGTVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:99)

FIG. 19M

DRA*0101 (N94C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTCSPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGVSFVFLPREDFHFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:100)

FIG. 19N

DRA*0101 (S95C)

IKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFE
AQGALANIAVDKANLEIMTKRSNYTPITNVPPEVTVLTNCPVELREPNVLICFIDK
FTPPVVNVTWLRNGKPVTGVSFVFLPREDFHFRKFHYLPFLPSTEDVYDCRVE
HWGLDEPLLKHWEFDAPSPLPET (SEQ ID NO:101)

FIG. 19O

PD-L1

FTVTVPKDLVVEYGSNMTIECKFPVEKQLDLAALIVYWEMEDKNIIQFVHGEE
DLKVQHSSYRQRARLLKDQLSLGNAALQITDVKLQDAGVYRCMISYGGADYKR
ITVKVNAPYNKINQRILVVDPVTSEHELTCQAEGYPKAEVIWTSSDHQVLSGKTT
TTNSKREEKLFNVTSTLRINTTTNEIFYCTFRRLDPEENHTAELVIPELPLAHPNE
R (SEQ ID NO:102)

FIG. 20A

DRB1*0401 (wild-type)

GDTRPRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPASIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTVIEWRARSESAQSKM (SEQ ID NO:103)

FIG. 20B

DRB1*0401 (P5C)

GDTRCRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPASIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTVIEWRARSESAQSKM (SEQ ID NO:104)

FIG. 20C

DRB1*0401 (F7C)

GDTRPRCLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPASIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTVIEWRARSESAQSKM (SEQ ID NO:105)

FIG. 20D

DRB1*0401 (Q10C)

GDTRPRFLECVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPASIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTVIEWRARSESAQSKM (SEQ ID NO:106)

FIG. 20E

DRB1*0401 (N19C)

GDTRPRFLEQVKHECHFFCGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPPASIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTV EWRARSESAQSKM (SEQ ID NO:107)

FIG. 20F

DRB1*0401 (G20C)

GDTRPRFLEQVKHECHFFNCTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPPASIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTV EWRARSESAQSKM (SEQ ID NO:108)

FIG. 20G

DRB1*0401 (H33C)

GDTRPRFLEQVKHECHFFNGTERVRFLDRYFYCQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPPASIEVRWFRNGQEEKTG VVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTV EWRARSESAQSKM (SEQ ID NO:109)

FIG. 20H

DRB1*0401 (G151C)

GDTRPRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYPPASIEVRWFRNGQEEKTG VVSTGLIQNC DWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTV EWRARSESAQSKM (SEQ ID NO:110)

FIG. 20I

DRB1*0401 (D152C)

GDTRPRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYFASIEVRWFRNGQEEKTG VVSTGLIQNGCWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTV EWRARSESAQSKM (SEQ ID NO:111)

FIG. 20J

DRB1*0401 (W153C)

GDTRPRFLEQVKHECHFFNGTERVRFLDRYFYHQEEYVRFDSDVGEYRAVTELG
RPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKT
QPLQHNNLLVCSVNGFYFASIEVRWFRNGQEEKTG VVSTGLIQNGDCTFQTLVM
LETVPRSGEVYTCQVEHPSLTSP LTV EWRARSESAQSKM (SEQ ID NO:112)

FIG. 21A

GenBank 3S7G_A

Homo sapiens **IgG1** Fc (SEQ ID NO:113)

227 aa

```
1 DKTHTCPPCP APELLGGPSV FLFPKPCKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD
61 GVEVHNAKTK PREEQNSTY RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK
121 GQPREPQVYT LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPPVLDL
181 DGSFFFLYSKL TVDKSRWQQG NVFSCSVMH E ALHNHYTQKS LSLSPGK
```

FIG. 21B**IgG1** Fc (L14A; L15A) (SEQ ID NO:114)

```
1 DKTHTCPPCP APEAAGGPSV FLFPKPCKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD
61 GVEVHNAKTK PREEQNSTY RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK
121 GQPREPQVYT LPPSRDELTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPPVLDL
181 DGSFFFLYSKL TVDKSRWQQG NVFSCSVMH E ALHNHYTQKS LSLSPGK
```

FIG. 21C

IgG1 Fc (E136; M138) (SEQ ID NO:115)

1 DKTHTCPPCP APE**LL**GGPSV FLFPKPCKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD
61 GVEVHNAKTK PREEQYNSTY RVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK
121 GQPREPQVYT LPPSR**EE**MTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPPVLDL
181 DGSFFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK

FIG. 21D

IgG1 Fc (E136; M138; L14A; L15A) (SEQ ID NO:116)

1 DKTHTCPPCP APE**AA**GGPSV FLFPKPCKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD
61 GVEVHNAKTK PREEQYNSTY RVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK
121 GQPREPQVYT LPPSR**EE**MTK NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPPVLDL
181 DGSFFFLYSKL TVDKSRWQQG NVFSCSVMHE ALHNHYTQKS LSLSPGK

FIG. 21E

Human IgG1 Fc Mutant: L234F/L235E/P331S (Triple Mutant “TM”) (L14F/L15E/P111S)
DKTHTCPPCPAPE**FE**GGPSVFLFPPKPKDILMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ**N**STYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAP**S**IEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:117)

FIG. 21F

Human IgG1 Fc Mutant: N297A (N77A)
DKTHTCPPCPAPE**LL**GGPSVFLFPPKPKDILMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ**A**STYRVVSVLTVLHQDWLNGKE
YKCKVSNKALPAP**P**IEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO:118)

FIG. 21G

GenBank AAN76044
Homo sapiens IgG2 Fc (amino acids 99-325) (SEQ ID NO:119)
227 aa (amino acids 99-325)
1 STKGPSVFPL APCRSTSES TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPAVLQSSG
61 LYSLSVVTV PSSNFGTQTY TCNVDHKPSN TKVDKTVRK CCVECPPCPA PPVAGPSVFL
121 FPPKPKDTLM ISRTPEVTCV VDVSHEDPE VQFNWYVDGV EVHNAKTKPR EEQFNSTFRV
181 VSVLTVVHQD WLNGKEYKCK VSNKGLPAPI EKTISKTKGQ PREPQVYITLP PSREEMTKNQ
241 VSLTCLVKGF YPSDIAVEWE SNGQPENNYK TTPPMLDSG SFFLYSKLTV DKSRWQQGNV
301 FSCSVMHEAL HNHYTQKSLS LSPGK

FIG. 21H

GenBank AAW65947

Homo sapiens IgG3 Fc (amino acids 19-246) (SEQ ID NO:120)
228 aa (amino acids 19-246)

1 HKPSNTKVDK RVELKTPLGD TTHTCPPCPA PELLGGPSVF LFPPKPKDIL MISRTPEVTC
61 VVVDVSHEDP EVKFNWYVDG VEVHNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC
121 KVSNKALPAP IEKTISKAKG QPREPQVYTL PPSRDELTKN QVSLTCLVKG FYPSDIAVEW
181 ESNQQPENNY KITPPVLDSD GSFFLYSKLT VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL
241 SLSPGK

Figure 21I

GenBank AAA52770

Homo sapiens IgD Fc (amino acids 162-383) (SEQ ID NO:121)
222 aa

1 PTKAPDVFPI ISGCRHPKDN SPVVLACLIT GYHPTSVTVT WYMGTSQSPQ RTFPEIQRRD
61 SYMYTSSQLS TPLQQWRQGE YKCVVQHTAS KSKKEIFRWP ESPKAQASSV PTAQPQAECS
121 LAKATTAPAT TRNTGRGGEK KKKEKEKEEQ EERETKTPEC PSHTQPLGVY LLTPAVQDLW
181 LRDKATFTCF VVGSDLKDAH LTWEVAGKVP TGGVEEGLLE RHNNGSQSQH SRLTLPRSLW
241 NAGTSVTCTL NHPSLPPQRL MALREPAQA PVKLSLNLLA SSDPPEAASW LLCEVSGFSP
301 PNILLMWLED QREVENTSGFA PARPPQPRS TTFWAWSVLR VPAPPSPQPA TYTCVVSHED
361 SRTLLNASRS LEVSYVTDHG PMK

FIG. 21J

GenBank 0308221A

Homo sapiens **IgM** Fc (SEQ ID NO:122)

276 aa

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1 VTSTLTIKZS DWLGESMFTC RVDHRGLTFQ QNASSMCVPD QDTAIRVFAI PPSFASIFLT
61 KSTKLTCLVT DLTTYBSVTI SWTREENGAV KHTNISESH PNATFSAVGE ASICEDBDWS
121 GERFTCTVTH TDLPSPLKQT ISRPKGVALH RPBVYLLPPA RZZLNLRESA TITCLVTFGS
181 PADVFVEWMQ RGEPLSPQKY VTSAPMPEPQ APGRYFAHSI LTVSEEEWNT GGTYTCVVAH
241 EALPNRVTER TVDKSTGKPT LYNVSLVMSD TAGTCY
```

Figure 21K

GenBank P01876

Homo sapiens **IgA** Fc (amino acids 120-353) (SEQ ID NO:123)

234 aa

```
1 ASPTSPKVFP LSLCSTQPDG NVVIACLVQG FFPQEPLSVT WSESGQGVTA RNFPPSQDAS
61 GDLYTTSSQL TLPATQCLAG KSVTCHVKHY TNPSQDVTVP CPVPSTPPTP SPSTPPTPSP
121 SCCHPRLSLH RPALEDLLG SEANLTCTLT GLRDASGVTF TWTPSSGKSA VQGPPERDLC
181 GCYSVSSVLP GCAEPWNHGK TFTCTAAYPE SKTPLTATLS KSGNTRPEV HLLPPFSEEL
241 ALNELVTLC LARGFSPKDV LVRWLQGSQE LPREKYLTTWA SRQEPSQGT TFAVTSILRV
301 AAEDWKKGDT FSCMVGHEAL PLAFTQKTID RLAGKPTHVN VSVVMAEVDG TCY
```


FIG. 21L

GenBank IF6A_B

Homo sapiens IgE Fc (amino acids 6-222) (SEQ ID NO:124)

212 aa

1 ADPCDSNPRG VSAYLSRPSP FDLFIRKSPT ITCLVVDLAP SKGTVNLTWS RASGKPVNHS
61 TRKEEKQRNG TLTVTSTLPV GTRDWIEGET YQCRVTHPHL PRALMRSTTK TSGPRAAPEV
121 YAFATPEWPG SRDKRTLACL IQNFMPEDIS VQWLHNEVQL PDARHSTTQP RKTGSGFFV
181 FSRLEVTRA EWEQDEFICR AVHEAASPSQ TVQRAVSVNP GK

FIG. 21M

GenBank P01861

Homo sapiens IgG4 Fc (amino acids 100-327) (SEQ ID NO:125)

228 aa (amino acids 100-327)

1 ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS
61 GLYSLSSVVT VPSSSLGTKT YTCNVVDHKPS NTKVDKRVES KYGPPCPSCP APEFLGGPSV
121 FLFPPKPKDT LMISRTPEVT CVVVDVSQED PEVQFNWYVD GVEVHNAKTK PREEQFNSTY
181 RVSVLTVLH QDWLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT LPPSQEEMTK
241 NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSRL TVDKSRWQEG
301 NVFSCSVME ALHNHYTQKS LSLSLGK

FIG. 22A

(wild-type IL-2)

APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCLE
EELKPLEEVNLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNR
WITFCQSIISTLT (SEQ ID NO:126)

FIG. 22B(IL-2R α)

1 **MDSYLLMWGL LTFIMVPGCQ** AELCDDDPPE IPHATFKAMA YKEGTM LNCE CKRGFRRIKS
61 GSLYMLCTGN SSHSSWDNQC QCTSSATRNT TKQVTPQPEE QKERKTTEMQ SPMQPV DQAS
121 LPGHCREPPP WENEATERIY HFVVGQMVYY QCVQGYRALH RGPAESVCKM THGKTRWTQP
181 QLICTGEMET SQFPGE EKPQ ASPEGRPESE TSCLVTTTDF QIQTEMAATM ETSIFTTEYQ
241 VAVAGCVFLL ISVLLLSGLT WQRRQRKSRR TI (SEQ ID NO:127)

Mature = amino acids 22-272

FIG. 22C(IL-2R β)

1 MAAPALSWRL PLLILLPLA TSWASAAVNG TSQFTCFYNS RANISCVWSQ DGALQDTSCQ
61 VHAWPDRRRW NQTCCELLPV S QASWACNLIL GAPDSQKLTT VDIVTLRVLC REGVRWRVMA
121 IQDFKPFENL RLMAPISLQV VHVETHRCNI SWEISQASHY FERHLEFEAR TLSPGHTWEE
181 APLLTLKQKQ EWICLET LTP DTQYEFQVRV KPLQGEFTTW SPWSQPLAFR TKPAALGKDT
241 IPWLGHLLVG LSGAFGF IIL VYLLINCRNT GPWLKKVLKC NTPDPSKFFS QLSSEHG G DV
301 QKWLSSPFPS SSFSPGGLAP EISPLEVLER DKVTQLLLQQ DKVPEPASLS SNHSLTSCFT
361 NQGYFFFHLP DALEIEACQV YFTYDPYSEE DPDEGVAGAP TGSSPQPLQP LSGEDDAYCT
421 FPSRDDLLLF SPSLLGGPSP PSTAPGGSGA GEERMPPSLQ ERVPRDWDPQ PLGPPTPGVP
481 DLVDFQPPPE LVLREAGEEV PDAGPREGVS FPWSRPPGQG EFRALNARLP LNTDAYLSLQ
541 ELQGQDPTHL V (SEQ ID NO:128)

Mature = amino acids 27-551

FIG. 22D(IL-2R γ)

1 MLKPSLPFTS LLFLQLPLL G VGLNTTILTP NGNEDTTADF FLTTMPTDSL SVSTLPLPEV
61 QCFVFNVEYM NCTWNSSSEP QPTNLTLHYW YKNSDNDKVQ KCSHYLFSEE ITSGCQLQKK
121 EIHLYQTFVV QLQDPREPRR QATQMLKLQN LVIPWAPENL TLHKLSESQL ELNWNRRFLN
181 HCLEHLVQYR TDWDHSWTEQ SVDYRHKFSL PSVDGQKRYT FRVRSRFPNPL CGSAQHWSEW
241 SHPIHWGSNT SKENPFLFAL EAVVISVGSM GLIISLLCVY FWLERTMPRI PTLKNLEDLV
301 TEYHGNFSAW SGVSKGLAES LQPDYSERLC LVSEIPPCKG ALGEGPGASP CNQHSPYWAP
361 PCYTLKPET (SEQ ID NO:129)

Mature = amino acids 23-369

FIG. 22E

PD-L1 ectodomain

FT VTPKDLVYV EYGSNMTIEC KFPVEKQLDL AALIVYWEME DKNIIQFVHG EEDLKVQHSS
YRQRARLLKD QLSLGNAALQ ITDVKLQDAG VYRCMISYGG ADYKRITVKV NAPYNKINQR
ILVVDPTSE HELTCQAEGY PKAEVIWTSS DHQVLSGKTT TTNSKREEKL FNVSTTLRIN
TTTNEIFYCT FRRLDPEENH TAEVIPGNI LNVSIKI (SEQ ID NO:130)

FIG. 22F

4-1BBL

DPAGLLDLRQG MFAQLVAQNV LLIDGPLSWY SDPGLAGVSL TGGLSYKEDT KELVVAKAGV
YYVFFQLELR RVVAGEGSGS VSLALHLQPL RSAAGAAALA LTVDLPPASS EARNSAFGFQ
GRLLHLSAGQ RLGVLHTEA RARHAWQLTQ GATVLGLFRV TPEIPA (SEQ ID NO:131)

FIG. 23A***Homo sapiens* TGF- β 1 preproprotein NCBI Ref. Seq. NP_000651.3**

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1   MPPSGLRLLP LLLPLLWLLV LTPGRPAAGL STCKTIDMEL VKRKRIEAIR GQILSKLRLA
61  SPPSQGEVPP GPLPEAVLAL YNSTRDRVAG ESAEPEPEPE ADYYAKEVTR VLMVETHNEI
121 YDKFKQSTHS IYMFFNTSEL REAVPEPVLL SRAELRLLRL KLVQEQHVLE YQKYSNNSWR
181 YLSNRLLAPS DSPEWLSFDV TGVVRQWLSR GGEIEGFRLS AHCSCDSRDN TLQVDINGFT
241 TGRRGDLATI HGMNRPFLLL MATPLERAQH LQSSRHRRAL DTNYCFSSTE KNCCVRQLYI
301 DFRKDLGWKW IHEPKGYHAN FCLGPCPYIW SLDTQYSKVL ALYNQHNPQA SAAPCCVPQA
361 LEPLPIVYYV GRKPKVEQLS NMIVRSCKCS (SEQ ID NO:132)

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1..29 Signal Peptide

29..261 TGF- β propeptide

244..246 Cell attachment site

279..390 mature peptide

See also UniProtKB - P01137 having a P10L substitution in the signal sequence

FIG. 23B**TGF- β 1 mature (279-390)**

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AL DTNYCFSSTE KNCCVRQLYI DFRKDLGWKW IHEPKGYHAN FCLGPCPYIW SLDTQYSKVL
ALYNQHNPQA SAAPCCVPQA LEPLPIVYYV GRKPKVEQLS NMIVRSCKCS (SEQ ID NO:133)

```


FIG. 23E

***Homo sapiens* TGF- β 3 preproprotein isoform 1 NCBI Ref. Seq. NP_001316868.1 UniProt Ref.: P10600.1**

```

1   MKMHLQRALV VLALLNFATV SLSLSTCTTL DFGHIKKKRV EAIRGQILSK LRLTSPPEPT
61  VMTHVPYQVL ALYNSTRELL EEMHGEREEG CTQENTESEY YAKEIHKFDM IQGLAEHNEL
121 AVCPKGITSK VFRFNVSSVE KNRTNLFRAE FRVLRVPNPS SKRNEQRIEL FQILRPDEHI
181 AKQRYIGGKN LPTRGTAEWL SFDVTDTVRE WLLRRESNLG LEISIHCPCH TFQPNGDILE
241 NIHEVMEIKF KGVDNEDDHG RGD LGRLKKQ KDHHNPHLIL MMIPPHRLDN PGQGGQRKKR
301 ALDTNYCFRN LEENCCVRPL YIDFRQDLGW KKWHEPKGY ANFCSGPCPY LRSADTTHTS
361 VLGLYNTLNP EASASPCCVP QDLEPLTILY YVGRTPKVEQ LSNMVVKSCS CS (SEQ ID
NO:136)

```

1..23	Signal Peptide
24..300	mature latency associated peptide
24..230	TGF- β propeptide`
261..263	Cell attachment site
301..412	mature peptide

FIG. 23F

***Homo sapiens* Mature TGF- β -3 isoform 1 NCBI Ref. Seq. NP_001316868.1 UniProt Ref.: P10600.1,**

```

1   ALDTNYCFRN LEENCCVRPL YIDFRQDLGW KKWHEPKGY ANFCSGPCPY LRSADTTHTS
61  VLGLYNTLNP EASASPCCVP QDLEPLTILY YVGRTPKVEQ LSNMVVKSCS CS (SEQ ID
NO:137)

```

FIG. 23G

***Homo sapiens* Mature TGF- β 3 isoform 1 Mutant: C77S NCBI Ref. Seq. NP_001316868.1 UniProt Ref.: P10600.1 (C77S substitution)**

```

1   ALDTNYCFRN LEENCCVRPL YIDFRQDLGW KKWHEPKGY ANFCSGPCPY LRSADTTHTS
61  VLGLYNTLNP EASASPSCVP QDLEPLTILY YVGRTPKVEQ LSNMVVKSCS CS (SEQ ID
NO:138)

```

C77S substitution bolded, underlined, and italicized.

FIG. 24 (cont'd)

NP_000651.3	PLERAQH--LQSSRRHRRALDTNYCFSSTEKNCCVRLYIDF	FKDLGKWKIHEPKGYHANF	321
P01137	PLERAQH--LQSSRRHRRALDTNYCFSSTEKNCCVRLYIDF	FKDLGKWKIHEPKGYHANF	321
AAA50405.1	PSYRLESEQ-TNRRKKRPRALDAAYCFRNVDNCCLRPLYIDF	FRDLGKWKIHEPKGYNANF	344
NP_0013168-	PPHRLDNPGGGGQKKRPRALDTNYCFRNLEENCCVRLYIDF	FRDLGKWKWHEPKGYIANF	343
68.1	* * : . *::*****: *** . :.*****: *****: *****		
NP_000651.3	CLGPCPYIWSLDTQYSKVLALYNQHNPGASAAP	CCVPOALEPLPIVYYVGRKPKVEQLSN	381
P01137	CLGPCPYIWSLDTQYSKVLALYNQHNPGASAAP	CCVPOALEPLPIVYYVGRKPKVEQLSN	381
AAA50405.1	CAGACPYLWSSDTQHSRVLSTYNTINPEASAP	CCVPSQDLEPLTILYYIGKTPKIEQLSN	404
NP_0013168-	CSGPCPYLRSADTTHSTVLGLYNTLNPEASAP	CCVPODLEPLTILYYVGRTPKVEQLSN	403
68.1	* * *****: *		
NP_000651.3	MIVRSCKCS	390 (SEQ ID NO:132)	
P01137	MIVRSCKCS	390 (SEQ ID NO:139)	
AAA50405.1	MIVKCKCS	413 (SEQ ID NO:140)	
NP_001316868.1	MVVKCKCS	412 (SEQ ID NO:136)	
	*: *: *****		

FIG. 25A

Homo sapiens TGF-β receptor type-1 isoform 1 precursor, NCBI Ref. Seq. NP_004603.1 and UniProtKB/Swiss-Prot: P36897.1

1 MEAAVAAPRP RLLLLVLAAA AAAAAALLPG ATALQCFC HL CTKDNFTCVT DGLCFVSVTE

61 TTDKVIHNSM CIAEIDLIPR DRPFVCA PSS KTGSVTTT YC CNQDHCNKIE LPTTVKSSPG

121 LGPVELAAVI AGPVCFVCIS LMLVYICHN RTVIHHRVPN EEDPSLDRPF ISEGTTLKDL

181 IYDMTTSGSG SGLPLLVRT IARTIVLQES IGKGRFGEVW RGKWRGEEVA VKIFSSREER

241 SWFREAEIYQ TVMLRHENIL GFIAADNKDN GTWTQLWLVS DYHEHGS�FD YLNRYTVTVE

301 GMIKLALSTA SGLAHLHMEI VGTQKPAIA HRDLKSKNIL VKKNGTCCIA DLGLAVRHDS

361 ATDTIDIAPN HRVGTKRYMA PEVLDDSI NM KHFESEFKRAD IYAMGLVFWE IARRCSIGGI

421 HEDYQLPYD LVPSPDPSVEE MRKVVCQKL RPNIPNRWQS CEALRVMAKI MRECWIYANGA

481 ARLTALRIKK TLSQLSQQEG IKM (SEQ ID NO:141)

1..33 signal peptide

34-126 extracellular region (ectodomain)

127-147 transmembrane region

176..203 Transforming growth factor beta type I GS-motif

205..492 Protein tyrosine kinase

209..496 Catalytic domain of the Serine/Threonine Kinases,

FIG. 25B

Homo sapiens TGF-β receptor type-1 isoform 1 ectodomain

34 LQCFCHL CTKDNFTCVT DGLCFVSVTE TTDKVIHNSM CIAEIDLIPR DRPFVCA PSS

91 KTGSVTTT YC CNQDHCNKIE LPTTVKSSPG LGPVEL (SEQ ID NO:142)

FIG. 25C

Homo sapiens TGF-β receptor type-2 (TβRII) isoform A precursor NCBI Ref. Seq. NP_001020018.1

1	MGRGLLRGLW	PLHIVLWTRI	ASTIPPHVQK	SDVEMEAQKD	EIICPSCNRT	AHPLRHINND
61	MIVTDNNGAV	KFPQLCKFCD	VRFSTCDNQK	SCMSNCSITS	ICEKPQEVCV	AVWRKNDENI
121	TLETVCHDPK	LPYHDFILED	AAPKGCIMKE	KKKPGETFFM	CSCSDECDND	NIIFSEEYNT
181	SNPDLILLVIF	QVTGISLLPP	LGVAISVIII	FYCYRVNRQQ	KLSTWETGK	TRKLMEFSEH
241	CAIILEDERS	DISSTCANNI	NHNTPELLPIE	LDTLVGKGRF	AEVYKAKLKQ	NTSEQFETVA
301	VKIFPYEEYA	SWKTEKDIFS	DINLKHENIL	QFLTAERKT	ELGKQYWLIT	AFHAKGNLQE
361	YLTRHVISWE	DLRKLGSSLA	RGLAHLHSDH	TPCGRPKMPI	VHRDLKSSNI	LVKNDLTCCL
421	CDFGLSLRLD	PTLSVDDLAN	SGQVGTARYM	APEVLESRMN	LENVESFKQT	DVYSMALVLW
481	EMTSRCNAVG	EVKDYEPFPG	SKVREHPCVE	SMKDNVLRDR	GRPEIPSFWL	NHQGIQMVCE
541	TLTECWDHDP	EARLTAQCVA	ERFSELEHLD	RLSGRSCSEE	KIPEDGSLNT	TK (SEQ ID NO:143)
1..23		signal peptide				
24..592		mature polypeptide				
24..177		extracellular region (ectodomain)				

FIG. 25D

Homo sapiens TGF-β receptor type-2 (TβRII) isoform A ectodomain

1	IPPHVQKSDV	EMEAQKDEII	CPSCNRTAHP	LRHINNDMIV	TDNNGAVKFP	QLCKE <u>CD</u> VRF
61	STCDNQKSCM	SNCSIT <u>SICE</u>	KPQEVCVAVW	RKNDENITILE	TVCHDPKLPY	HDFILEDAAAS
121	PKCIMKEKKK	PGETFFMCSC	SS <u>DECNDNII</u>	FSEE (SEQ ID NO:144)		

FIG. 25E

Homo sapiens TGF-β receptor type-2 (TβRII) isoform B precursor, UniProtKB Ref. P37173, NCBI Ref. Seq. NP_003233.4

1	MGRGILLRLW	PLHIVLWTRI	ASTIPPHVQK	SVNNDMIVTD	NNGAVKFPQL	CK EC DVRFST
61	CDNQKSCMSN	CSIT S ICEKP	QEVCAVWRK	NDENITLETV	CHDPKLPYHD	FILEDAASP
121	CIMKEKKKPG	ETFFMCSCSS	D ECNDNIIFS	EEYNTSNPDL	LLVIFQVTGI	SLLPPLGVAI
181	SVIIIFYCYR	VNRQKLSST	WETGKTRKLM	EFSEHCAIIL	EDDRSDISST	CANNINHTE
241	LLPIELDTLV	GKGRFAEVYK	AKLKQNTSEQ	FETVAVKIFP	YEEYASWKTE	KDIFSDINLK
301	HENILQFLTA	EERKTELKQ	YWLITAFHAK	GNLQEYLTRH	VISWEDLRKL	GSSLARGIAH
361	LHSDHTPCGR	PKMPIVHRDL	KSSNIIKVND	LTCCLCDFGL	SLRLDPTLSV	DDLANSQQVG
421	TARYMAPEVL	ESRMLENVE	SFKQTDVISM	ALVLWEMTSR	CNAVGEVKDY	EPFFGSKVRE
481	HPCVESMKDN	VLRDRGRPEI	PSFWLNHQGI	QMVCELTLEC	WDHDPPEARLT	AQCVAEFSE
541	LEHLDRLSGR	SCSEKIPED	GSLNTTK	(SEQ ID NO:145)		
1..23	Signal peptide (NCBI records report the signal sequence to be aas 1-22.)					
24..567	Mature polypeptide					
24..166	Transforming growth factor beta receptor 2 ectodomain					

FIG. 25F

Homo sapiens TGF-β receptor type-2 (TβRII) isoform B, ectodomain sequence

		30	32			52	55
1	IPPHVQKSVN	NDMIVTDNNG	AVKFPQLCKE	CDVRFSTCDN	QKSCMSNC	TSIC	EKPQEV
61	CVAVWRKNDE	NITLETVCHD	PKLPYHDFIL	EDAAAPK	CIM	KEKKKPGETF	FMCS
							SSDEC
							118
121	NDNIIFSEY	NTSNPDLLIV	IFQ	(SEQ ID NO:146)			

FIG. 25G

Homo sapiens TGF-β receptor type-2 (TβRII) isoform B, ectodomain fragment sequence

		30	32			52	55
1	IPPHVQKSVN	NDMIVTDNNG	AVKFPQLCKE	CDVRFSTCDN	QKSCMSNC	TSIC	EKPQEV
61	CVAVWRKNDE	NITLETVCHD	PKLPYHDFIL	EDAAAPK	CIM	KEKKKPGETF	FMCS
							SSDEC
							118
121	NDNIIFSEE	(SEQ ID NO:147)					

FIG. 25H

Homo sapiens TGF-β receptor type-2 isoform B, ectodomain fragment Δ14 (N-terminus) D118A

15 TDNNG AVKFPQLCKF CDVRFSTCDN QKSCMSNC SI TSICEKPQEV CVAVWRKNDE
30 32 52 55
| | | |
80 NITLETVCHD PKLPYHDFIL EDAASPKCIM KEKKKPGETF FMCSCSSAEC NDNIIFSEE (SEQ ID NO:148)
118
|

FIG. 25I

Homo sapiens TGF-β receptor type-2 (TβRII) isoform B, ectodomain fragment Δ25 (N-terminus) D118A

26 QLCKF CDVRFSTCDN QKSCMSNC SI TSICEKPQEV CVAVWRKNDE NITLETVCHD
30 32 52 55
| | | |
81 PKLPYHDFIL EDAASPKCIM KEKKKPGETF FMCSCSSAEC NDNIIFSEE (SEQ ID NO:149)
118
|

FIG. 25J

Homo sapiens TGF-β receptor type-2 (TβRII) isoform B, ectodomain fragment Δ25 (N-terminus), D118A ectodomain sequence

26 QLCKF CDVRFSTCDN QKSCMSNC SI TSICEKPQEV CVAVWRKNDE NITLETVCHD
81 PKLPYHDFIL EDAASPKCIM KEKKKPGETF FMCSCSSAEC NDNIIFSEE
131 NTSNPD (SEQ ID NO:150)

FIG. 25K

Homo sapiens TGF-β receptor type 3 isoform A precursor, (BETA Glycan), NCBI Ref. Seq. NP_003234.2 and UniProtKB/Swiss-Prot: Q03167.3

1	MTSHYVIAIF	ALMSSCLATA	GPEPGALCEL	SPVSASHPVQ	ALMESFTVLS	GCASRGTTGL
61	PQEVHVLNLR	TAGQPGQLQ	REVTLLHNP	SSVHIHHSV	VFLNSPHPL	VWHLKTERLA
121	TGVSRLFLVS	EGSVVQFSSA	NFSLTAETEE	RNFPHGNEHL	LNWARKEYGA	VTSFTELKIA
181	RNIYIKVGED	QVFPPKCNIG	KNFLSLNYLA	EYLQPKAAEG	CVMSSQPQNE	EVHIIELITP
241	NSNPYSAFQV	DITIDIRPSQ	EDLEVVKNLI	LILCKKSVN	WVIKSFVKG	SLKIIAPNSI
301	GFGKESERSM	TMTKSIRDDI	PSTQGNLVKW	ALDNGYSPIT	SYTMAPVANR	FHLRLENNAE
361	EMGDEEVHTI	PPELRILLDP	GALPALQNPP	IRGEGQNGG	LPFFFPDISR	RVWNEEGEDG
421	LPRPKDPVIP	SIQLFPGLRE	PEEVQGSVDI	ALSVKCDNEK	MIVAVEKDSF	QASGYSGMDV
481	TLLDPTCKAK	MNGTHFVLES	PLNGCGTRPR	WSALDGVVYY	NSIVIQVPAL	GDSSGWPDGY
541	EDLESGDNGF	PGDMDEGDAS	LFTRPEIVVF	NCSLQQVRNP	SSFQEQPHGN	ITFNMELYNT
601	DLFLVPSQGV	FVSPENGHVV	VEVSVTKAEQ	ELGFAIQTCF	ISPYSNPDRM	SHYTIIEINIC
661	PKDESVKFYS	PKRVHFPIQ	ADMDKKRFSF	VFKPVFNTSL	LFLQCELTLC	TKMEKHPQKL
721	PKCVPPDEAC	TSLDASIIWA	MMQNKKFTFK	PLAVIHHEAE	SKEKGPSMKE	PNPISPPIFH
781	GLDTLTVMGI	AFAAFVIGAL	LTGALWYIYS	HTGETAGRQQ	VPTSPPASEN	SSAAHSIGST
841	QSTPCSSSST	A (SEQ ID NO:151)				

1..18	Signal peptide
27..787	Extracellular domain (ectodomain)
788-809	Transmembrane domain
567..724	Zona pellucida-like domain
737..751	Interaction with TGF-beta ligand
788..809	site_type="transmembrane region"

FIG. 25L

Homo sapiens TGF-β receptor type 3 isoform A ectodomain

				CEL	SPVSASHPVQ	ALMESFTVLS	GCASRGTTGL
61	PQEVHVLNLR	TAGQGPGLQ	REVTLHLNPI	SSVHIHHSV	VFLNSPHPL	VWHLKTERLA	
121	TGVSRLFLVS	EGSVVQFSSA	NFSLTAETEE	RNFPHGNEHL	LNWARKEYGA	VTSFTELKIA	
181	RNIYIKVGED	QVFPPKCNIG	KNFLSLNYLA	EYLQPKAAEG	CVMSSQPQNE	EVHIIELITP	
241	NSNPYSAFQV	DITIDIRPSQ	EDLEVKNLI	LILCKKSVN	WVIKSFVKG	SLKIIAPNSI	
301	GFGKESERSM	TMTKSIRDDI	PSTQGNLVKW	ALDNGYSPIT	SYTMAPVANR	FHLRLENNAE	
361	EMGDEEVHTI	PPELRILLDP	GALPALQNPP	IRGEGQNGG	LPFFFPDISR	RVWNEEGEDG	
421	LPRPKDPVIP	SIQLFPGLRE	PEEVQGSVDI	ALSVKCDNEK	MIVAVEKDSF	QASGYSGMDV	
481	TLLDPTCKAK	MNGTHFVLES	PLNGCGTRPR	WSALDGVVY	NSIVIQVPAL	GDSSGWPDPY	
541	EDLESGDNGF	PGDMDEGDAS	LFTRPEIVVF	NCSLQQVRNP	SSFQEQPHGN	ITFNMELYNT	
601	DLFLVPSQGV	FVSPENGHVV	VEVSVTKAEQ	ELGFAIQTCF	ISPYSNPDRM	SHYTIIEINIC	
661	PKDESVKFYS	PKRVHFPPIQ	ADMDKKRFSF	VFKPVFNTSL	LFLQCELTLC	TKMEKHPQKL	
721	PKCVFPDEAC	TSLDASIIWA	MMQNKKTFTK	PLAVIHHEAE	SKEKGPSMKE	PNPISPP	(SEQ ID NO:152)

FIG. 25M

Homo sapiens TGF-β receptor type 3 isoform B precursor, (BETA Glycan) NCBI Ref. Seq. NP_001182612.1

1	MTSHYVIAIF	ALMSSCLATA	GPEPGALCEL	SPVSASHPVQ	ALMESFTVLS	GCASRGTTG
61	PQEVHVLNLR	TAGQPGQLQ	REVTLHLNPI	SSVHIHHSV	VFLNPSHPL	VWHLKTERLA
121	TGVSRLFLVS	EGSVVQFSSA	NFSLTAETEE	RNFPHGNEHL	LNWARKEYGA	VTSFTELKIA
181	RNIYIKVGED	QVFPPKCNIG	KNFLSLNYLA	EYLQPKAAEG	CVMSSQPQNE	EVHIIELITP
241	NSNPYSAFQV	DITIDIRPSQ	EDLEVVKNLI	LILCKKSVN	WVIKSFVKG	SLKIIAPNSI
301	GFGKESERSM	TMTKSIRDDI	PSTQGNLVKW	ALDNGYSPIT	SYTMAPVANR	FHLRLENNEE
361	MGDEEVHTIP	PELRILLDPG	ALPALQNPPI	RGEGQNGGL	PFFPDISRR	VWNEEGEDGL
421	PRPKDPVIPS	IQLFPGLREP	EEVQGSVDIA	LSVKCDNEKM	IVAVEKDSFQ	ASGYSGMDVT
481	LLDPTCKAKM	NGTHFVLESP	LNGCGTRPRW	SALDGVVYIN	SIVIQVPALG	DSSGWPDGYE
541	DLESGDNGFP	GMDDEGDASL	FTRPEIVVFN	CSLQQVRNPS	SFQEOPHGNI	TFNMELYNTD
601	LFLVPSQGVF	SVPENGHVYV	EVSVTKAEQE	LGFAIQTCFI	SPYSNPD RMS	HYTIIENICP
661	KDESVKFYSP	KRVHFPQPQA	DMDKKRFSFV	FKPVFNTSLL	FLQCELTLCI	KMEKHPQKLP
721	KCVPPDEACT	SLDASIIWAM	MQNKKTFTKP	LAVIHHEAES	KEKGPSMKEP	NPISPPIFHG
781	LDTLTVMGIA	FAAFVIGALL	TGALWYIYSH	TGETAGRQQV	PTSPPASENS	SAAHSIGSTQ
841	STPCSSSSTA	(SEQ ID NO:153)				
1..18	Signal peptide					
27..786	Extracellular domain (ectodomain)					
566..723	Zona pellucida-like domain					
736..750	Interaction with TGF-beta ligand					
787..808	site_type="transmembrane region"					

FIG. 25N

Homo sapiens TGF-β receptor type 3 isoform B ectodomain

61 PQEVHVLNLR TAGQPGQLQ REVTLHLNPI LCEL SPVSASHPVQ ALMESFTVLS GCASRGTTGL
121 TGVSRFLVLS EGSVVQFSSA NFSLTAETEE RNFPHGNEHL VFLNLSPHPL VVHLKTERLA
181 RNIYIKVGED QVFPKCNIG KNFLSLNYLA EYLQPKAAEG CVMSSQPQNE EVHIIELITP
241 NSNPYSAFQV DITIDIRPSQ EDLEVVKNLI LILCKKSVN WVIKSFQVKG SLKIIAPNSI
301 GFGESESRM TMTKSIRDDI PSTQGNLVKW ALDNGYSPIT SYTMAPVANR FHLRLENNEE
361 MGDEEVHTIP PELRILLDPG ALPALQNPP I RGEGQNGGL PFFPDISRR VMNEEGEDGL
421 PRPKDPVIPS IQLFPGLREP EEVQGSVDIA LSVKCDNEKM IVAVEKDSFQ ASGYSGMDVT
481 LLDPTCKAKM NGTHFVLESP LNGCGTRPRW SALDGVVYVN SIVIQVPALG DSSGWPDGYE
541 DLESGDNGFP GDMDEGDASL FTRPEIVVFN CSLQQVRNPS SFQEQPHGNI TFNMELYNTD
601 LFLVPSQGVF SVPENGHVYV EVSVTKAEQE LGFAIQICFI SPYSNPD RMS HYTIIENICP
661 KDESVKFYSP KRVHFPIPQA DMDKKRFSFV FKPVFNTSLL FLQCELTLC T KMEKHPQKLP
721 KCVPPDEACT SLDASIIWAM MQNKKTF TKP LAVIHHEAES KEKGPSMKEP NPISPPIFHG
781 LDTLTVM (SEQ ID NO:154)

FIG. 26A

4415

SLQPLALEGSLQSRGGGGGSGGGGSGGGGSGDTRCRFLEQVKHECHFFNGTERVRFLDRYFYH
QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
YPEVTVYPAKTQPLQHHNLLVCSVNGFYPPASIEVRWFRNGQEEKTG VVSTGLIONGDWTFOTLV
MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGGSGGGGSGGGGSG
GGGSIKEEHVIIQAEFYLNPDQSGEFMFDFDGD EIFHVDMAKKETVWRLEEFGRFASF EAQ GAL
ANIAVDKANLEIMTKRSNYTCITNPPEVTVL TNSPVELREPNVLCFIDKFTPPVVNVTWLRNGK
PVT TGVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGG
SAAAGGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
LPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGALDTNYCFRN
LEENCCVRPLYIDFRQDLGWKWWHEPKGYANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASA
SPSCVPQDLEPLTILYYVGRTPKVEQLSNMVKCKCS (SEQ ID NO:155)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)5 (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162) – bold

DRB1*0401 (P5C) -- underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain A (S354C; T366W) – italicized

TGF-beta-3 (C77S) – bold and italicized

FIG. 26B

4417

SLQPLALEGSLQSRGGGGSGGGSGGGSGDTRCRFLEQVKHECHFFNGTERVRFLDRYFYH
QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
YPEVTVYPAKTQPLQHHNLLVCSVNGFYPPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFQTLV
MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGSGGGSGGGSGG
GGGSIKEEHVIIQAEFYLNPDQSGEFMFDFDGDGEIFHVDMAKKETVWRLEEFGRFASF EAQ GAL
ANIAVDKANLEIMTKRSNYTCITNPPEVTVLTNSPVELREPNVLCFIDKFTPPVVNVTLWRNGK
PVTTGVS ETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGG
SAAAGGDKTHTCPPCPAPEAAGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVC
TLPPSREEMTKNQVSLTSCAVKGFPYSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRW
QQGNVFSCSVMHEALHNHYTQKSLSLSPGGGGSGGGSGGGSGGGSGQLCKFC D VRFSTCDNQKSC
MSNCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGET
FFMCSCSSAECNDNIIFSEEYNTSNPDGGGGSGGGSGGGSGGGSGGGGSAPTSSSTKKTQLQLEAL
LLDLQMILNGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDL
ISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT (SEQ ID NO:156)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)5 (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162) – bold

DRB1*0401 (P5C) -- underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain B (Y349C, T366S, L368A, Y407V) – italicized

TBR11 (delta 25; D118A) – bold and italicized

IL-2 (H16A; F42A) – italicized and underlined

FIG. 27A

4418

NFIRMVISNPAATGGGGSGGGGSGGGGSGDTRCRFLEQVKHECHFFNGTERVRFLDRYFYHQE
 EYVRFSDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYP
 EVTVYPAKTQPLQHHNLLVCSVNGFYFPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFTQTLVM
 LETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGGSGGGGSGGGGSGGGG
 GSIKEEHVIIQAEFYLNPDQSGEFMFDFDGDIEFHVDMAKKETVWRLEEFGRFASFEAQGALANI
 AVDKANLEIMTKRSNYTCITNVPPEVTVLTNSPVELREPNVLICFIDKFPPVVNVTLWRNGKPV
 TGVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGGSA
 AGGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
 HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP
 CREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQG
 NVFSCSVSMHEALHNHYTQKSLSLSPGGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGG
 ENCCVRPLYIDFRQDLGWKWWHEPKGYANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASASP
 SCVPQDLEPLTILYYVGRTPKVEQLSNMVVKCKCS (SEQ ID NO:157)

GAD – NFIRMVISNPAAT (SEQ ID NO:163)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)5 (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162) – bold

DRB1*0401 (P5C) -- underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain A (S354C; T366W) – italicized

TGF-beta-3 (C77S) – bold and italicized

FIG. 27B

4420

NFIRMVISNPAAT**GGGGSGGGSGGGSG**GDTRCRFLEQVKHECHFFNGTERVRFLDRYFYHQE
EYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYP
EVTVYPAKTQPLQHHNLLVCSVNGFYPPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFTQTLVM
LETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKM**GGGGSGGGSGGGSGGGSGGGSGGG**
GSIKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFEAQGALANI
AVDKANLEIMTKRSNYTCITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTWLRNGKPVT
TGVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPET**GG****SAA**
AGGDKTHTC**PPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV**
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLP
SREEMTKNQVSLTSCAVKG**FYP****SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGN**
VFSCSV**MHEALHNHYTQKSLSLSP****GGGGSGGGSGGGSGGGSGQLCKFCDVRFSTCDNQKSCMSNCS**
ITSICEKPQ**EV****CVAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCS**
CSSAECNDNIIFSE**EYNTSNPD****GGGGSGGGSGGGSGGGSGGGSGAPTSSSTKKTQLQLEALLDL**
QMILNGINNYKNPKLTRMLTAKFYMPKKATEL**KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDL**
ISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT (SEQ ID NO:158)

GAD – NFIRMVISNPAAT (SEQ ID NO:163)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)5 (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 (P5C) – underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain B (Y349C, T366S, L368A, Y407V) – italicized

TBR11 (delta 25; D118A) – bold and italicized

IL-2 (H16A; F42A) – italicized and underlined

FIG. 28

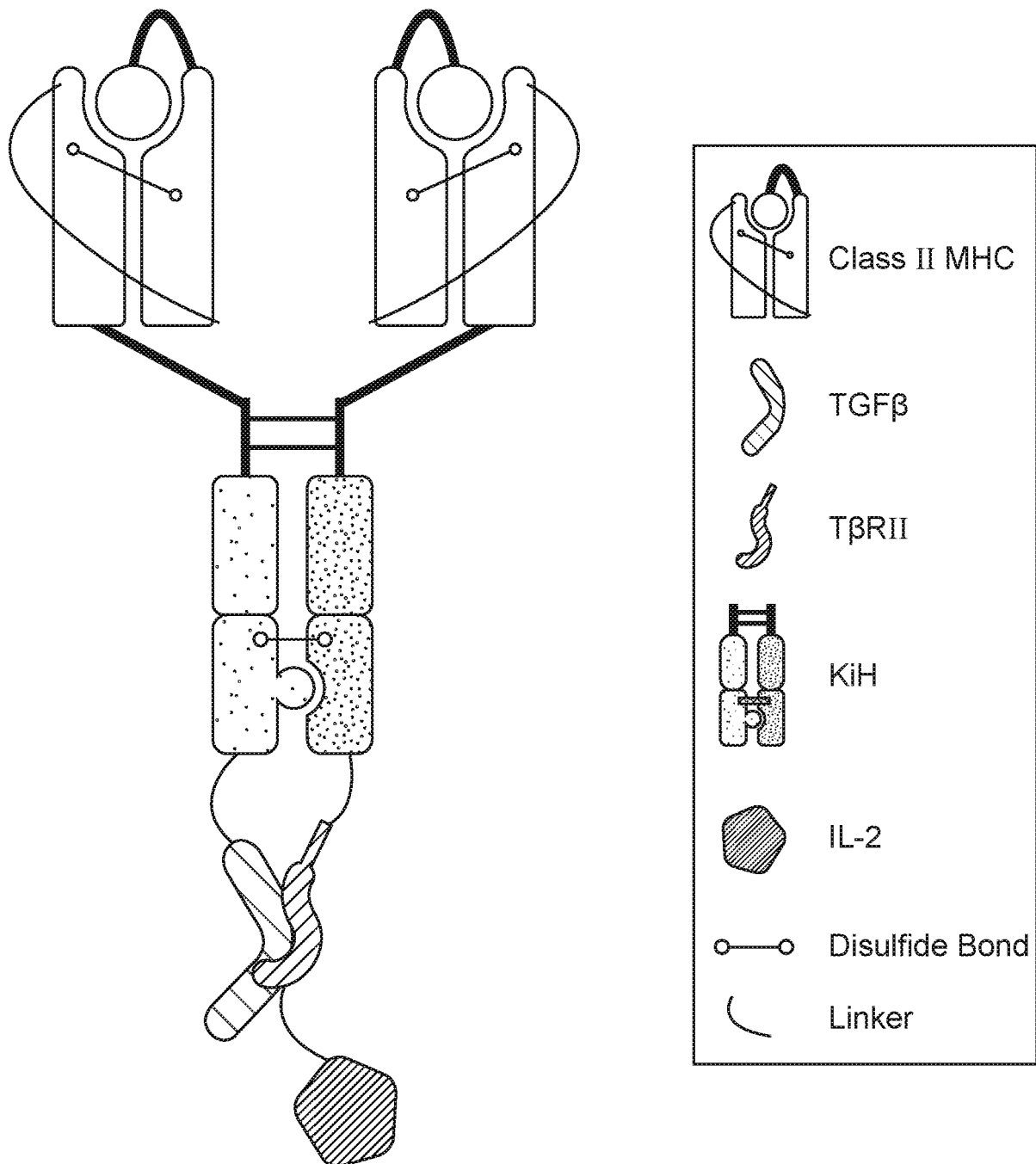


FIG. 29A

4415

SLQPLALEGSLQSRGGGGGSGGGGSGGGGSGDTRCRFLEQVKHECHFFNGTERVRFLDRYFYH
QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
YPEVTVYPAKTQPLQHHNLLVCSVNGFYPPASIEVRWFRNGQEEKTG VVSTGLIONGDWTFOTLV
MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGGSGGGGSGGGGSG
GGGSIKEEHVIIQAEFYLNPDQSGEFMFDFDGD EIFHVDMAKKETVWRLEEFGRFASF EAQ GAL
ANIAVDKANLEIMTKRSNYTCITNVPPEVTVL TNSPVELREPNVLCFIDKFTPPVVNVTWLRNGK
PVT TGVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGG
SAAAGGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDG
VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSG
LEENCCVRPLYIDFRQDLGWKWWHEPKGYIANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASA
SPSCVPQDLEPLTILYYVGRTPKVEQLSNMVKSKCS (SEQ ID NO:155)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)5 (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162) – bold

DRB1*0401 (P5C) -- underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain A (S354C; T366W) – italicized

TGF-beta-3 (C77S) – bold and italicized

FIG. 29B

4416

SLQPLALEGSLQSRGGGGGGSGGGGGSGGGSGDTRCRFLEQVKHECHFFNGTERVRFLDRYFYH
 QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
 YPEVTVYPAKTQPLQHNNLLVCSVNGFYFASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFTLV
 MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGGGSGGGGGSGGGGGSG
 GGGSIKEEHVIIQAEFYLNPDQSGEFMFEDFDGDEIFHVDMAKKETVWRLEEFGRFASF EAQ GAL
 ANIAVDKANLEIMTKRSNYTCITNVPPEVTVLTNSPVELREPNVLCIFIDKF TPPVVNVTWLRNGK
 PVT TGVS ETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGG
 SAAAGGDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
 VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVC
 TLPPSREEMTKNQVSLTSCAVKGFFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRW
 QQGNV FSCSV MHEALHNHYTQKSLSLSPGGGGGGSGGGGGSGGGGGSQLCKFCDVRFSTCDNQKSC
 MSNCSITSICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILED AASPKCIMKEKKKPGET
 FFMCS CSSAECNDNIIFSEEYNTSNPD (SEQ ID NO:164)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)5 (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 (P5C) -- underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain B (Y349C, T366S, L368A, Y407V) – italicized

TBR II (delta 25; D118A) – bold and italicized

FIG. 30A

4418

NFIRMVISNPAAT**GGGGSGGGSGGGSG**GDTRCRFLEQVKHECHFFNGTERVRFLDRYFYHQE
EYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTCRHNYGVGESFTVQRRVYP
EVTVYPAKTQPLQHHNLLVCSVNGFYPPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFTQTLVM
LETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKM**GGGGSGGGSGGGSGGGSGGGSGGG**
GSIKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFEAQGALANI
AVDKANLEIMTKRSNYTCITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTWLRNGKPVT
TGVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPET**GG****SAA**
AGGDKTHTC**PPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV**
HNAKTKPREEQ**YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP**
CREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYK**TPPVLDSDGSFFLYSKLTVDKSRWQQG**
NVFSCSV**MHEALHNHYTQKSLSLSP****GGGGSGGGSGGGSGGGSGGGSGGGSGGGSGGG****SALDTNYCFRNLE**
ENCCVRPLYIDFRQDLGWKWWHEPKGYANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASASP
SCVPQDLEPLTILYYVGRTPKVEQLSNMVVK**SCKCS** (SEQ ID NO:157)

GAD – NFIRMVISNPAAT (SEQ ID NO:163)

linkers – (GGGGSG)³ (SEQ ID NO:160), (GGGGSG)⁵ (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162) – bold

DRB1*0401 (P5C) -- underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain A (S354C; T366W) – italicized

TGF-beta-3 (C77S) – bold and italicized

FIG. 30B

4419

NFIRMVISNPAAT**GGGGSGGGSGGGSG**GDTRCRFLEQVKHECHFFNGTERVRFLDRYFYHQE
EYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRVYP
EVTVYPAKTQPLQHHNLLVCSVNGFYPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFQTLVM
LETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKM**GGGGSGGGSGGGSGGGSGGGSGGG**
GSIKEEHVIIQAEFYLNPDQSGEFMFDFDGDEIFHVDMAKKETVWRLEEFGRFASFEAOGALANI
AVDKANLEIMTKRSNYTCITNPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTWLRNGKPVT
TGVSETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPET**GG****SAA**
AGGDK**TH****TCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV**
HNA**TKPREEQYN****STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLPP**
SREEMTKNQVSL**SCAVKG****FYP****SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGN**
VFSCSV**MHEALHNHYTQKSLSLSP****GGGGSGGGSGGGSGGGSGQLCKFCDVRFSTCDNQKSCMSNCS**
ITSICEK**PQ****EV****CVAVWRKNDENIT****LET****VCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCS**
CSSAECNDNIIFSE**EYNTS****NPD** (SEQ ID NO:165)

GAD – NFIRMVISNPAAT (SEQ ID NO:163)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)5 (SEQ ID NO:161), and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 (P5C) – underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain B (Y349C, T366S, L368A, Y407V) – italicized

TBR11 (delta 25; D118A) – bold and italicized

FIG. 31A

3858

SLQPLALEGSLQSRG**GGGGSGGGSGGGSGD**TRPRFLEQVKHECHFFNGTERVRFLDRYFYH
 QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
 YPEVTVYPAKTQPLQHNNLLVCSVNGFYPPASIEVRWFRNGQEEKTGVVSTGLIONGDWTFOTLV
 MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKM**GGGGSGGGSGGGSGGGSGGGSGIK**
 EEHVIIQAEFYLNPDQSGEFMFDFDGDIEFHVDMAKKETVWRLEEFGRFASFEAQGALANIAVD
 KANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTLRNGKPVTTG
 SETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPET**GGSAAG**
GDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
 AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV
 FSCSVMHEALHNHYTQKSLSLSPG**GGGGSGGGSGGGSGGGSGGGSGGGSGGGSGALDTNYCFRNLEEN**
CCVRPLYIDFRQDLGWKQVHEPKGYYANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASASPSCV
PQDLEPLTILYYVGRTPKVEQLSNMVVKSCCKS (SEQ ID NO:166)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGGS)3 (SEQ ID NO:160), (GGGGS)4 (SEQ ID NO:171), (GGGGS)5 (SEQ ID NO:161),
 and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 – underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain A (T366W) – italicized

TGF-beta-3 (C77S) – bold and italicized

FIG. 31B

3859

SLQPLALEGSLQSRGGGGSGGGSGGGSGDTRPRFLEQVKHECHFFNGTERVRFLDRYFYH
 QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
 YPEVTVYPAKTQPLQHNNLLVCSVNGFYFASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFQTLV
 MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGSGGGSGGGSGIK
 EEHVIIQAEFYLNPDQSGEFMFEDFDGDEIFHVDMAKKETVWRLEEFGRFASFEAQGALANIAVD
 KANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTLWRNGKPVTTGV
 SETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGGSAAG
 GDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
 AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLVSKLTVDKSRWQQGNVF
 SCSVMHEALHNHYTQKSLSLSPGGGGSGGGSGGGSGGGSGQLCKFCDFRSTCDNQKSCMSNCSIT
 SICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILEDAAAPKCIMKEKKKPGETFFMCSCS
 SAECNDNIIFSEEYNTSNPD (SEQ ID NO:167)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)4 (SEQ ID NO:171), and GGSAAAGG (SEQ ID NO:162) – bold

DRB1*0401 – underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain B (T366S, L368A, Y407V) – italicized

TBR11 (delta 25; D118A) – bold and italicized

FIG. 32A

3858

SLQPLALEGSLQSRGGGGGSGGGSGGGSGDTRPRFLEQVKHECHFFNGTERVRFLDRYFYH
 QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
 YPEVTVYPAKTQPLQHNNLLVCSVNGFYPPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFQTLV
 MLETVPRSGEVYTCQVEHPSLTSP~~LT~~VEWRARSESAQSKMGGGGSGGGSGGGSGGGSGIK
 EEHVIIQAEFYLNPDQSGEFMFEDFDGDEIFHVDMAKKETVWRLEEFGRFASFEAQGALANIAVD
 KANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTVLNRNGKPVTTGV
 SETVFLPREDHLERKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGGSAAG
 GDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
 AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSLKTVLTKSRWQQGNV
 FSCSVMH~~EA~~LHNHYTQKSLSLSPGGGGSGGGSGGGSGGGSGGGSGGGSGGGSGALDTNYCFRNLEEN
 CCVRPLYIDFRQDLGWKQVHEPKGYANFCSGPCPYLRSA~~DT~~THSTVLGLYNTLNPEASASPSCV
 PQDLEPLTILYYVGRTPKVEQLSNMVVKCKCS (SEQ ID NO:166)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)4 (SEQ ID NO:171), (GGGS)5 (SEQ ID NO:161),
 and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 – underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain A (T366W) – italicized

TGF-beta-3 (C77S) – bold and italicized

FIG. 32B

3869

SLQPLALEGSLQSRGGGGSGGGSGGGSGDTRPRFLEQVKHECHFFNGTERVRFLDRYFYH
 QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
 YPEVTVYPAKTQPLQHNNLLVCSVNGFYFASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFTQTLV
 MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGSGGGSGGGSGGGSGIK
 EEHVIIQAEFYLNPDQSGEFMFEDFDGDEIFHVDMAKKETVWRLEEFGRFASFEAQGALANIAVD
 KANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTLWRNGKPVTGTV
 SETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGGSAAG
 GDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
 AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLVSKLTVDKSRWQQGNVF
 SCSVMHEALHNHYTQKSLSLSPGGGGSGGGSGGGSGGGSGQLCKFCDVRFSTCDNQKSCMSNCST
 SICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCS
 SAECNDNIIFSEEYNTSNPDGGGGSGGGSGGGSGGGSGGGSGAPTSSSTKKTQLQLEALLDLQML
 NGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVL
 ELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT (SEQ ID NO:168)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)4 (SEQ ID NO:171), and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 – underlined

DRA1 – double underlined

IgG Fc (LALA) KiH Chain B (T366S, L368A, Y407V) – italicized

TBR11 (delta 25; D118A) – bold and italicized

IL-2 (H16A; F42A) – italicized and underlined

FIG. 33A

3870

SLQPLALEGSLQSRG**GGGGSGGGSGGGSGDTRPRFLEQVKHECHFFNGTERVRFLDRYFYH**
QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
YPEVTVYPAKTOPLQHHNLLVCSVNGFYPPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFQTFV
MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGSGGGSGGGSGGGGSIK
EEHVIIQAEFYLNPDQSGEFMFDFDGDDEIFHVDMAKKETVWRLEEFGRFASFEAQGALANIAVD
KANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTLWRNGKPVTGTV
SETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGGSAAG
GDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
EEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNV
FSCSVMHEALHNHYTQKSLSLSPGGGGSGGGSGGGSGGGSGGGSGGGSGGGGSALDTNYCFRNLEEN
CCVRPLYIDFRQDLGWKWWHEPKGYANFCSGPCPYLRSDTTHSTVLGLYNTLNPEASASPSCV
PQDLEPLTILYVGRTPKVEQLSNMVVKSCCKCS (SEQ ID NO:169)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGGS)3 (SEQ ID NO:160), (GGGGS)4 (SEQ ID NO:171), (GGGGS)5 (SEQ ID NO:161),
and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 (L158F) – underlined (L158F substitution in bold)

DRA1 – double underlined

IgG Fc (LALA) KiH Chain A (T366W) – italicized

TGF-beta-3 (C77S) – bold and italicized

FIG. 33B

3871

SLQPLALEGSLQSRGGGGSGGGSGGGSGDTRPRFLEQVKHECHFFNGTERVRFLDRYFYH
 QEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRAAVDTYCRHNYGVGESFTVQRRV
 YPEVTVYPAKTQPLQHHNLLVCSVNGFYYPASIEVRWFRNGQEEKTGVVSTGLIQNGDWTFQTFV
 MLETVPRSGEVYTCQVEHPSLTSPLTVEWRARSESAQSKMGGGGSGGGSGGGSGGGSGIK
 EEHVIIQAEFYLNPDQSGEFMFEDFDGDEIFHVDMAKKETVWRLEEFGRFASF EAQ GALANIAVD
 KANLEIMTKRSNYTPITNVPPEVTVLTNSPVELREPNVLICFIDKFTPPVVNVTLWRNGKPVTGTV
 SETVFLPREDHLFRKFHYLPFLPSTEDVYDCRVEHWGLDEPLLKHWEFDAPSPLPETGGSAAG
 GDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN
 AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLVSKLTVDKSRWQQGNVF
 SCSVMHEALHNHYTQKSLSLSPGGGGSGGGSGGGSGGGSGQLCKFCDVRFSTCDNQKSCMSNCST
 SICEKPQEVCAVWRKNDENITLETVCHDPKLPYHDFILED AASP KCIMKEKKKPGETFFMCSCS
 SAECNDNIIFSEEYNTSNPDGGGGSGGGSGGGSGGGSGGGSGAPTSSSTKKTQLQLEALLDLQ MIL
 NGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVL
 ELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT (SEQ ID NO:170)

proIns – SLQPLALEGSLQSRG (SEQ ID NO:159)

linkers – (GGGS)3 (SEQ ID NO:160), (GGGS)4 (SEQ ID NO:171), and GGSAAAGG (SEQ ID NO:162)– bold

DRB1*0401 (L158F) – underlined (L158F substitution in bold)

DRA1 – double underlined

IgG Fc (LALA) KiH Chain B (T366S, L368A, Y407V) – italicized

TBR II (delta 25; D118A) – bold and italicized

IL-2 (H16A; F42A) – italicized and underlined

FIG. 34A

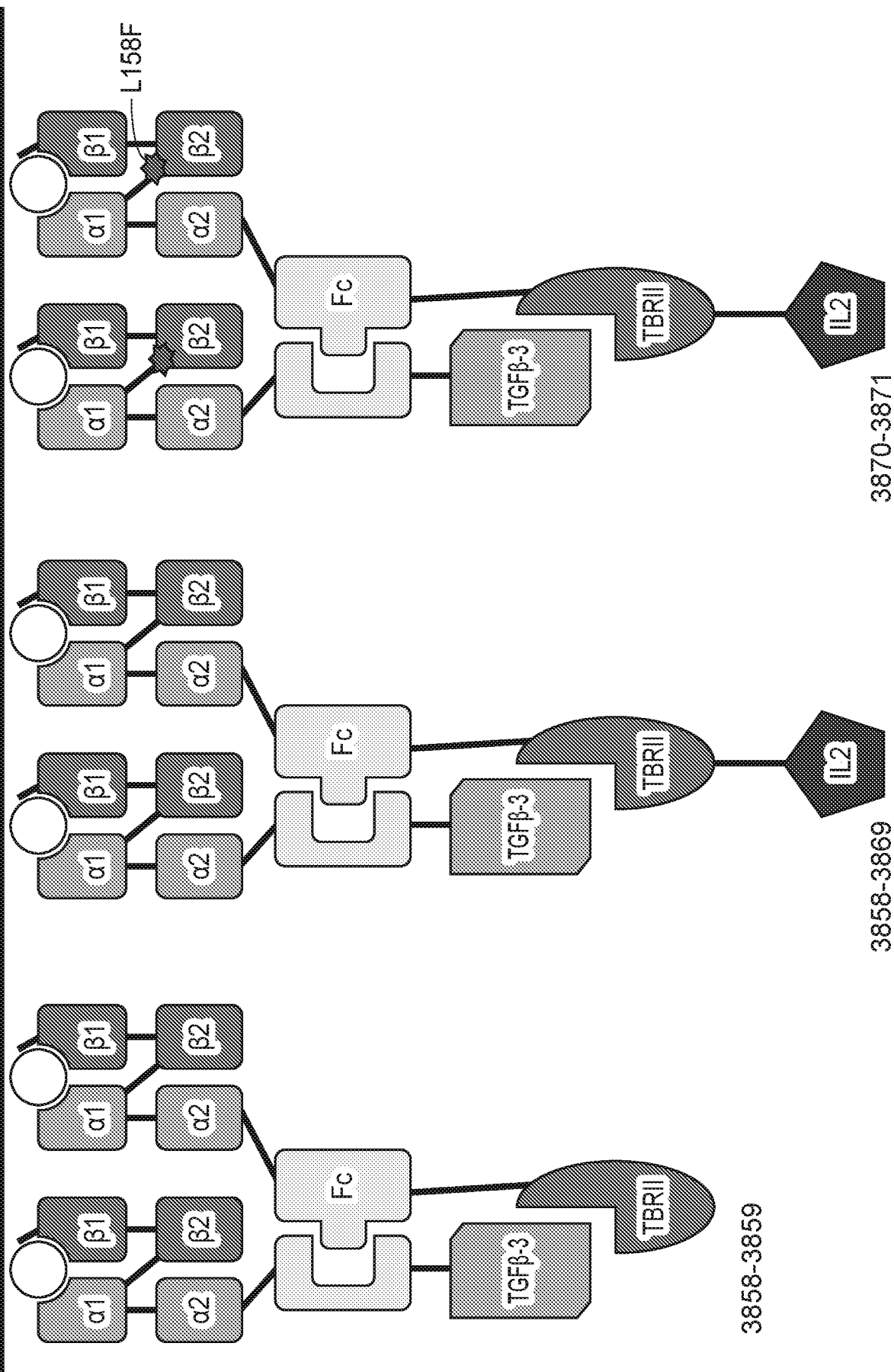


FIG. 34B

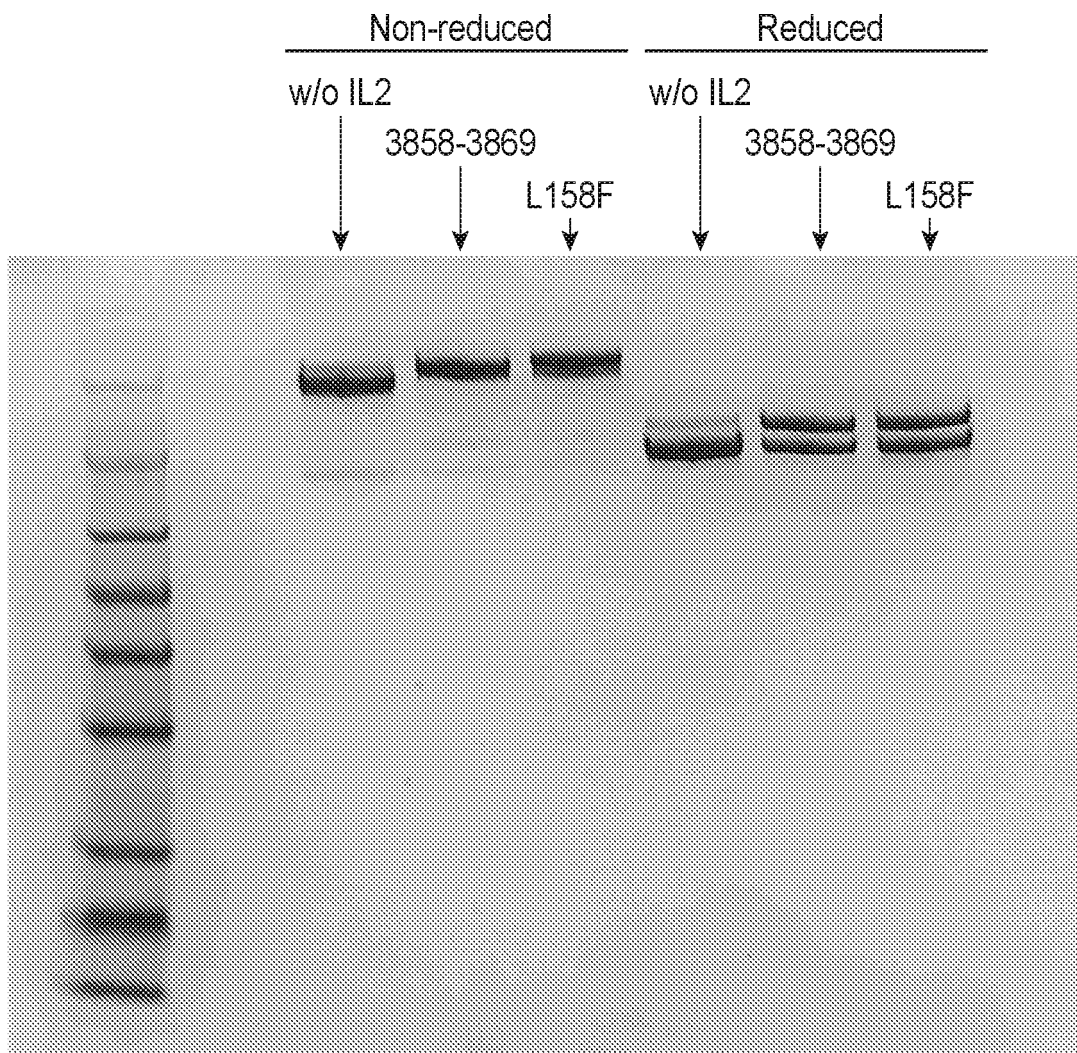


FIG. 35

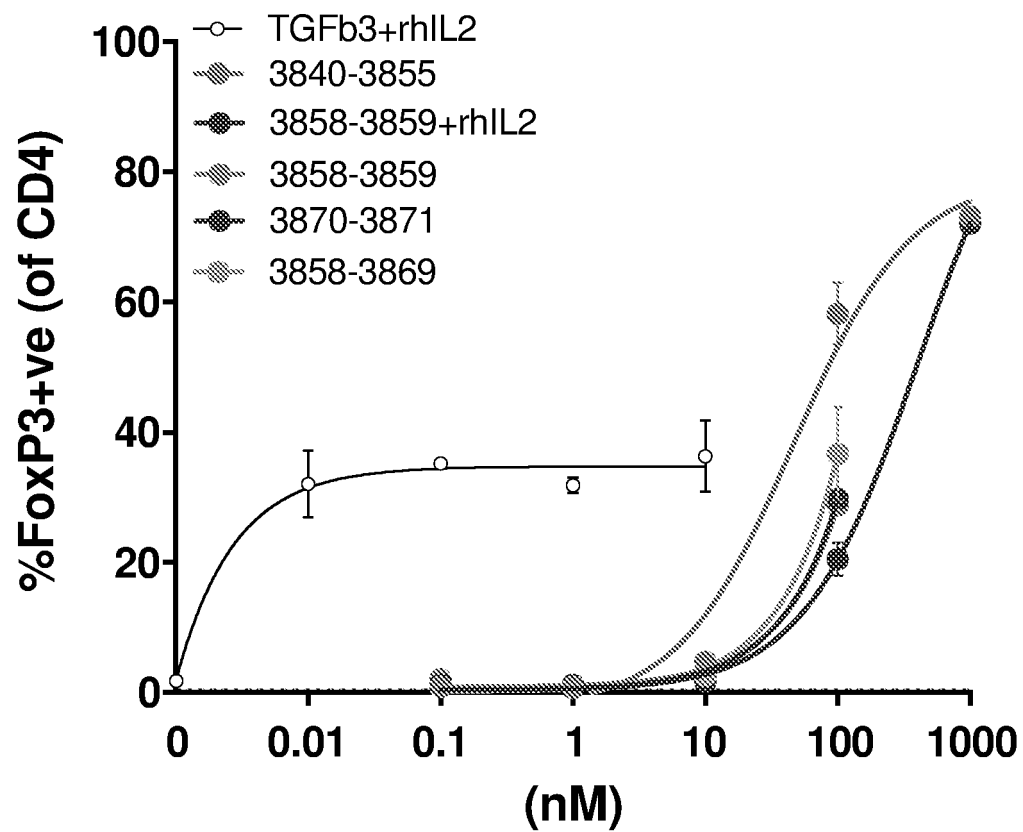
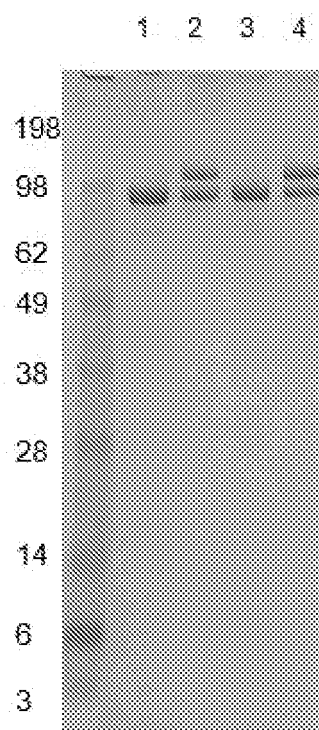


FIG. 36

*Reduced SDS-PAGE*

SEQUENCE LISTING

<110> Cue Biopharma, Inc.
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 Low, Chee Meng

<120> MHC CLASS II T-CELL MODULATORY POLYPEPTIDES FOR TREATING TYPE 1
 DIABETES MELLITUS (T1D) AND METHODS OF USE THEREOF

<130> CUEB-142W0

<150> US 63/177,641
 <151> 2021-04-21

<160> 259

<170> PatentIn version 3.5

<210> 1
 <211> 254
 <212> PRT
 <213> Homo sapiens

<400> 1

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

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> 2
<211> 266
<212> PRT
<213> Homo sapiens

<400> 2

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

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> 3

<211> 266

<212> PRT

<213> Homo sapiens

<400> 3

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 Ala Val 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

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> 4
<211> 266
<212> PRT
<213> Homo sapiens

<400> 4

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 Ile
85 90 95

Leu Glu Asp Glu 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

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> 5

<211> 266

<212> PRT

<213> Homo sapiens

<400> 5

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
 50 55 60

Glu Asn Val Arg Phe Asp Ser Asp Val Gly Glu Phe 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 Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 6
<211> 266
<212> PRT
<213> Homo sapiens

<400> 6

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Glu Arg Tyr Phe His Asn Gln Glu
50 55 60

Glu Asn 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 Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 7

<211> 266

<212> PRT

<213> Homo sapiens

<400> 7

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
 50 55 60

Glu Ser Val Arg Phe Asp Ser Asp Val Gly Glu Phe 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 Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 8
<211> 266
<212> PRT
<213> Homo sapiens

<400> 8

Met Val Cys Leu Lys Phe Pro Gly Gly Ser Cys Met Ala 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 Glu Gln Val Lys His Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu
50 55 60

Glu Tyr 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 Lys 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 Tyr Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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

Leu 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

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> 9

<211> 266

<212> PRT

<213> Homo sapiens

<400> 9

Met Val Cys Leu Lys Phe Pro Gly Gly Ser Cys Met Ala 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 Glu Gln Val Lys His Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu
 50 55 60

Glu Tyr 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 Ile
 85 90 95

Leu Glu Asp Glu Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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

Leu 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

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> 10
<211> 266
<212> PRT
<213> Homo sapiens

<400> 10

Met Val Cys Leu Lys Phe Pro Gly Gly Ser Cys Met Ala 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 Glu Gln Val Lys His Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu
50 55 60

Glu Tyr 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 Glu Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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

Leu 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

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> 11

<211> 266

<212> PRT

<213> Homo sapiens

<400> 11

Met Val Cys Leu Lys Phe Pro Gly Gly Ser Cys Met Ala 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 Glu Gln Val Lys His Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu
 50 55 60

Glu Tyr 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 Val Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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

Leu 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

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> 12
<211> 266
<212> PRT
<213> Homo sapiens

<400> 12

Met Val Cys Leu Lys Phe Pro Gly Gly Ser Cys Met Ala 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 Glu Gln Val Lys His Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu
50 55 60

Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65 70 75 80

Glu Leu Gly Arg Pro Ser 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 Tyr Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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

Leu 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

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> 13

<211> 266

<212> PRT

<213> Homo sapiens

<400> 13

Met Val Cys Leu Lys Phe Pro Gly Gly Ser Cys Met Ala 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 Glu Gln Val Lys His Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His 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 Glu Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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

Leu 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

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> 14
<211> 266
<212> PRT
<213> Homo sapiens

<400> 14

Met Val Cys Leu Lys Phe Pro Gly Gly Ser Cys Met Ala 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 Glu Gln Val Lys His Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu
50 55 60

Glu Tyr 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 Tyr Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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

Leu 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

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> 15

<211> 266

<212> PRT

<213> Homo sapiens

<400> 15

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Ala 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

Gln Pro Arg Phe Leu Trp Gln Gly Lys Tyr Lys Cys His Phe Phe Asn
 35 40 45

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

Glu Phe Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
 65 70 75 80

Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys Asp Ile
 85 90 95

Leu Glu Asp Arg Arg Gly Gln Val Asp Thr Val Cys Arg His Asn Tyr
 100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala 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 Met 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

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> 16
<211> 266
<212> PRT
<213> Homo sapiens

<400> 16

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Gly Glu Cys Tyr Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
50 55 60

Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65 70 75 80

Glu Leu Gly Arg Pro Ser Ala Glu Tyr Trp Asn Ser Gln Lys Asp Phe
85 90 95

Leu Glu Asp Arg Arg Ala Leu Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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 Ser 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

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> 17

<211> 266

<212> PRT

<213> Homo sapiens

<400> 17

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Gly Glu Cys Tyr Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
 50 55 60

Glu Tyr 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 Phe
 85 90 95

Leu Glu Asp Arg Arg Ala Leu Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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 Ser 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

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> 18
<211> 266
<212> PRT
<213> Homo sapiens

<400> 18

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Gly Glu Cys Tyr Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
50 55 60

Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65 70 75 80

Glu Leu Gly Arg Pro Ser Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile
85 90 95

Leu Glu Asp Arg Arg Ala Leu Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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 Ser 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

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> 19

<211> 266

<212> PRT

<213> Homo sapiens

<400> 19

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Ala 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

Gln Pro Arg Phe Leu Lys Gln Asp Lys Phe Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Tyr Leu His Arg Gly Ile Tyr Asn Gln Glu
 50 55 60

Glu Asn Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
 65 70 75 80

Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys Asp Phe
 85 90 95

Leu Glu Arg Arg Arg Ala Glu Val Asp Thr Val Cys Arg His Asn Tyr
 100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Glu Val
115 120 125

Thr Val Tyr Pro Ala 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 Met 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

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> 20
<211> 266
<212> PRT
<213> Homo sapiens

<400> 20

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Glu Val Lys Phe Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Leu Leu Glu Arg Arg Val His Asn Gln Glu
50 55 60

Glu Tyr Ala Arg Tyr 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 Arg 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 Gln 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 Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Gly Gln Glu Glu Lys Thr 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 Gln Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser
195 200 205

Val Met 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

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

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

<210> 21

<211> 266

<212> PRT

<213> Homo sapiens

<400> 21

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
 50 55 60

Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val Thr
 65 70 75 80

Glu Leu Gly Arg Pro Asp Glu Glu Tyr Trp Asn Ser Gln Lys Asp Phe
 85 90 95

Leu Glu Asp 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 His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 22
<211> 266
<212> PRT
<213> Homo sapiens

<400> 22

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
50 55 60

Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val Thr
65 70 75 80

Glu Leu Gly Arg Pro Asp Glu Glu Tyr Trp Asn Ser Gln Lys Asp Phe
85 90 95

Leu Glu Asp Glu Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 23

<211> 266

<212> PRT

<213> Homo sapiens

<400> 23

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
 50 55 60

Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val Thr
 65 70 75 80

Glu Leu Gly Arg Pro Asp Glu Glu Tyr Trp Asn Ser Gln Lys Asp Phe
 85 90 95

Leu Glu Asp Arg Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 24
<211> 266
<212> PRT
<213> Homo sapiens

<400> 24

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Gly Glu Cys Tyr Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Leu Leu Glu Arg His Phe His Asn Gln Glu
50 55 60

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

Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys Asp Ile
85 90 95

Leu Glu Asp Arg Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

Gly Ala Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 25

<211> 266

<212> PRT

<213> Homo sapiens

<400> 25

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe His Asn Gln Glu
 50 55 60

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

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile
 85 90 95

Leu Glu Asp Glu Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 26
<211> 266
<212> PRT
<213> Homo sapiens

<400> 26

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
50 55 60

Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65 70 75 80

Glu Leu Gly Arg Pro Ser Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile
85 90 95

Leu Glu Asp Lys 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 His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 27

<211> 266

<212> PRT

<213> Homo sapiens

<400> 27

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe His Asn Gln Glu
 50 55 60

Glu Phe Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
 65 70 75 80

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

Leu Glu Arg Arg Arg Ala Glu Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Lys Val
115 120 125

Thr Val Tyr Pro Ser Lys Thr Gln Pro Leu Gln His Tyr 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 28
<211> 266
<212> PRT
<213> Homo sapiens

<400> 28

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Glu Arg Tyr Phe His Asn Gln Glu
50 55 60

Glu Asn 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 His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 29

<211> 266

<212> PRT

<213> Homo sapiens

<400> 29

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys Gln Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe His Asn Gln Glu
 50 55 60

Glu Phe 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 Arg Arg Arg Ala Glu Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 30
<211> 266
<212> PRT
<213> Homo sapiens

<400> 30

Met Val Cys Leu Arg Leu Pro Gly Gly Ser Cys Met Ala Val 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 Glu Tyr Ser Thr Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Glu Arg Tyr Phe His Asn Gln Glu
50 55 60

Glu Asn 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 Val Glu Ser Phe Thr Val Gln Arg Arg Val His 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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

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

<210> 31
 <211> 266
 <212> PRT
 <213> Homo sapiens

<400> 31

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 Ser Gly Asp Thr
 20 25 30

Arg Pro Arg Phe Leu Trp Gln Pro Lys Arg Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
 50 55 60

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

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile
 85 90 95

Leu Glu Gln Ala Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Gln 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 Leu Asn Gly Gln Glu Glu Lys Ala Gly Met 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

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> 32
<211> 266
<212> PRT
<213> Homo sapiens

<400> 32

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 Ser Gly Asp Thr
20 25 30

Arg Pro Arg Phe Leu Trp Gln Pro Lys Arg Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
50 55 60

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

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile
85 90 95

Leu Glu Gln Ala 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 Gln 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 Leu Asn Gly Gln Glu Glu Lys Ala Gly Met 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

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> 33

<211> 266

<212> PRT

<213> Homo sapiens

<400> 33

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 Ser Gly Asp Thr
 20 25 30

Arg Pro Arg Phe Leu Trp Gln Pro Lys Arg Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg His Phe Tyr Asn Gln Glu
 50 55 60

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

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Ile
 85 90 95

Leu Glu Gln Ala Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Gln 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 Leu Asn Gly Gln Glu Glu Lys Ala Gly Met 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

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> 34
<211> 266
<212> PRT
<213> Homo sapiens

<400> 34

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 Ser Gly Asp Thr
20 25 30

Arg Pro Arg Phe Leu Trp Gln Pro Lys Arg Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr Asn Gln Glu
50 55 60

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

Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Phe
85 90 95

Leu Glu Gln Ala Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Gln 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 Leu Asn Gly Gln Glu Glu Lys Ala Gly Met 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

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> 35

<211> 266

<212> PRT

<213> Homo sapiens

<400> 35

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 Ser Gly Asp Thr
 20 25 30

Arg Pro Arg Phe Leu Trp Gln Pro Lys Arg Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe 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 Ile
 85 90 95

Leu Glu Gln Ala Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Gln 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 Leu Asn Gly Gln Glu Glu Lys Ala Gly Met 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

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> 36
<211> 266
<212> PRT
<213> Homo sapiens

<400> 36

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 Pro Lys Arg Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe 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 Phe
85 90 95

Leu Glu Asp 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 Gln 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 Leu Asn Gly Gln Glu Glu Lys Ala Gly Met 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

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> 37

<211> 266

<212> PRT

<213> Homo sapiens

<400> 37

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
 1 5 10 15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
 20 25 30

Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
 50 55 60

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

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

Leu Glu Gln Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
115 120 125

Thr Val Tyr Pro Ala 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 Ala 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

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> 38
<211> 266
<212> PRT
<213> Homo sapiens

<400> 38

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
1 5 10 15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
20 25 30

Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn Gln Glu
50 55 60

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

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

Leu Glu Gln Lys Arg Gly Gln Val Asp Asn Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
115 120 125

Thr Val Tyr Pro Ala 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 Ala 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

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> 39

<211> 266

<212> PRT

<213> Homo sapiens

<400> 39

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
 1 5 10 15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
 20 25 30

Arg Pro Arg Phe Leu Glu Leu Leu Lys Ser Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Glu Arg His Phe His Asn Gln Glu
 50 55 60

Glu Tyr Ala Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Arg
 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 Lys Arg Gly Gln Val Asp Asn Tyr Cys Arg His Asn Tyr
 100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
115 120 125

Thr Val Tyr Pro Ala 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

Phe 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 Ser 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

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> 40
<211> 266
<212> PRT
<213> Homo sapiens

<400> 40

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
1 5 10 15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala Gly Asp Thr
20 25 30

Arg Pro Arg Phe Leu Glu Leu Leu Lys Ser Glu Cys His Phe Phe Asn
35 40 45

Gly Thr Glu Arg Val Arg Phe Leu Glu Arg Tyr Phe His Asn Gln Glu
50 55 60

Glu Phe Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr
65 70 75 80

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

Leu Glu Gln Lys Arg Gly Gln Val Asp Asn Tyr Cys Arg His Asn Tyr
100 105 110

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val His Pro Gln Val
115 120 125

Thr Val Tyr Pro Ala 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 Thr Gly Val Val Ser Thr Gly Leu
165 170 175

Ile His 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

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> 41

<211> 266

<212> PRT

<213> Homo sapiens

<400> 41

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Ala Ala Leu Thr
 1 5 10 15

Val Thr Leu Thr Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr
 20 25 30

Gln Pro Arg Phe Leu Glu Gln Ala Lys Cys Glu Cys His Phe Leu Asn
 35 40 45

Gly Thr Glu Arg Val Trp Asn Leu Ile Arg Tyr Ile Tyr Asn Gln Glu
 50 55 60

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

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Gln 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 Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Ser 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

Met Met Ser Pro Leu Thr Val Gln Trp Ser 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

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

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

<210> 42
<211> 266
<212> PRT
<213> Homo sapiens

<400> 42

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Ala Ala Leu Thr
1 5 10 15

Val Thr Leu Thr Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr
20 25 30

Gln Pro Arg Phe Leu Glu Gln Ala Lys Cys Glu Cys His Phe Leu Asn
35 40 45

Gly Thr Glu Arg Val Trp Asn Leu Ile Arg Tyr Ile Tyr Asn Gln Glu
50 55 60

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

Gly Val Val Glu Ser Phe Thr Val Gln Arg Arg Val Gln 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 Asn 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

Met Met Ser Pro Leu Thr Val Gln Trp Ser 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

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

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

<210> 43

<211> 266

<212> PRT

<213> Homo sapiens

<400> 43

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Tyr Met Ala Lys 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 Gln Gln Asp Lys Tyr Glu Cys His Phe Phe Asn
 35 40 45

Gly Thr Glu Arg Val Arg Phe Leu His Arg Asp Ile Tyr Asn Gln Glu
 50 55 60

Glu Asp Leu 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 Phe
 85 90 95

Leu Glu Asp 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 Ala Arg Thr Gln Thr Leu Gln His His Asn Leu Leu
130 135 140

Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile Glu Val Arg Trp
145 150 155 160

Phe Arg Asn Ser 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 Gln 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

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

Ser Gly Leu His Pro Thr Gly Leu Val Ser
260 265

<210> 44
<211> 261
<212> PRT
<213> Homo sapiens

<400> 44

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

Pro Cys Ser Gly Asp
 260

<210> 45
 <211> 263
 <212> PRT
 <213> Homo sapiens

<400> 45

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

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> 46
<211> 250
<212> PRT
<213> Homo sapiens

<400> 46

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

Pro Ile Pro Pro Pro Asp Ala Met Glu Thr Leu Val Cys Ala Leu Gly

210

215

220

Leu Ala Ile Gly Leu Val Gly Phe Leu Val Gly Thr Val Leu Ile Ile
 225 230 235 240

Met Gly Thr Tyr Val Ser Ser Val Pro Arg
 245 250

<210> 47

<211> 273

<212> PRT

<213> Homo sapiens

<400> 47

Met Gly Ser Gly Trp Val Pro Trp Val Val Ala Leu Leu Val Asn Leu
 1 5 10 15

Thr Arg Leu Asp Ser Ser Met Thr Gln Gly Thr Asp Ser Pro Glu Asp
 20 25 30

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
 115 120 125

Pro Glu Arg Thr Pro Leu Leu His Gln His Asn Leu Leu His Cys Ser
130 135 140

Val Thr Gly Phe Tyr Pro Gly Asp Ile Lys Ile Lys Trp Phe Leu Asn
145 150 155 160

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
195 200 205

Pro Val Ser Val Glu Trp Arg Ala Gln Ser Glu Tyr Ser Trp Arg Lys
210 215 220

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
260 265 270

Cys

<210> 48
<211> 260
<212> PRT
<213> Homo sapiens

<400> 48

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

<210> 49
 <211> 260
 <212> PRT
 <213> Homo sapiens

<400> 49

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 Gln 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

Arg 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 Ala 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 Arg Phe Phe
130 135 140

Pro Pro Val Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Pro 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 Val 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 Pro Leu
260

<210> 50
<211> 258
<212> PRT
<213> Homo sapiens

<400> 50

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> 51
 <211> 258
 <212> PRT
 <213> Homo sapiens

<400> 51

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 Leu Phe 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 Phe
 50 55 60

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

Gly Arg Pro Asp Glu Glu Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu
 85 90 95

Glu Glu Arg Ala Val Pro Asp Arg Met Cys Arg His Asn Tyr Glu Leu
 100 105 110

Gly Gly Pro Met Thr Leu Gln Arg Arg Val Gln Pro Arg 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 Thr 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 Arg 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> 52
<211> 258
<212> PRT
<213> Homo sapiens

<400> 52

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 Leu 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 Phe
50 55 60

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

Gly Arg Pro Asp Glu Asp Tyr Trp Asn Ser Gln Lys Asp Leu 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 Arg 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> 53

<211> 258

<212> PRT

<213> Homo sapiens

<400> 53

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 Leu Phe 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 Phe
 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 Met Cys Arg His Asn Tyr Glu Leu
 100 105 110

Gly Gly Pro Met Thr Leu Gln Arg Arg Val Gln Pro Arg 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 Thr 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 Arg 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> 54
<211> 258
<212> PRT
<213> Homo sapiens

<400> 54

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 Leu 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 Phe
50 55 60

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

Gly Arg Pro Asp Glu Asp Tyr Trp Asn Ser Gln Lys Asp Leu Leu Glu
85 90 95

Glu Glu Arg Ala Val Pro Asp Arg Met 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 Arg 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> 55

<211> 258

<212> PRT

<213> Homo sapiens

<400> 55

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 His Gln Leu 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 Phe
 50 55 60

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

Gly Arg Pro Asp Glu Asp Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu
 85 90 95

Glu Glu 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 Arg 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> 56
<211> 258
<212> PRT
<213> Homo sapiens

<400> 56

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 Leu Arg Gln Glu Cys Tyr Ala Phe Asn
35 40 45

Gly Thr Gln Arg Phe Leu Glu Arg Tyr Ile Tyr Asn Arg Gln 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 Leu Leu Glu
85 90 95

Glu Arg Arg Ala Val Pro Asp Arg Met 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 Arg 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> 57
 <211> 258
 <212> PRT
 <213> Homo sapiens

<400> 57

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 Leu 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 Glu Arg Ala Val Pro Asp Arg Ile 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 Arg 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> 58
<211> 258
<212> PRT
<213> Homo sapiens

<400> 58

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 His Gln Leu 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 Phe
50 55 60

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

Gly Arg Pro Asp Glu Asp 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 Arg 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> 59

<211> 258

<212> PRT

<213> Homo sapiens

<400> 59

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 Leu Phe 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 Phe
 50 55 60

Val 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 Glu Arg Ala Val Pro Asp Arg Met Cys Arg His Asn Tyr Glu Leu
 100 105 110

Gly Gly Pro Met Thr Leu Gln Arg Arg Val Gln Pro Arg 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 Thr 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 Arg 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> 60
<211> 258
<212> PRT
<213> Homo sapiens

<400> 60

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 Leu 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 Phe
50 55 60

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

Gly Arg Pro Asp Glu Asp Tyr Trp Asn Ser Gln Lys Asp Leu 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 Arg Ser

210

215

220

Lys Thr Leu Thr Gly Ala Gly Gly Phe Met 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> 61
 <211> 258
 <212> PRT
 <213> Homo sapiens

<400> 61

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 Leu Phe 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 Phe
 50 55 60

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

Gly Arg Pro Asp Glu Glu Tyr Trp Asn Ser Gln Lys Asp Ile Leu Glu
 85 90 95

Glu Glu Arg Ala Val Pro Asp Arg Met Cys Arg His Asn Tyr Glu Leu
 100 105 110

Gly Gly Pro Met Thr Leu Gln Arg Arg Val Gln Pro Arg 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 Gln 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 Thr 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 Arg 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> 62
<211> 255
<212> PRT
<213> Homo sapiens

<400> 62

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

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> 63

<211> 255

<212> PRT

<213> Homo sapiens

<400> 63

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 Gln 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

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 Met 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> 64
<211> 255
<212> PRT
<213> Homo sapiens

<400> 64

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 Phe
35 40 45

Thr His Glu Phe Asp Gly Asp Glu Gln Phe Tyr Val Asp Leu Glu Lys
50 55 60

Lys Glu Thr Ala Trp Arg Trp Pro Glu Phe Ser Lys Phe Gly Gly Phe
65 70 75 80

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 His Ala 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> 65
 <211> 255
 <212> PRT
 <213> Homo sapiens

<400> 65

Met Ile Leu Asn Lys Ala Leu Leu Leu Gly Ala Leu Ala Leu Thr Thr
 1 5 10 15

Met Met Ser Pro Cys Gly Gly Glu Gly 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

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 Thr 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> 66
<211> 254
<212> PRT
<213> Homo sapiens

<400> 66

Met Ile Leu Asn Lys Ala Leu Met 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 Tyr Gly Val Asn Leu Tyr Gln Ser Tyr Gly Pro Ser Gly Gln Phe
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 Val Trp Lys Leu Pro Leu Phe His Arg Leu Arg Phe Asp
65 70 75 80

Pro Gln Phe Ala Leu Thr Asn Ile Ala Val Leu Lys His Asn Leu Asn
85 90 95

Ile Leu Ile Lys Arg Ser Asn Ser Thr Ala Ala Thr Asn Glu Val Pro
100 105 110

Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro Asn
115 120 125

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

Thr Trp Leu Ser Asn Gly His Ser Val Thr Glu Gly Val Ser Glu Thr
145 150 155 160

Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr Leu
165 170 175

Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu His
180 185 190

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Pro Glu Ile Pro
195 200 205

Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly Leu
210 215 220

Ser Val Gly Leu Val Gly Ile Val Val Gly Thr Val Leu Ile Ile Arg
225 230 235 240

Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
245 250

<210> 67
<211> 254
<212> PRT
<213> Homo sapiens

<400> 67

Met Ile Leu Asn Lys Ala Leu Met 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 Tyr Gly Val Asn Leu Tyr Gln Ser Tyr Gly Pro Ser Gly Gln Tyr
35 40 45

Ser His Glu Phe Asp Gly Asp Glu Glu Phe Tyr Val Asp Leu Glu Arg
50 55 60

Lys Glu Thr Val Trp Gln Leu Pro Leu Phe Arg Arg Phe Arg Arg Phe
65 70 75 80

Asp Pro Gln Phe Ala Leu Thr Asn Ile Ala Val Leu Lys His Asn Leu
85 90 95

Asn Ile Val Ile Lys Arg Ser 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 His Ser Val Thr Glu Gly Val Ser Thr
145 150 155 160

Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr Leu
165 170 175

Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu His
180 185 190

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Pro Glu Ile Pro
195 200 205

Thr Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly Leu
210 215 220

Ser Val Gly Leu Val Gly Ile Val Val Gly Thr Val Leu Ile Ile Arg
225 230 235 240

Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
245 250

<210> 68
<211> 255
<212> PRT
<213> Homo sapiens

<400> 68

Met Ile Leu Asn Lys Ala Leu Met Leu Gly Ala Leu Ala Leu Thr Thr
1 5 10 15

Val Thr Ser Pro Cys Gly Gly Glu Asp Ile Val Ala Asp His Val Ala
20 25 30

Ser Tyr Gly Val Asn Leu Tyr Gln Ser Tyr Gly Pro Ser Gly Gln Tyr
35 40 45

Ser His Glu Phe Asp Gly Asp Glu Glu Phe Tyr Val Asp Leu Glu Arg
50 55 60

Lys Glu Thr Val Trp Gln Leu Pro Leu Phe Arg Arg Phe Arg Arg Phe
65 70 75 80

Asp Pro Gln Phe Ala Leu Thr Asn Ile Ala Val Leu Lys His Asn Leu
85 90 95

Asn Ile Val Ile Lys Arg Ser 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 His 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 Asp Asp Glu Ile Tyr Asp Cys Lys Val Glu
180 185 190

His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Pro Glu Ile
195 200 205

Pro Thr 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 Leu Ile Ile
225 230 235 240

Arg Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
245 250 255

<210> 69
<211> 254
<212> PRT
<213> Homo sapiens

<400> 69

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 Tyr Gly Val Asn Leu Tyr Gln Ser Tyr Gly Pro Ser Gly Gln Tyr
35 40 45

Thr His Glu Phe Asp Gly Asp Glu Gln Phe Tyr Val Asp Leu Gly Arg
50 55 60

Lys Glu Thr Val Trp Cys Leu Pro Val Leu Arg Gln Phe Arg Phe Asp
65 70 75 80

Pro Gln Phe Ala Leu Thr Asn Ile Ala Val Thr Lys His Asn Leu Asn
85 90 95

Ile Leu Ile Lys Arg Ser Asn Ser Thr Ala Ala Thr Asn Glu Val Pro
100 105 110

Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro Asn
115 120 125

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

Thr Trp Leu Ser Asn Gly His Ser Val Thr Glu Gly Val Ser Glu Thr
145 150 155 160

Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr Leu
165 170 175

Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu His
180 185 190

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Pro Glu Ile Pro
195 200 205

Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly Leu
210 215 220

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

Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
245 250

<210> 70
<211> 254
<212> PRT
<213> Homo sapiens

<400> 70

Met Ile Leu Asn Lys Ala Leu Met 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 Tyr Gly Val Asn Leu Tyr Gln Ser Tyr Gly Pro Ser Gly Gln Tyr
35 40 45

Thr His Glu Phe Asp Gly Asp Glu Gln Phe Tyr Val Asp Leu Gly Arg
50 55 60

Lys Glu Thr Val Trp Cys Leu Pro Val Leu Arg Gln Phe Arg Phe Asp
65 70 75 80

Pro Gln Phe Ala Leu Thr Asn Ile Ala Val Leu Lys His Asn Leu Asn
85 90 95

Ser Leu Ile Lys Arg Ser Asn Ser Thr Ala Ala Thr Asn Glu Val Pro
100 105 110

Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro Asn
115 120 125

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

Thr Trp Leu Ser Asn Gly His Ser Val Thr Glu Gly Val Ser Glu Thr
145 150 155 160

Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr Leu
165 170 175

Thr Leu Leu Pro Ser Ala Glu Glu Ser Tyr Asp Cys Lys Val Glu His
180 185 190

Trp Gly Leu Asp Lys Pro Leu Leu Lys His Trp Glu Pro Glu Ile Pro
195 200 205

Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly Leu
210 215 220

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

Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
245 250

<210> 71
<211> 254
<212> PRT
<213> Homo sapiens

<400> 71

Met Ile Leu Asn Lys Ala Leu Met Leu Gly Thr 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 Tyr Gly Val Asn Leu Tyr Gln Ser Tyr Gly Pro Ser Gly Gln Tyr
35 40 45

Thr His Glu Phe Asp Gly Asp Glu Gln Phe Tyr Val Asp Leu Gly Arg
50 55 60

Lys Glu Thr Val Trp Cys Leu Pro Val Leu Arg Gln Phe Arg Phe Asp
65 70 75 80

Pro Gln Phe Ala Leu Thr Asn Ile Ala Val Leu Lys His Asn Leu Asn
85 90 95

Ser Leu Ile Lys Arg Ser Asn Ser Thr Ala Ala Thr Asn Glu Val Pro
100 105 110

Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro Asn
115 120 125

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

Thr Trp Leu Ser Asn Gly His Ser Val Thr Glu Gly Val Ser Glu Thr
145 150 155 160

Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr Leu
165 170 175

Thr Leu Leu Pro Ser Ala Glu Glu Ser Tyr Asp Cys Lys Val Glu His
180 185 190

Trp Gly Leu Asp Lys Pro Leu Leu Lys His Trp Glu Pro Glu Ile Pro
195 200 205

Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly Leu
210 215 220

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

Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
245 250

<210> 72
<211> 254
<212> PRT
<213> Homo sapiens

<400> 72

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 Tyr Gly Val Asn Leu Tyr Gln Ser Tyr Gly Pro Ser Gly Gln Phe
35 40 45

Thr His Glu Phe Asp Gly Asp Glu Gln Phe Tyr Val Asp Leu Gly Arg
50 55 60

Lys Glu Thr Val Trp Cys Leu Pro Val Leu Arg Gln Phe Arg Phe Asp
65 70 75 80

Pro Gln Phe Ala Leu Thr Asn Ile Ala Val Thr Lys His Asn Leu Asn
85 90 95

Ile Leu Ile Lys Arg Ser Asn Ser Thr Ala Ala Thr Asn Glu Val Pro
100 105 110

Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly Gln Pro Asn
115 120 125

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

Thr Trp Leu Ser Asn Gly His Ser Val Thr Glu Gly Val Ser Glu Thr
145 150 155 160

Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile Ser Tyr Leu
165 170 175

Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys Val Glu His
180 185 190

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Pro Glu Ile Pro
195 200 205

Ala Pro Met Ser Glu Leu Thr Glu Thr Val Val Cys Ala Leu Gly Leu
210 215 220

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

Gly Leu Arg Ser Val Gly Ala Ser Arg His Gln Gly Pro Leu
245 250

<210> 73
<211> 255
<212> PRT
<213> Homo sapiens

<400> 73

Met Ile Leu Asn Lys Ala Leu Leu Leu Gly Ala Leu Ala Leu Thr Ala
1 5 10 15

Val Met Ser Pro Cys Gly Gly Glu Asp Ile Val Ala Asp His Val Ala
20 25 30

Ser Tyr Gly Val Asn Phe Tyr Gln Ser His Gly Pro Ser Gly Gln Tyr
35 40 45

Thr His Glu Phe Asp Gly Asp Glu Glu Phe Tyr Val Asp Leu Glu Thr
50 55 60

Lys Glu Thr Val Trp Gln Leu Pro Met Phe Ser Lys Phe Ile Ser Phe
65 70 75 80

Asp Pro Gln Ser Ala Leu Arg Asn Met Ala Val Gly Lys His Thr Leu
85 90 95

Glu Phe Met Met Arg Gln Ser Asn Ser Thr Ala Ala Thr Asn Glu Val
100 105 110

Pro Glu Val Thr Val Phe Ser Lys Phe 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 His 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 Glu Pro Leu Leu Lys His Trp Glu Pro Glu Ile
195 200 205

Pro Ala Pro Met Ser Glu Leu Thr Glu Thr Leu Val Cys Ala Leu Gly
210 215 220

Leu Ser Val Gly Leu Met 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 Leu Leu
245 250 255

<210> 74

<211> 261

<212> PRT

<213> Homo sapiens

<400> 74

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
225 230 235 240

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> 75
<211> 261
<212> PRT
<213> Homo sapiens

<400> 75

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 Gly 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
225 230 235 240

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> 76

<211> 261

<212> PRT

<213> Homo sapiens

<400> 76

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 Ala Met	Leu Ser Thr Pro Val	Ala Glu Gly
	20	25	30
Arg Asp Ser	Pro Glu Asp Phe Val Tyr Gln Phe Lys	Ala Met Cys Tyr	
	35	40	45
Phe Thr Asn Gly Thr Glu Arg Val Arg Tyr Val Thr Arg Tyr Ile Tyr			
50	55	60	
Asn Arg Glu Glu Tyr Ala Arg Phe Asp Ser Asp Val Glu Val Tyr Arg			
65	70	75	80
Ala Val Thr Pro Leu Gly Pro Pro Asp Ala Glu Tyr Trp Asn Ser Gln			
	85	90	95
Lys Glu Val Leu Glu Arg Thr Arg Ala Glu Leu Asp Thr 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 Thr 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 His Gly Asp Val Tyr Thr Cys His Val Glu			
	195	200	205

His Pro Ser Leu Gln Asn 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
225 230 235 240

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> 77
<211> 261
<212> PRT
<213> Homo sapiens

<400> 77

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

Thr Val Thr Leu Met Leu Ala 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 Thr Arg Tyr Ile Tyr
50 55 60

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

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

Lys Glu Val Leu Glu Arg Thr Arg Ala Glu Leu Asp Thr 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 Thr 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 Asn Pro Ile Ile 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
225 230 235 240

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> 78
<211> 261
<212> PRT
<213> Homo sapiens

<400> 78

Met Ser Trp Lys Lys Ala Leu Arg Ile Pro Gly Gly Leu Arg Val Ala

1	5	10	15
Thr Val Thr	Leu Met Leu Ala 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 Thr Arg Tyr Ile Tyr			
50	55	60	
Asn Arg Glu Glu Tyr Ala Arg Phe Asp Ser Asp Val Gly Val Tyr Arg			
65	70	75	80
Ala Val Thr Pro Leu Gly Pro Pro Asp Ala Glu Tyr Trp Asn Ser Gln			
	85	90	95
Lys Glu Val Leu Glu Arg Thr Arg Ala Glu Leu Asp Thr 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 Thr 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 Asn Pro Ile Ile 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
225 230 235 240

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> 79
<211> 261
<212> PRT
<213> Homo sapiens

<400> 79

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

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

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

Asn Arg Glu Glu Tyr Ala Arg Phe Asp Ser Asp Val Glu Val Tyr Arg
65 70 75 80

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

Lys Glu Val Leu Glu Arg Thr Arg Ala Glu Leu Asp Thr 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 Thr 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 His Gly Asp Val Tyr Thr Cys His Val Glu
195 200 205

His Pro Ser Leu Gln Asn 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
225 230 235 240

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> 80
<211> 261
<212> PRT
<213> Homo sapiens

<400> 80

Met Ser Trp Lys Lys Ala Leu Arg Ile Pro Gly Gly Leu Arg Val Ala

1	5	10	15
Thr Val Thr	Leu Met Leu Ala Met	Leu Ser Thr Pro Val	Ala Glu Gly
	20	25	30
Arg Asp Ser	Pro Glu Asp Phe Val	Phe Gln Phe Lys	Gly Met Cys Tyr
	35	40	45
Phe Thr Asn	Gly Thr Glu Leu Val	Arg Gly Val Thr	Arg Tyr Ile Tyr
	50	55	60
Asn Arg Glu	Glu Tyr Ala Arg Phe	Asp Ser Asp Val	Gly Val Tyr Arg
65	70	75	80
Ala Val Thr	Pro Leu Gly Arg Leu	Asp Ala Glu Tyr	Trp Asn Ser Gln
	85	90	95
Lys Asp Ile	Leu Glu Glu Asp Arg	Ala Ser Val Asp	Thr 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	Thr 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 Asn Pro Ile Ile 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
225 230 235 240

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> 81
<211> 261
<212> PRT
<213> Homo sapiens

<400> 81

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

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

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

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

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

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

Lys Asp Ile Leu Glu Glu Asp Arg Ala Ser Val Asp Thr 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 Thr 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 Asn Pro Ile Ile 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
225 230 235 240

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> 82

<211> 261

<212> PRT

<213> Homo sapiens

<400> 82

Met Ser Trp Lys Lys Ser Leu Arg Ile Pro Gly Asp Leu Arg Val Ala

1	5	10	15
Thr Val Thr	Leu Met Leu Ala Ile	Leu Ser Ser Ser	Leu Ala Glu Gly
	20	25	30
Arg Asp Ser	Pro Glu Asp Phe Val Tyr	Gln Phe Lys Gly	Leu Cys Tyr
	35	40	45
Phe Thr Asn Gly Thr	Glu Arg Val Arg Gly Val	Thr Arg His Ile Tyr	
	50	55	60
Asn Arg Glu Glu Tyr Val	Arg Phe Asp Ser Asp Val Gly Val Tyr Arg		
65	70	75	80
Ala Val Thr Pro Gln Gly Arg Pro Val	Ala Glu Tyr Trp Asn Ser Gln		
	85	90	95
Lys Glu Val Leu Glu Gly Ala Arg Ala Ser Val Asp Arg Val Cys Arg			
	100	105	110
His Asn Tyr Glu Val Ala Tyr Arg Gly Ile 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 Ile Cys Ser Val Thr Asp Phe Tyr Pro Ser 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 Val Gly Gly Phe Val Leu
225 230 235 240

Gly Leu Ile Phe Leu Gly Leu Gly Leu Ile Ile Arg Gln Arg Ser Arg
245 250 255

Lys Gly Leu Leu His
260

<210> 83
<211> 269
<212> PRT
<213> Homo sapiens

<400> 83

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

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

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

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

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

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

Lys Glu Val Leu Glu Gly Ala Arg Ala Ser Val Asp Arg Val Cys Arg
100 105 110

His Asn Tyr Glu Val Ala Tyr Arg Gly Ile 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 Ile Cys Ser Val Thr Asp Phe Tyr Pro Ser 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 Val Gly Gly Phe Val Leu
225 230 235 240

Gly Leu Ile Phe Leu Gly Leu Gly Leu Ile Ile Arg Gln Arg Ser Arg
245 250 255

Lys Gly Pro Gln Gly Pro Pro Pro Ala Gly Leu Leu His
260 265

<210> 84

<211> 269

<212> PRT

<213> Homo sapiens

<400> 84

Met Ser Trp Lys Lys Ala Leu Arg Ile Pro Gly Gly Leu Arg Ala Pro

1	5	10	15
Thr Val Thr	Leu Met Leu Ala Met	Leu Ser Thr Pro Val	Ala Glu Gly
	20	25	30
Arg Asp Pro	Pro Glu Asp Phe Val	Leu Gln Phe Lys	Ala Met Cys Tyr
	35	40	45
Phe Thr Asn	Gly Thr Glu Arg Val	Arg Tyr Val Thr	Arg Tyr Ile Tyr
	50	55	60
Asn Arg Glu	Glu Asp Val Arg Phe	Asp Ser Asp Val	Gly Val Tyr Arg
65	70	75	80
Ala Val Thr	Pro Gln Gly Arg Pro	Asp Ala Glu Tyr	Trp Asn Ser Gln
	85	90	95
Lys Asp Ile	Leu Glu Arg Thr Arg	Ala Glu Leu Asp	Thr Val Cys Arg
	100	105	110
His Asn Tyr	Glu Val Ala Phe Arg	Gly Ile 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	Gly Gln Ile Lys
145	150	155	160
Val Arg Trp	Phe Arg Asn Asp	Gln Glu Glu Thr	Ala Gly Val Val
	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 His 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 Asn Lys Met Leu Ser Gly Ile Gly Gly Phe Val Leu
225 230 235 240

Gly Leu Ile Phe Leu Gly Leu Gly Leu Ile Ile Arg Gln Arg Ser Gln
245 250 255

Lys Gly Pro Gln Gly Pro Pro Pro Ala Gly Leu Leu His
260 265

<210> 85
<211> 269
<212> PRT
<213> Homo sapiens

<400> 85

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

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

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

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

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

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

Lys Glu Val Leu Glu Gly Thr Arg Ala Glu Leu Asp Thr Val Cys Arg
100 105 110

His Asn Tyr Glu Val Ala Phe Arg Gly Ile 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 Gly 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 Val Gly Gly Phe Val Leu
225 230 235 240

Gly Leu Ile Phe Leu Gly Leu Gly Leu Ile Ile Arg Gln Arg Ser Gln
245 250 255

Lys Gly Pro Gln Gly Pro Pro Pro Ala Gly Leu Leu His
260 265

<210> 86

<211> 227

<212> PRT

<213> Homo sapiens

<400> 86

Met Ala Leu Gln Ile Pro Gly Gly Phe Trp Ala Ala Ala Val Thr Val

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

Ser Pro Ile Thr Val Glu Trp Arg Pro Arg Gly Pro Pro Pro Ala Gly
210 215 220

Leu Leu His
225

<210> 87
<211> 264
<212> PRT
<213> Homo sapiens

<400> 87

Met Ala Leu Gln Ile Pro Gly Gly Phe Trp Ala Ala Ala Val Thr Val
1 5 10 15

Met Leu Val Met Leu Ser Thr Pro Val Ala Glu Ala Arg Asp Phe Pro
20 25 30

Lys Asp Phe Leu Val Gln Phe Lys Gly Met Cys Tyr Phe Thr Asn Gly
35 40 45

Thr Glu Arg Val Arg Gly Val Ala Arg Tyr Ile Tyr Asn Arg Glu Glu
50 55 60

Tyr Gly Arg Phe Asp Ser Asp Val Gly Glu Phe Gln Ala Val Thr Glu
65 70 75 80

Leu Gly Arg Ser Ile Glu Asp Trp Asn Asn Tyr Lys Asp Phe Leu Glu
85 90 95

Gln Glu Arg Ala Ala Val Asp Lys Val Cys Arg His Asn Tyr Glu Ala
100 105 110

Glu Leu Arg Thr Thr Leu Gln Arg Gln Val Glu Pro Thr Val Thr Ile
115 120 125

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

Ser Val Thr Asp Phe Tyr Pro Ala Gln Ile Lys Val Arg Trp Phe Arg
145 150 155 160

Asn Asp Gln Glu Glu Thr Ala Gly Val Val Ser Thr Ser Leu Ile Arg
165 170 175

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

Gln Arg Gly Asp Ile Tyr Thr Cys Gln Val Glu His Pro Ser Leu Gln
195 200 205

Ser Pro Ile Thr Val Glu Trp Arg Ala Gln Ser Glu Ser Ala Gln Ser
210 215 220

Lys Met Leu Ser Gly Ile Gly Gly Phe Val Leu Gly Leu Ile Phe Leu
225 230 235 240

Gly Leu Gly Leu Ile Ile Arg His Arg Gly Gln Lys Gly Pro Arg Gly
245 250 255

Pro Pro Pro Ala Gly Leu Leu His
260

<210> 88
<211> 189
<212> PRT
<213> Homo sapiens

<400> 88

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe

35

40

45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
 50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
 65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
 85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
 100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
 115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
 130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
 145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
 165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
 180 185

<210> 89

<211> 189

<212> PRT

<213> Homo sapiens

<400> 89

Ile Lys Cys Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
 1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 90

<211> 189

<212> PRT

<213> Homo sapiens

<400> 90

Ile Lys Glu Cys His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 91

<211> 189
<212> PRT
<213> Homo sapiens

<400> 91

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Cys Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 92
<211> 189
<212> PRT
<213> Homo sapiens

<400> 92

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Cys Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 93
<211> 189
<212> PRT
<213> Homo sapiens

<400> 93

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Cys Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 94
<211> 189
<212> PRT
<213> Homo sapiens

<400> 94

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Cys Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val

115

120

125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
 130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
 145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
 165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
 180 185

<210> 95

<211> 189

<212> PRT

<213> Homo sapiens

<400> 95

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
 1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
 20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
 35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
 50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Cys Arg Ser Asn Tyr Thr
 65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
 85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 96
<211> 189
<212> PRT
<213> Homo sapiens

<400> 96

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Cys
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 97
<211> 189
<212> PRT
<213> Homo sapiens

<400> 97

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Cys Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 98
<211> 189
<212> PRT
<213> Homo sapiens

<400> 98

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe

35

40

45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
 50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
 65 70 75 80

Pro Cys Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
 85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
 100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
 115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
 130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
 145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
 165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
 180 185

<210> 99

<211> 189

<212> PRT

<213> Homo sapiens

<400> 99

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
 1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Cys Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 100

<211> 189

<212> PRT

<213> Homo sapiens

<400> 100

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Cys Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 101

<211> 189
<212> PRT
<213> Homo sapiens

<400> 101

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Cys Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr
180 185

<210> 102
<211> 220
<212> PRT
<213> Homo sapiens

<400> 102

Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr Gly Ser
1 5 10 15

Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
20 25 30

Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
35 40 45

Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser Tyr Arg
50 55 60

Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
65 70 75 80

Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
85 90 95

Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
100 105 110

Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
115 120 125

Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
130 135 140

Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
145 150 155 160

Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
165 170 175

Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
180 185 190

Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
195 200 205

Pro Glu Leu Pro Leu Ala His Pro Pro Asn Glu Arg
210 215 220

<210> 103
<211> 199
<212> PRT
<213> Homo sapiens

<400> 103

Gly Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
180 185 190

Glu Ser Ala Gln Ser Lys Met
195

<210> 104
<211> 199
<212> PRT
<213> Homo sapiens

<400> 104

Gly Asp Thr Arg Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg

65		70		75		80									
His	Asn	Tyr	Gly	Val	Gly	Glu	Ser	Phe	Thr	Val	Gln	Arg	Arg	Val	Tyr
			85						90					95	

Pro	Glu	Val	Thr	Val	Tyr	Pro	Ala	Lys	Thr	Gln	Pro	Leu	Gln	His	His
		100						105					110		

Asn	Leu	Leu	Val	Cys	Ser	Val	Asn	Gly	Phe	Tyr	Pro	Ala	Ser	Ile	Glu
		115					120					125			

Val	Arg	Trp	Phe	Arg	Asn	Gly	Gln	Glu	Glu	Lys	Thr	Gly	Val	Val	Ser
	130					135					140				

Thr	Gly	Leu	Ile	Gln	Asn	Gly	Asp	Trp	Thr	Phe	Gln	Thr	Leu	Val	Met
145					150					155					160

Leu	Glu	Thr	Val	Pro	Arg	Ser	Gly	Glu	Val	Tyr	Thr	Cys	Gln	Val	Glu
			165						170					175	

His	Pro	Ser	Leu	Thr	Ser	Pro	Leu	Thr	Val	Glu	Trp	Arg	Ala	Arg	Ser
		180						185					190		

Glu	Ser	Ala	Gln	Ser	Lys	Met
	195					

<210> 105
 <211> 199
 <212> PRT
 <213> Homo sapiens

<400> 105

Gly	Asp	Thr	Arg	Pro	Arg	Cys	Leu	Glu	Gln	Val	Lys	His	Glu	Cys	His
1				5					10					15	

Phe	Phe	Asn	Gly	Thr	Glu	Arg	Val	Arg	Phe	Leu	Asp	Arg	Tyr	Phe	Tyr
		20						25					30		

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
180 185 190

Glu Ser Ala Gln Ser Lys Met
195

<210> 106

<211> 199

<212> PRT

<213> Homo sapiens

<400> 106

Gly Asp Thr Arg Pro Arg Phe Leu Glu Cys Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
180 185 190

Glu Ser Ala Gln Ser Lys Met

195

<210> 107
<211> 199
<212> PRT
<213> Homo sapiens

<400> 107

Gly Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Cys Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
180 185 190

Glu Ser Ala Gln Ser Lys Met
195

<210> 108
<211> 199
<212> PRT
<213> Homo sapiens

<400> 108

Gly Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Cys Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
180 185 190

Glu Ser Ala Gln Ser Lys Met
195

<210> 109
<211> 199
<212> PRT
<213> Homo sapiens

<400> 109

Gly Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

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

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
180 185 190

Glu Ser Ala Gln Ser Lys Met
195

<210> 110
<211> 199
<212> PRT
<213> Homo sapiens

<400> 110

Gly Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln

50

55

60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
 65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
 85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
 100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
 115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
 130 135 140

Thr Gly Leu Ile Gln Asn Cys Asp Trp Thr Phe Gln Thr Leu Val Met
 145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
 165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
 180 185 190

Glu Ser Ala Gln Ser Lys Met
 195

<210> 111

<211> 199

<212> PRT

<213> Homo sapiens

<400> 111

Gly Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His
 1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Cys Trp Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser
180 185 190

Glu Ser Ala Gln Ser Lys Met
195

<210> 112

<211> 199

<212> PRT

<213> Homo sapiens

<400> 112

Gly Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr
20 25 30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr
85 90 95

Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His
100 105 110

Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu
115 120 125

Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser
130 135 140

Thr Gly Leu Ile Gln Asn Gly Asp Cys Thr Phe Gln Thr Leu Val Met
145 150 155 160

Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu
165 170 175

His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser

180

185

190

Glu Ser Ala Gln Ser Lys Met
195

<210> 113
<211> 227
<212> PRT
<213> Homo sapiens

<400> 113

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 114
<211> 227
<212> PRT
<213> Homo sapiens

<400> 114

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 115
<211> 227
<212> PRT
<213> Homo sapiens

<400> 115

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 116
<211> 227
<212> PRT
<213> Homo sapiens

<400> 116

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 117
<211> 227
<212> PRT
<213> Homo sapiens

<400> 117

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Ser Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

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

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 118
<211> 227
<212> PRT
<213> Homo sapiens

<400> 118

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly

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

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 119
<211> 325
<212> PRT
<213> Homo sapiens

<400> 119

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser
1 5 10 15

Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
20 25 30

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
35 40 45

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
50 55 60

Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr
65 70 75 80

Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr
85 90 95

Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro
100 105 110

Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
115 120 125

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
130 135 140

Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
145 150 155 160

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
165 170 175

Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu
180 185 190

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala
195 200 205

Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro
210 215 220

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
225 230 235 240

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
245 250 255

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
260 265 270

Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
275 280 285

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
290 295 300

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
305 310 315 320

Leu Ser Pro Gly Lys
325

<210> 120
<211> 246
<212> PRT
<213> Homo sapiens

<400> 120

His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Leu Lys Thr
1 5 10 15

Pro Leu Gly Asp Thr Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
20 25 30

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
35 40 45

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
50 55 60

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
65 70 75 80

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
85 90 95

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
100 105 110

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
115 120 125

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
130 135 140

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
145 150 155 160

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
165 170 175

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
180 185 190

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
195 200 205

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
210 215 220

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
225 230 235 240

Ser Leu Ser Pro Gly Lys
245

<210> 121
<211> 383
<212> PRT
<213> Homo sapiens

<400> 121

Pro Thr Lys Ala Pro Asp Val Phe Pro Ile Ile Ser Gly Cys Arg His
1 5 10 15

Pro Lys Asp Asn Ser Pro Val Val Leu Ala Cys Leu Ile Thr Gly Tyr
20 25 30

His Pro Thr Ser Val Thr Val Thr Trp Tyr Met Gly Thr Gln Ser Gln
35 40 45

Pro Gln Arg Thr Phe Pro Glu Ile Gln Arg Arg Asp Ser Tyr Tyr Met
50 55 60

Thr Ser Ser Gln Leu Ser Thr Pro Leu Gln Gln Trp Arg Gln Gly Glu
65 70 75 80

Tyr Lys Cys Val Val Gln His Thr Ala Ser Lys Ser Lys Lys Glu Ile
85 90 95

Phe Arg Trp Pro Glu Ser Pro Lys Ala Gln Ala Ser Ser Val Pro Thr
100 105 110

Ala Gln Pro Gln Ala Glu Gly Ser Leu Ala Lys Ala Thr Thr Ala Pro
115 120 125

Ala Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu
130 135 140

Lys Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys
145 150 155 160

Pro Ser His Thr Gln Pro Leu Gly Val Tyr Leu Leu Thr Pro Ala Val
165 170 175

Gln Asp Leu Trp Leu Arg Asp Lys Ala Thr Phe Thr Cys Phe Val Val
180 185 190

Gly Ser Asp Leu Lys Asp Ala His Leu Thr Trp Glu Val Ala Gly Lys
195 200 205

Val Pro Thr Gly Gly Val Glu Glu Gly Leu Leu Glu Arg His Ser Asn
210 215 220

Gly Ser Gln Ser Gln His Ser Arg Leu Thr Leu Pro Arg Ser Leu Trp
225 230 235 240

Asn Ala Gly Thr Ser Val Thr Cys Thr Leu Asn His Pro Ser Leu Pro
245 250 255

Pro Gln Arg Leu Met Ala Leu Arg Glu Pro Ala Ala Gln Ala Pro Val
260 265 270

Lys Leu Ser Leu Asn Leu Leu Ala Ser Ser Asp Pro Pro Glu Ala Ala
275 280 285

Ser Trp Leu Leu Cys Glu Val Ser Gly Phe Ser Pro Pro Asn Ile Leu
290 295 300

Leu Met Trp Leu Glu Asp Gln Arg Glu Val Asn Thr Ser Gly Phe Ala
305 310 315 320

Pro Ala Arg Pro Pro Pro Gln Pro Arg Ser Thr Thr Phe Trp Ala Trp
325 330 335

Ser Val Leu Arg Val Pro Ala Pro Pro Ser Pro Gln Pro Ala Thr Tyr
340 345 350

Thr Cys Val Val Ser His Glu Asp Ser Arg Thr Leu Leu Asn Ala Ser
355 360 365

Arg Ser Leu Glu Val Ser Tyr Val Thr Asp His Gly Pro Met Lys
370 375 380

<210> 122
<211> 276
<212> PRT
<213> Homo sapiens

<400> 122

Val Thr Ser Thr Leu Thr Ile Lys Glx Ser Asp Trp Leu Gly Glu Ser
1 5 10 15

Met Phe Thr Cys Arg Val Asp His Arg Gly Leu Thr Phe Gln Gln Asn
20 25 30

Ala Ser Ser Met Cys Val Pro Asp Gln Asp Thr Ala Ile Arg Val Phe
35 40 45

Ala Ile Pro Pro Ser Phe Ala Ser Ile Phe Leu Thr Lys Ser Thr Lys
50 55 60

Leu Thr Cys Leu Val Thr Asp Leu Thr Thr Tyr Asx Ser Val Thr Ile
65 70 75 80

Ser Trp Thr Arg Glu Glu Asn Gly Ala Val Lys Thr His Thr Asn Ile
85 90 95

Ser Glu Ser His Pro Asn Ala Thr Phe Ser Ala Val Gly Glu Ala Ser
100 105 110

Ile Cys Glu Asp Asx Asp Trp Ser Gly Glu Arg Phe Thr Cys Thr Val
115 120 125

Thr His Thr Asp Leu Pro Ser Pro Leu Lys Gln Thr Ile Ser Arg Pro
130 135 140

Lys Gly Val Ala Leu His Arg Pro Asx Val Tyr Leu Leu Pro Pro Ala
145 150 155 160

Arg Glx Glx Leu Asn Leu Arg Glu Ser Ala Thr Ile Thr Cys Leu Val
165 170 175

Thr Gly Phe Ser Pro Ala Asp Val Phe Val Glu Trp Met Gln Arg Gly
180 185 190

Glu Pro Leu Ser Pro Gln Lys Tyr Val Thr Ser Ala Pro Met Pro Glu
195 200 205

Pro Gln Ala Pro Gly Arg Tyr Phe Ala His Ser Ile Leu Thr Val Ser
210 215 220

Glu Glu Glu Trp Asn Thr Gly Gly Thr Tyr Thr Cys Val Val Ala His
225 230 235 240

Glu Ala Leu Pro Asn Arg Val Thr Glu Arg Thr Val Asp Lys Ser Thr
245 250 255

Gly Lys Pro Thr Leu Tyr Asn Val Ser Leu Val Met Ser Asp Thr Ala
260 265 270

Gly Thr Cys Tyr

275

<210> 123
<211> 353
<212> PRT
<213> Homo sapiens

<400> 123

Ala Ser Pro Thr Ser Pro Lys Val Phe Pro Leu Ser Leu Cys Ser Thr
1 5 10 15

Gln Pro Asp Gly Asn Val Val Ile Ala Cys Leu Val Gln Gly Phe Phe
20 25 30

Pro Gln Glu Pro Leu Ser Val Thr Trp Ser Glu Ser Gly Gln Gly Val
35 40 45

Thr Ala Arg Asn Phe Pro Pro Ser Gln Asp Ala Ser Gly Asp Leu Tyr
50 55 60

Thr Thr Ser Ser Gln Leu Thr Leu Pro Ala Thr Gln Cys Leu Ala Gly
65 70 75 80

Lys Ser Val Thr Cys His Val Lys His Tyr Thr Asn Pro Ser Gln Asp
85 90 95

Val Thr Val Pro Cys Pro Val Pro Ser Thr Pro Pro Thr Pro Ser Pro
100 105 110

Ser Thr Pro Pro Thr Pro Ser Pro Ser Cys Cys His Pro Arg Leu Ser
115 120 125

Leu His Arg Pro Ala Leu Glu Asp Leu Leu Leu Gly Ser Glu Ala Asn
130 135 140

Leu Thr Cys Thr Leu Thr Gly Leu Arg Asp Ala Ser Gly Val Thr Phe
145 150 155 160

Thr Trp Thr Pro Ser Ser Gly Lys Ser Ala Val Gln Gly Pro Pro Glu
165 170 175

Arg Asp Leu Cys Gly Cys Tyr Ser Val Ser Ser Val Leu Pro Gly Cys
180 185 190

Ala Glu Pro Trp Asn His Gly Lys Thr Phe Thr Cys Thr Ala Ala Tyr
195 200 205

Pro Glu Ser Lys Thr Pro Leu Thr Ala Thr Leu Ser Lys Ser Gly Asn
210 215 220

Thr Phe Arg Pro Glu Val His Leu Leu Pro Pro Pro Ser Glu Glu Leu
225 230 235 240

Ala Leu Asn Glu Leu Val Thr Leu Thr Cys Leu Ala Arg Gly Phe Ser
245 250 255

Pro Lys Asp Val Leu Val Arg Trp Leu Gln Gly Ser Gln Glu Leu Pro
260 265 270

Arg Glu Lys Tyr Leu Thr Trp Ala Ser Arg Gln Glu Pro Ser Gln Gly
275 280 285

Thr Thr Thr Phe Ala Val Thr Ser Ile Leu Arg Val Ala Ala Glu Asp
290 295 300

Trp Lys Lys Gly Asp Thr Phe Ser Cys Met Val Gly His Glu Ala Leu
305 310 315 320

Pro Leu Ala Phe Thr Gln Lys Thr Ile Asp Arg Leu Ala Gly Lys Pro
325 330 335

Thr His Val Asn Val Ser Val Val Met Ala Glu Val Asp Gly Thr Cys
340 345 350

Tyr

<210> 124
<211> 222
<212> PRT
<213> Homo sapiens

<400> 124

Ala Asp Pro Cys Asp Ser Asn Pro Arg Gly Val Ser Ala Tyr Leu Ser
1 5 10 15

Arg Pro Ser Pro Phe Asp Leu Phe Ile Arg Lys Ser Pro Thr Ile Thr
20 25 30

Cys Leu Val Val Asp Leu Ala Pro Ser Lys Gly Thr Val Asn Leu Thr
35 40 45

Trp Ser Arg Ala Ser Gly Lys Pro Val Asn His Ser Thr Arg Lys Glu
50 55 60

Glu Lys Gln Arg Asn Gly Thr Leu Thr Val Thr Ser Thr Leu Pro Val
65 70 75 80

Gly Thr Arg Asp Trp Ile Glu Gly Glu Thr Tyr Gln Cys Arg Val Thr
85 90 95

His Pro His Leu Pro Arg Ala Leu Met Arg Ser Thr Thr Lys Thr Ser
100 105 110

Gly Pro Arg Ala Ala Pro Glu Val Tyr Ala Phe Ala Thr Pro Glu Trp
115 120 125

Pro Gly Ser Arg Asp Lys Arg Thr Leu Ala Cys Leu Ile Gln Asn Phe
130 135 140

Met Pro Glu Asp Ile Ser Val Gln Trp Leu His Asn Glu Val Gln Leu
145 150 155 160

Pro Asp Ala Arg His Ser Thr Thr Gln Pro Arg Lys Thr Lys Gly Ser

165

170

175

Gly Phe Phe Val Phe Ser Arg Leu Glu Val Thr Arg Ala Glu Trp Glu
 180 185 190

Gln Lys Asp Glu Phe Ile Cys Arg Ala Val His Glu Ala Ala Ser Pro
 195 200 205

Ser Gln Thr Val Gln Arg Ala Val Ser Val Asn Pro Gly Lys
 210 215 220

<210> 125

<211> 327

<212> PRT

<213> Homo sapiens

<400> 125

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
 1 5 10 15

Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
 20 25 30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
 35 40 45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50 55 60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
 65 70 75 80

Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95

Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
 100 105 110

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
130 135 140

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
165 170 175

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
195 200 205

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Leu Gly Lys
325

<210> 126
<211> 133
<212> PRT
<213> Homo sapiens

<400> 126

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 127

<211> 272
<212> PRT
<213> Homo sapiens

<400> 127

Met Asp Ser Tyr Leu Leu Met Trp Gly Leu Leu Thr Phe Ile Met Val
1 5 10 15

Pro Gly Cys Gln Ala Glu Leu Cys Asp Asp Asp Pro Pro Glu Ile Pro
20 25 30

His Ala Thr Phe Lys Ala Met Ala Tyr Lys Glu Gly Thr Met Leu Asn
35 40 45

Cys Glu Cys Lys Arg Gly Phe Arg Arg Ile Lys Ser Gly Ser Leu Tyr
50 55 60

Met Leu Cys Thr Gly Asn Ser Ser His Ser Ser Trp Asp Asn Gln Cys
65 70 75 80

Gln Cys Thr Ser Ser Ala Thr Arg Asn Thr Thr Lys Gln Val Thr Pro
85 90 95

Gln Pro Glu Glu Gln Lys Glu Arg Lys Thr Thr Glu Met Gln Ser Pro
100 105 110

Met Gln Pro Val Asp Gln Ala Ser Leu Pro Gly His Cys Arg Glu Pro
115 120 125

Pro Pro Trp Glu Asn Glu Ala Thr Glu Arg Ile Tyr His Phe Val Val
130 135 140

Gly Gln Met Val Tyr Tyr Gln Cys Val Gln Gly Tyr Arg Ala Leu His
145 150 155 160

Arg Gly Pro Ala Glu Ser Val Cys Lys Met Thr His Gly Lys Thr Arg
165 170 175

Trp Thr Gln Pro Gln Leu Ile Cys Thr Gly Glu Met Glu Thr Ser Gln
180 185 190

Phe Pro Gly Glu Glu Lys Pro Gln Ala Ser Pro Glu Gly Arg Pro Glu
195 200 205

Ser Glu Thr Ser Cys Leu Val Thr Thr Thr Asp Phe Gln Ile Gln Thr
210 215 220

Glu Met Ala Ala Thr Met Glu Thr Ser Ile Phe Thr Thr Glu Tyr Gln
225 230 235 240

Val Ala Val Ala Gly Cys Val Phe Leu Leu Ile Ser Val Leu Leu Leu
245 250 255

Ser Gly Leu Thr Trp Gln Arg Arg Gln Arg Lys Ser Arg Arg Thr Ile
260 265 270

<210> 128
<211> 551
<212> PRT
<213> Homo sapiens

<400> 128

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

Leu Pro Leu Ala Thr Ser Trp Ala Ser Ala Ala Val Asn Gly Thr Ser
20 25 30

Gln Phe Thr Cys Phe Tyr Asn Ser Arg Ala Asn Ile Ser Cys Val Trp
35 40 45

Ser Gln Asp Gly Ala Leu Gln Asp Thr Ser Cys Gln Val His Ala Trp
50 55 60

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

Gln Ala Ser Trp Ala Cys Asn Leu Ile Leu Gly Ala Pro Asp Ser Gln
85 90 95

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

Gly Val Arg Trp Arg Val Met Ala Ile Gln Asp Phe Lys Pro Phe Glu
115 120 125

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

Thr His Arg Cys Asn Ile Ser Trp Glu Ile Ser Gln Ala Ser His Tyr
145 150 155 160

Phe Glu Arg His Leu Glu Phe Glu Ala Arg Thr Leu Ser Pro Gly His
165 170 175

Thr Trp Glu Glu Ala Pro Leu Leu Thr Leu Lys Gln Lys Gln Glu Trp
180 185 190

Ile Cys Leu Glu Thr Leu Thr Pro Asp Thr Gln Tyr Glu Phe Gln Val
195 200 205

Arg Val Lys Pro Leu Gln Gly Glu Phe Thr Thr Trp Ser Pro Trp Ser
210 215 220

Gln Pro Leu Ala Phe Arg Thr Lys Pro Ala Ala Leu Gly Lys Asp Thr
225 230 235 240

Ile Pro Trp Leu Gly His Leu Leu Val Gly Leu Ser Gly Ala Phe Gly
245 250 255

Phe Ile Ile Leu Val Tyr Leu Leu Ile Asn Cys Arg Asn Thr Gly Pro
260 265 270

Trp Leu Lys Lys Val Leu Lys Cys Asn Thr Pro Asp Pro Ser Lys Phe

275

280

285

Phe Ser Gln Leu Ser Ser Glu His Gly Gly Asp Val Gln Lys Trp Leu
 290 295 300

Ser Ser Pro Phe Pro Ser Ser Ser Phe Ser Pro Gly Gly Leu Ala Pro
 305 310 315 320

Glu Ile Ser Pro Leu Glu Val Leu Glu Arg Asp Lys Val Thr Gln Leu
 325 330 335

Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn
 340 345 350

His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His
 355 360 365

Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Val Tyr Phe Thr Tyr
 370 375 380

Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val Ala Gly Ala Pro
 385 390 395 400

Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp
 405 410 415

Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro
 420 425 430

Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala Pro Gly Gly Ser
 435 440 445

Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu Gln Glu Arg Val Pro
 450 455 460

Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr Pro Gly Val Pro
 465 470 475 480

Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu Val Leu Arg Glu Ala
485 490 495

Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly Val Ser Phe Pro
500 505 510

Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg
515 520 525

Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly
530 535 540

Gln Asp Pro Thr His Leu Val
545 550

<210> 129
<211> 369
<212> PRT
<213> Homo sapiens

<400> 129

Met Leu Lys Pro Ser Leu Pro Phe Thr Ser Leu Leu Phe Leu Gln Leu
1 5 10 15

Pro Leu Leu Gly Val Gly Leu Asn Thr Thr Ile Leu Thr Pro Asn Gly
20 25 30

Asn Glu Asp Thr Thr Ala Asp Phe Phe Leu Thr Thr Met Pro Thr Asp
35 40 45

Ser Leu Ser Val Ser Thr Leu Pro Leu Pro Glu Val Gln Cys Phe Val
50 55 60

Phe Asn Val Glu Tyr Met Asn Cys Thr Trp Asn Ser Ser Ser Glu Pro
65 70 75 80

Gln Pro Thr Asn Leu Thr Leu His Tyr Trp Tyr Lys Asn Ser Asp Asn
85 90 95

Asp Lys Val Gln Lys Cys Ser His Tyr Leu Phe Ser Glu Glu Ile Thr
100 105 110

Ser Gly Cys Gln Leu Gln Lys Lys Glu Ile His Leu Tyr Gln Thr Phe
115 120 125

Val Val Gln Leu Gln Asp Pro Arg Glu Pro Arg Arg Gln Ala Thr Gln
130 135 140

Met Leu Lys Leu Gln Asn Leu Val Ile Pro Trp Ala Pro Glu Asn Leu
145 150 155 160

Thr Leu His Lys Leu Ser Glu Ser Gln Leu Glu Leu Asn Trp Asn Asn
165 170 175

Arg Phe Leu Asn His Cys Leu Glu His Leu Val Gln Tyr Arg Thr Asp
180 185 190

Trp Asp His Ser Trp Thr Glu Gln Ser Val Asp Tyr Arg His Lys Phe
195 200 205

Ser Leu Pro Ser Val Asp Gly Gln Lys Arg Tyr Thr Phe Arg Val Arg
210 215 220

Ser Arg Phe Asn Pro Leu Cys Gly Ser Ala Gln His Trp Ser Glu Trp
225 230 235 240

Ser His Pro Ile His Trp Gly Ser Asn Thr Ser Lys Glu Asn Pro Phe
245 250 255

Leu Phe Ala Leu Glu Ala Val Val Ile Ser Val Gly Ser Met Gly Leu
260 265 270

Ile Ile Ser Leu Leu Cys Val Tyr Phe Trp Leu Glu Arg Thr Met Pro
275 280 285

Arg Ile Pro Thr Leu Lys Asn Leu Glu Asp Leu Val Thr Glu Tyr His
290 295 300

Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys Gly Leu Ala Glu Ser
305 310 315 320

Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys Leu Val Ser Glu Ile Pro
325 330 335

Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Ala Ser Pro Cys Asn
340 345 350

Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys Pro Glu
355 360 365

Thr

<210> 130
<211> 219
<212> PRT
<213> Homo sapiens

<400> 130

Phe Thr Val Thr Val Pro Lys Asp Leu Tyr Val Val Glu Tyr Gly Ser
1 5 10 15

Asn Met Thr Ile Glu Cys Lys Phe Pro Val Glu Lys Gln Leu Asp Leu
20 25 30

Ala Ala Leu Ile Val Tyr Trp Glu Met Glu Asp Lys Asn Ile Ile Gln
35 40 45

Phe Val His Gly Glu Glu Asp Leu Lys Val Gln His Ser Ser Tyr Arg
50 55 60

Gln Arg Ala Arg Leu Leu Lys Asp Gln Leu Ser Leu Gly Asn Ala Ala
65 70 75 80

Leu Gln Ile Thr Asp Val Lys Leu Gln Asp Ala Gly Val Tyr Arg Cys
85 90 95

Met Ile Ser Tyr Gly Gly Ala Asp Tyr Lys Arg Ile Thr Val Lys Val
100 105 110

Asn Ala Pro Tyr Asn Lys Ile Asn Gln Arg Ile Leu Val Val Asp Pro
115 120 125

Val Thr Ser Glu His Glu Leu Thr Cys Gln Ala Glu Gly Tyr Pro Lys
130 135 140

Ala Glu Val Ile Trp Thr Ser Ser Asp His Gln Val Leu Ser Gly Lys
145 150 155 160

Thr Thr Thr Thr Asn Ser Lys Arg Glu Glu Lys Leu Phe Asn Val Thr
165 170 175

Ser Thr Leu Arg Ile Asn Thr Thr Thr Asn Glu Ile Phe Tyr Cys Thr
180 185 190

Phe Arg Arg Leu Asp Pro Glu Glu Asn His Thr Ala Glu Leu Val Ile
195 200 205

Pro Gly Asn Ile Leu Asn Val Ser Ile Lys Ile
210 215

<210> 131
<211> 167
<212> PRT
<213> Homo sapiens

<400> 131

Asp Pro Ala Gly Leu Leu Asp Leu Arg Gln Gly Met Phe Ala Gln Leu
1 5 10 15

Val Ala Gln Asn Val Leu Leu Ile Asp Gly Pro Leu Ser Trp Tyr Ser
20 25 30

Asp Pro Gly Leu Ala Gly Val Ser Leu Thr Gly Gly Leu Ser Tyr Lys
35 40 45

Glu Asp Thr Lys Glu Leu Val Val Ala Lys Ala Gly Val Tyr Tyr Val
50 55 60

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

Ser Val Ser Leu Ala Leu His Leu Gln Pro Leu Arg Ser Ala Ala Gly
85 90 95

Ala Ala Ala Leu Ala Leu Thr Val Asp Leu Pro Pro Ala Ser Ser Glu
100 105 110

Ala Arg Asn Ser Ala Phe Gly Phe Gln Gly Arg Leu Leu His Leu Ser
115 120 125

Ala Gly Gln Arg Leu Gly Val His Leu His Thr Glu Ala Arg Ala Arg
130 135 140

His Ala Trp Gln Leu Thr Gln Gly Ala Thr Val Leu Gly Leu Phe Arg
145 150 155 160

Val Thr Pro Glu Ile Pro Ala
165

<210> 132
<211> 390
<212> PRT
<213> Homo sapiens

<400> 132

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

Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr

20

25

30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala
 35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
 50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu
 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Glu Pro Glu
 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu
 100 105 110

Met Val Glu Thr His Asn Glu Ile Tyr Asp Lys Phe Lys Gln Ser Thr
 115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Glu Leu Arg Glu Ala Val
 130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu
 145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn
 165 170 175

Asn Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser
 180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu
 195 200 205

Ser Arg Gly Gly Glu Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser
 210 215 220

Cys Asp Ser Arg Asp Asn Thr Leu Gln Val Asp Ile Asn Gly Phe Thr
225 230 235 240

Thr Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu Gln
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser
275 280 285

Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys
290 295 300

Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn
305 310 315 320

Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr
325 330 335

Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala
340 345 350

Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr
355 360 365

Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val
370 375 380

Arg Ser Cys Lys Cys Ser
385 390

<210> 133
<211> 112
<212> PRT
<213> Homo sapiens

<400> 133

Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys
1 5 10 15

Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp
20 25 30

Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys
35 40 45

Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu
50 55 60

Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Cys Cys Val Pro
65 70 75 80

Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro
85 90 95

Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser
100 105 110

<210> 134

<211> 413

<212> PRT

<213> Homo sapiens

<400> 134

Met His Tyr Cys Val Leu Ser Ala Phe Leu Ile Leu His Leu Val Thr
1 5 10 15

Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe
20 25 30

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu
35 40 45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Glu Glu Val Pro

50

55

60

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

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Asp Glu
85 90 95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Pro Phe Phe
100 105 110

Pro Ser Glu Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg Ile
115 120 125

Val Arg Phe Asp Val Ser Ala Met Glu Lys Asn Ala Ser Asn Leu Val
130 135 140

Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg Val
145 150 155 160

Pro Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp Leu
165 170 175

Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr Arg
180 185 190

Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val His Glu
195 200 205

Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu His
210 215 220

Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro Asn
225 230 235 240

Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr Ser
245 250 255

Thr Tyr Thr Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys Lys
260 265 270

Asn Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser Tyr
275 280 285

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

Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro
305 310 315 320

Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp Ile His Glu
325 330 335

Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu
340 345 350

Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu Tyr Asn Thr
355 360 365

Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu
370 375 380

Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro Lys Ile Glu
385 390 395 400

Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser
405 410

<210> 135
<211> 112
<212> PRT
<213> Homo sapiens

<400> 135

Ala Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys
1 5 10 15

Leu Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp
20 25 30

Ile His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys
35 40 45

Pro Tyr Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu
50 55 60

Tyr Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser
65 70 75 80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro
85 90 95

Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser
100 105 110

<210> 136

<211> 412

<212> PRT

<213> Homo sapiens

<400> 136

Met Lys Met His Leu Gln Arg Ala Leu Val Val Leu Ala Leu Leu Asn
1 5 10 15

Phe Ala Thr Val Ser Leu Ser Leu Ser Thr Cys Thr Thr Leu Asp Phe
20 25 30

Gly His Ile Lys Lys Lys Arg Val Glu Ala Ile Arg Gly Gln Ile Leu
35 40 45

Ser Lys Leu Arg Leu Thr Ser Pro Pro Glu Pro Thr Val Met Thr His
50 55 60

Val Pro Tyr Gln Val Leu Ala Leu Tyr Asn Ser Thr Arg Glu Leu Leu

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

His His Asn Pro His Leu Ile Leu Met Met Ile Pro Pro His Arg Leu
275 280 285

Asp Asn Pro Gly Gln Gly Gly Gln Arg Lys Lys Arg Ala Leu Asp Thr
290 295 300

Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu
305 310 315 320

Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro
325 330 335

Lys Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg
340 345 350

Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu
355 360 365

Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro Gln Asp Leu Glu
370 375 380

Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln
385 390 395 400

Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser
405 410

<210> 137
<211> 112
<212> PRT
<213> Homo sapiens

<400> 137

Ala Leu Asp Thr Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys
1 5 10 15

Val Arg Pro Leu Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp
20 25 30

Val His Glu Pro Lys Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys
35 40 45

Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu
50 55 60

Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Pro
65 70 75 80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro
85 90 95

Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser
100 105 110

<210> 138
<211> 112
<212> PRT
<213> Homo sapiens

<400> 138

Ala Leu Asp Thr Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys
1 5 10 15

Val Arg Pro Leu Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp
20 25 30

Val His Glu Pro Lys Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys
35 40 45

Pro Tyr Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu
50 55 60

Tyr Asn Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Ser Cys Val Pro
65 70 75 80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro

85

90

95

Lys Val Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser
 100 105 110

<210> 139

<211> 390

<212> PRT

<213> Homo sapiens

<400> 139

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

Trp Leu Leu Val Leu Thr Pro Gly Arg Pro Ala Ala Gly Leu Ser Thr
 20 25 30

Cys Lys Thr Ile Asp Met Glu Leu Val Lys Arg Lys Arg Ile Glu Ala
 35 40 45

Ile Arg Gly Gln Ile Leu Ser Lys Leu Arg Leu Ala Ser Pro Pro Ser
 50 55 60

Gln Gly Glu Val Pro Pro Gly Pro Leu Pro Glu Ala Val Leu Ala Leu
 65 70 75 80

Tyr Asn Ser Thr Arg Asp Arg Val Ala Gly Glu Ser Ala Glu Pro Glu
 85 90 95

Pro Glu Pro Glu Ala Asp Tyr Tyr Ala Lys Glu Val Thr Arg Val Leu
 100 105 110

Met Val Glu Thr His Asn Glu Ile Tyr Asp Lys Phe Lys Gln Ser Thr
 115 120 125

His Ser Ile Tyr Met Phe Phe Asn Thr Ser Glu Leu Arg Glu Ala Val
 130 135 140

Pro Glu Pro Val Leu Leu Ser Arg Ala Glu Leu Arg Leu Leu Arg Leu
145 150 155 160

Lys Leu Lys Val Glu Gln His Val Glu Leu Tyr Gln Lys Tyr Ser Asn
165 170 175

Asn Ser Trp Arg Tyr Leu Ser Asn Arg Leu Leu Ala Pro Ser Asp Ser
180 185 190

Pro Glu Trp Leu Ser Phe Asp Val Thr Gly Val Val Arg Gln Trp Leu
195 200 205

Ser Arg Gly Gly Glu Ile Glu Gly Phe Arg Leu Ser Ala His Cys Ser
210 215 220

Cys Asp Ser Arg Asp Asn Thr Leu Gln Val Asp Ile Asn Gly Phe Thr
225 230 235 240

Thr Gly Arg Arg Gly Asp Leu Ala Thr Ile His Gly Met Asn Arg Pro
245 250 255

Phe Leu Leu Leu Met Ala Thr Pro Leu Glu Arg Ala Gln His Leu Gln
260 265 270

Ser Ser Arg His Arg Arg Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser
275 280 285

Thr Glu Lys Asn Cys Cys Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys
290 295 300

Asp Leu Gly Trp Lys Trp Ile His Glu Pro Lys Gly Tyr His Ala Asn
305 310 315 320

Phe Cys Leu Gly Pro Cys Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr
325 330 335

Ser Lys Val Leu Ala Leu Tyr Asn Gln His Asn Pro Gly Ala Ser Ala
340 345 350

Ala Pro Cys Cys Val Pro Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr
355 360 365

Tyr Val Gly Arg Lys Pro Lys Val Glu Gln Leu Ser Asn Met Ile Val
370 375 380

Arg Ser Cys Lys Cys Ser
385 390

<210> 140
<211> 413
<212> PRT
<213> Homo sapiens

<400> 140

Met His Tyr Cys Val Leu Ser Ala Phe Leu Ile Leu His Leu Val Thr
1 5 10 15

Val Ala Leu Ser Leu Ser Thr Cys Ser Thr Leu Asp Met Asp Gln Phe
20 25 30

Met Arg Lys Arg Ile Glu Ala Ile Arg Gly Gln Ile Leu Ser Lys Leu
35 40 45

Lys Leu Thr Ser Pro Pro Glu Asp Tyr Pro Glu Pro Glu Glu Val Pro
50 55 60

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

Lys Ala Ser Arg Arg Ala Ala Ala Cys Glu Arg Glu Arg Ser Asp Glu
85 90 95

Glu Tyr Tyr Ala Lys Glu Val Tyr Lys Ile Asp Met Pro Pro Phe Phe
100 105 110

Pro Ser Glu Ala Ile Pro Pro Thr Phe Tyr Arg Pro Tyr Phe Arg Ile

115

120

125

Val Arg Phe Asp Val Ser Ala Met Glu Lys Asn Ala Ser Asn Leu Val
130 135 140

Lys Ala Glu Phe Arg Val Phe Arg Leu Gln Asn Pro Lys Ala Arg Val
145 150 155 160

Pro Glu Gln Arg Ile Glu Leu Tyr Gln Ile Leu Lys Ser Lys Asp Leu
165 170 175

Thr Ser Pro Thr Gln Arg Tyr Ile Asp Ser Lys Val Val Lys Thr Arg
180 185 190

Ala Glu Gly Glu Trp Leu Ser Phe Asp Val Thr Asp Ala Val His Glu
195 200 205

Trp Leu His His Lys Asp Arg Asn Leu Gly Phe Lys Ile Ser Leu His
210 215 220

Cys Pro Cys Cys Thr Phe Val Pro Ser Asn Asn Tyr Ile Ile Pro Asn
225 230 235 240

Lys Ser Glu Glu Leu Glu Ala Arg Phe Ala Gly Ile Asp Gly Thr Ser
245 250 255

Thr Tyr Thr Ser Gly Asp Gln Lys Thr Ile Lys Ser Thr Arg Lys Lys
260 265 270

Asn Ser Gly Lys Thr Pro His Leu Leu Leu Met Leu Leu Pro Ser Tyr
275 280 285

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

Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys Leu Arg Pro
305 310 315 320

Leu Tyr Ile Asp Phe Arg Arg Asp Leu Gly Trp Lys Trp Ile His Glu
325 330 335

Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys Pro Tyr Leu
340 345 350

Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu Tyr Asn Thr
355 360 365

Ile Asn Pro Glu Ala Ser Ala Ser Pro Cys Cys Val Ser Gln Asp Leu
370 375 380

Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro Lys Ile Glu
385 390 395 400

Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser
405 410

<210> 141
<211> 503
<212> PRT
<213> Homo sapiens

<400> 141

Met Glu Ala Ala Val Ala Ala Pro Arg Pro Arg Leu Leu Leu Leu Val
1 5 10 15

Leu Ala Ala Ala Ala Ala Ala Ala Ala Leu Leu Pro Gly Ala Thr
20 25 30

Ala Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys
35 40 45

Val Thr Asp Gly Leu Cys Phe Val Ser Val Thr Glu Thr Thr Asp Lys
50 55 60

Val Ile His Asn Ser Met Cys Ile Ala Glu Ile Asp Leu Ile Pro Arg
65 70 75 80

Asp Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr
85 90 95

Thr Thr Tyr Cys Cys Asn Gln Asp His Cys Asn Lys Ile Glu Leu Pro
100 105 110

Thr Thr Val Lys Ser Ser Pro Gly Leu Gly Pro Val Glu Leu Ala Ala
115 120 125

Val Ile Ala Gly Pro Val Cys Phe Val Cys Ile Ser Leu Met Leu Met
130 135 140

Val Tyr Ile Cys His Asn Arg Thr Val Ile His His Arg Val Pro Asn
145 150 155 160

Glu Glu Asp Pro Ser Leu Asp Arg Pro Phe Ile Ser Glu Gly Thr Thr
165 170 175

Leu Lys Asp Leu Ile Tyr Asp Met Thr Thr Ser Gly Ser Gly Ser Gly
180 185 190

Leu Pro Leu Leu Val Gln Arg Thr Ile Ala Arg Thr Ile Val Leu Gln
195 200 205

Glu Ser Ile Gly Lys Gly Arg Phe Gly Glu Val Trp Arg Gly Lys Trp
210 215 220

Arg Gly Glu Glu Val Ala Val Lys Ile Phe Ser Ser Arg Glu Glu Arg
225 230 235 240

Ser Trp Phe Arg Glu Ala Glu Ile Tyr Gln Thr Val Met Leu Arg His
245 250 255

Glu Asn Ile Leu Gly Phe Ile Ala Ala Asp Asn Lys Asp Asn Gly Thr
260 265 270

Trp Thr Gln Leu Trp Leu Val Ser Asp Tyr His Glu His Gly Ser Leu
275 280 285

Phe Asp Tyr Leu Asn Arg Tyr Thr Val Thr Val Glu Gly Met Ile Lys
290 295 300

Leu Ala Leu Ser Thr Ala Ser Gly Leu Ala His Leu His Met Glu Ile
305 310 315 320

Val Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp Leu Lys Ser
325 330 335

Lys Asn Ile Leu Val Lys Lys Asn Gly Thr Cys Cys Ile Ala Asp Leu
340 345 350

Gly Leu Ala Val Arg His Asp Ser Ala Thr Asp Thr Ile Asp Ile Ala
355 360 365

Pro Asn His Arg Val Gly Thr Lys Arg Tyr Met Ala Pro Glu Val Leu
370 375 380

Asp Asp Ser Ile Asn Met Lys His Phe Glu Ser Phe Lys Arg Ala Asp
385 390 395 400

Ile Tyr Ala Met Gly Leu Val Phe Trp Glu Ile Ala Arg Arg Cys Ser
405 410 415

Ile Gly Gly Ile His Glu Asp Tyr Gln Leu Pro Tyr Tyr Asp Leu Val
420 425 430

Pro Ser Asp Pro Ser Val Glu Glu Met Arg Lys Val Val Cys Glu Gln
435 440 445

Lys Leu Arg Pro Asn Ile Pro Asn Arg Trp Gln Ser Cys Glu Ala Leu
450 455 460

Arg Val Met Ala Lys Ile Met Arg Glu Cys Trp Tyr Ala Asn Gly Ala
465 470 475 480

Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Ser Gln Leu Ser
485 490 495

Gln Gln Glu Gly Ile Lys Met
500

<210> 142
<211> 93
<212> PRT
<213> Homo sapiens

<400> 142

Leu Gln Cys Phe Cys His Leu Cys Thr Lys Asp Asn Phe Thr Cys Val
1 5 10 15

Thr Asp Gly Leu Cys Phe Val Ser Val Thr Glu Thr Thr Asp Lys Val
20 25 30

Ile His Asn Ser Met Cys Ile Ala Glu Ile Asp Leu Ile Pro Arg Asp
35 40 45

Arg Pro Phe Val Cys Ala Pro Ser Ser Lys Thr Gly Ser Val Thr Thr
50 55 60

Thr Tyr Cys Cys Asn Gln Asp His Cys Asn Lys Ile Glu Leu Pro Thr
65 70 75 80

Thr Val Lys Ser Ser Pro Gly Leu Gly Pro Val Glu Leu
85 90

<210> 143
<211> 592
<212> PRT
<213> Homo sapiens

<400> 143

Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro Leu His Ile Val Leu
1 5 10 15

Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Asp
20 25 30

Val Glu Met Glu Ala Gln Lys Asp Glu Ile Ile Cys Pro Ser Cys Asn
35 40 45

Arg Thr Ala His Pro Leu Arg His Ile Asn Asn Asp Met Ile Val Thr
50 55 60

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
65 70 75 80

Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
85 90 95

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
100 105 110

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
115 120 125

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
130 135 140

Lys Cys Ile Met Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met
145 150 155 160

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
165 170 175

Glu Tyr Asn Thr Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln Val
180 185 190

Thr Gly Ile Ser Leu Leu Pro Pro Leu Gly Val Ala Ile Ser Val Ile
195 200 205

Ile Ile Phe Tyr Cys Tyr Arg Val Asn Arg Gln Gln Lys Leu Ser Ser
210 215 220

Thr Trp Glu Thr Gly Lys Thr Arg Lys Leu Met Glu Phe Ser Glu His
225 230 235 240

Cys Ala Ile Ile Leu Glu Asp Asp Arg Ser Asp Ile Ser Ser Thr Cys
245 250 255

Ala Asn Asn Ile Asn His Asn Thr Glu Leu Leu Pro Ile Glu Leu Asp
260 265 270

Thr Leu Val Gly Lys Gly Arg Phe Ala Glu Val Tyr Lys Ala Lys Leu
275 280 285

Lys Gln Asn Thr Ser Glu Gln Phe Glu Thr Val Ala Val Lys Ile Phe
290 295 300

Pro Tyr Glu Glu Tyr Ala Ser Trp Lys Thr Glu Lys Asp Ile Phe Ser
305 310 315 320

Asp Ile Asn Leu Lys His Glu Asn Ile Leu Gln Phe Leu Thr Ala Glu
325 330 335

Glu Arg Lys Thr Glu Leu Gly Lys Gln Tyr Trp Leu Ile Thr Ala Phe
340 345 350

His Ala Lys Gly Asn Leu Gln Glu Tyr Leu Thr Arg His Val Ile Ser
355 360 365

Trp Glu Asp Leu Arg Lys Leu Gly Ser Ser Leu Ala Arg Gly Ile Ala
370 375 380

His Leu His Ser Asp His Thr Pro Cys Gly Arg Pro Lys Met Pro Ile
385 390 395 400

Val His Arg Asp Leu Lys Ser Ser Asn Ile Leu Val Lys Asn Asp Leu
405 410 415

Thr Cys Cys Leu Cys Asp Phe Gly Leu Ser Leu Arg Leu Asp Pro Thr
420 425 430

Leu Ser Val Asp Asp Leu Ala Asn Ser Gly Gln Val Gly Thr Ala Arg
435 440 445

Tyr Met Ala Pro Glu Val Leu Glu Ser Arg Met Asn Leu Glu Asn Val
450 455 460

Glu Ser Phe Lys Gln Thr Asp Val Tyr Ser Met Ala Leu Val Leu Trp
465 470 475 480

Glu Met Thr Ser Arg Cys Asn Ala Val Gly Glu Val Lys Asp Tyr Glu
485 490 495

Pro Pro Phe Gly Ser Lys Val Arg Glu His Pro Cys Val Glu Ser Met
500 505 510

Lys Asp Asn Val Leu Arg Asp Arg Gly Arg Pro Glu Ile Pro Ser Phe
515 520 525

Trp Leu Asn His Gln Gly Ile Gln Met Val Cys Glu Thr Leu Thr Glu
530 535 540

Cys Trp Asp His Asp Pro Glu Ala Arg Leu Thr Ala Gln Cys Val Ala
545 550 555 560

Glu Arg Phe Ser Glu Leu Glu His Leu Asp Arg Leu Ser Gly Arg Ser
565 570 575

Cys Ser Glu Glu Lys Ile Pro Glu Asp Gly Ser Leu Asn Thr Thr Lys
580 585 590

<210> 144
<211> 154
<212> PRT
<213> Homo sapiens

<400> 144

Ile Pro Pro His Val Gln Lys Ser Asp Val Glu Met Glu Ala Gln Lys
1 5 10 15

Asp Glu Ile Ile Cys Pro Ser Cys Asn Arg Thr Ala His Pro Leu Arg
20 25 30

His Ile Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val Lys
35 40 45

Phe Pro Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp
50 55 60

Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu
65 70 75 80

Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn
85 90 95

Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp
100 105 110

Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys
115 120 125

Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu
130 135 140

Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu
145 150

<210> 145

<211> 567

<212> PRT

<213> Homo sapiens

<400> 145

Met Gly Arg Gly Leu Leu Arg Gly Leu Trp Pro Leu His Ile Val Leu
1 5 10 15

Trp Thr Arg Ile Ala Ser Thr Ile Pro Pro His Val Gln Lys Ser Val
20 25 30

Asn Asn Asp Met Ile Val Thr Asp Asn Asn Gly Ala Val Lys Phe Pro
35 40 45

Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
50 55 60

Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
65 70 75 80

Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
85 90 95

Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
100 105 110

Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
115 120 125

Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
130 135 140

Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp Leu
145 150 155 160

Leu Leu Val Ile Phe Gln Val Thr Gly Ile Ser Leu Leu Pro Pro Leu
165 170 175

Gly Val Ala Ile Ser Val Ile Ile Ile Phe Tyr Cys Tyr Arg Val Asn
180 185 190

Arg Gln Gln Lys Leu Ser Ser Thr Trp Glu Thr Gly Lys Thr Arg Lys
195 200 205

Leu Met Glu Phe Ser Glu His Cys Ala Ile Ile Leu Glu Asp Asp Arg
210 215 220

Ser Asp Ile Ser Ser Thr Cys Ala Asn Asn Ile Asn His Asn Thr Glu
225 230 235 240

Leu Leu Pro Ile Glu Leu Asp Thr Leu Val Gly Lys Gly Arg Phe Ala
245 250 255

Glu Val Tyr Lys Ala Lys Leu Lys Gln Asn Thr Ser Glu Gln Phe Glu
260 265 270

Thr Val Ala Val Lys Ile Phe Pro Tyr Glu Glu Tyr Ala Ser Trp Lys
275 280 285

Thr Glu Lys Asp Ile Phe Ser Asp Ile Asn Leu Lys His Glu Asn Ile
290 295 300

Leu Gln Phe Leu Thr Ala Glu Glu Arg Lys Thr Glu Leu Gly Lys Gln
305 310 315 320

Tyr Trp Leu Ile Thr Ala Phe His Ala Lys Gly Asn Leu Gln Glu Tyr
325 330 335

Leu Thr Arg His Val Ile Ser Trp Glu Asp Leu Arg Lys Leu Gly Ser
340 345 350

Ser Leu Ala Arg Gly Ile Ala His Leu His Ser Asp His Thr Pro Cys
355 360 365

Gly Arg Pro Lys Met Pro Ile Val His Arg Asp Leu Lys Ser Ser Asn
370 375 380

Ile Leu Val Lys Asn Asp Leu Thr Cys Cys Leu Cys Asp Phe Gly Leu
385 390 395 400

Ser Leu Arg Leu Asp Pro Thr Leu Ser Val Asp Asp Leu Ala Asn Ser
405 410 415

Gly Gln Val Gly Thr Ala Arg Tyr Met Ala Pro Glu Val Leu Glu Ser
420 425 430

Arg Met Asn Leu Glu Asn Val Glu Ser Phe Lys Gln Thr Asp Val Tyr
435 440 445

Ser Met Ala Leu Val Leu Trp Glu Met Thr Ser Arg Cys Asn Ala Val
450 455 460

Gly Glu Val Lys Asp Tyr Glu Pro Pro Phe Gly Ser Lys Val Arg Glu
465 470 475 480

His Pro Cys Val Glu Ser Met Lys Asp Asn Val Leu Arg Asp Arg Gly
485 490 495

Arg Pro Glu Ile Pro Ser Phe Trp Leu Asn His Gln Gly Ile Gln Met
500 505 510

Val Cys Glu Thr Leu Thr Glu Cys Trp Asp His Asp Pro Glu Ala Arg
515 520 525

Leu Thr Ala Gln Cys Val Ala Glu Arg Phe Ser Glu Leu Glu His Leu
530 535 540

Asp Arg Leu Ser Gly Arg Ser Cys Ser Glu Glu Lys Ile Pro Glu Asp
545 550 555 560

Gly Ser Leu Asn Thr Thr Lys
565

<210> 146

<211> 143

<212> PRT

<213> Homo sapiens

<400> 146

Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr
1 5 10 15

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
20 25 30

Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
35 40 45

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
50 55 60

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
65 70 75 80

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
85 90 95

Lys Cys Ile Met Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met
100 105 110

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
115 120 125

Glu Tyr Asn Thr Ser Asn Pro Asp Leu Leu Leu Val Ile Phe Gln
130 135 140

<210> 147
<211> 129
<212> PRT
<213> Homo sapiens

<400> 147

Ile Pro Pro His Val Gln Lys Ser Val Asn Asn Asp Met Ile Val Thr
1 5 10 15

Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys Asp
20 25 30

Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys
35 40 45

Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val
50 55 60

Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp
65 70 75 80

Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro
85 90 95

Lys Cys Ile Met Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met
100 105 110

Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu
115 120 125

Glu

<210> 148
<211> 114
<212> PRT
<213> Homo sapiens

<400> 148

Thr Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys
1 5 10 15

Asp Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn
20 25 30

Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala
35 40 45

Val Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His

50

55

60

Asp Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser
 65 70 75 80

Pro Lys Cys Ile Met Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe
 85 90 95

Met Cys Ser Cys Ser Ser Ala Glu Cys Asn Asp Asn Ile Ile Phe Ser
 100 105 110

Glu Glu

<210> 149
 <211> 104
 <212> PRT
 <213> Homo sapiens

<400> 149

Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
 1 5 10 15

Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
 20 25 30

Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
 35 40 45

Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
 50 55 60

Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
 65 70 75 80

Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Ala Glu Cys Asn
 85 90 95

Asp Asn Ile Ile Phe Ser Glu Glu
100

<210> 150
<211> 111
<212> PRT
<213> Homo sapiens

<400> 150

Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
1 5 10 15

Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
20 25 30

Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
35 40 45

Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
50 55 60

Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
65 70 75 80

Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Ala Glu Cys Asn
85 90 95

Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp
100 105 110

<210> 151
<211> 851
<212> PRT
<213> Homo sapiens

<400> 151

Met Thr Ser His Tyr Val Ile Ala Ile Phe Ala Leu Met Ser Ser Cys
1 5 10 15

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

Val Ser Ala Ser His Pro Val Gln Ala Leu Met Glu Ser Phe Thr Val
35 40 45

Leu Ser Gly Cys Ala Ser Arg Gly Thr Thr Gly Leu Pro Gln Glu Val
50 55 60

His Val Leu Asn Leu Arg Thr Ala Gly Gln Gly Pro Gly Gln Leu Gln
65 70 75 80

Arg Glu Val Thr Leu His Leu Asn Pro Ile Ser Ser Val His Ile His
85 90 95

His Lys Ser Val Val Phe Leu Leu Asn Ser Pro His Pro Leu Val Trp
100 105 110

His Leu Lys Thr Glu Arg Leu Ala Thr Gly Val Ser Arg Leu Phe Leu
115 120 125

Val Ser Glu Gly Ser Val Val Gln Phe Ser Ser Ala Asn Phe Ser Leu
130 135 140

Thr Ala Glu Thr Glu Glu Arg Asn Phe Pro His Gly Asn Glu His Leu
145 150 155 160

Leu Asn Trp Ala Arg Lys Glu Tyr Gly Ala Val Thr Ser Phe Thr Glu
165 170 175

Leu Lys Ile Ala Arg Asn Ile Tyr Ile Lys Val Gly Glu Asp Gln Val
180 185 190

Phe Pro Pro Lys Cys Asn Ile Gly Lys Asn Phe Leu Ser Leu Asn Tyr
195 200 205

Leu Ala Glu Tyr Leu Gln Pro Lys Ala Ala Glu Gly Cys Val Met Ser
210 215 220

Ser Gln Pro Gln Asn Glu Glu Val His Ile Ile Glu Leu Ile Thr Pro
225 230 235 240

Asn Ser Asn Pro Tyr Ser Ala Phe Gln Val Asp Ile Thr Ile Asp Ile
245 250 255

Arg Pro Ser Gln Glu Asp Leu Glu Val Val Lys Asn Leu Ile Leu Ile
260 265 270

Leu Lys Cys Lys Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp Val
275 280 285

Lys Gly Ser Leu Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly Lys
290 295 300

Glu Ser Glu Arg Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp Ile
305 310 315 320

Pro Ser Thr Gln Gly Asn Leu Val Lys Trp Ala Leu Asp Asn Gly Tyr
325 330 335

Ser Pro Ile Thr Ser Tyr Thr Met Ala Pro Val Ala Asn Arg Phe His
340 345 350

Leu Arg Leu Glu Asn Asn Ala Glu Glu Met Gly Asp Glu Glu Val His
355 360 365

Thr Ile Pro Pro Glu Leu Arg Ile Leu Leu Asp Pro Gly Ala Leu Pro
370 375 380

Ala Leu Gln Asn Pro Pro Ile Arg Gly Gly Glu Gly Gln Asn Gly Gly
385 390 395 400

Leu Pro Phe Pro Phe Pro Asp Ile Ser Arg Arg Val Trp Asn Glu Glu
405 410 415

Gly Glu Asp Gly Leu Pro Arg Pro Lys Asp Pro Val Ile Pro Ser Ile
420 425 430

Gln Leu Phe Pro Gly Leu Arg Glu Pro Glu Glu Val Gln Gly Ser Val
435 440 445

Asp Ile Ala Leu Ser Val Lys Cys Asp Asn Glu Lys Met Ile Val Ala
450 455 460

Val Glu Lys Asp Ser Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp Val
465 470 475 480

Thr Leu Leu Asp Pro Thr Cys Lys Ala Lys Met Asn Gly Thr His Phe
485 490 495

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

Ala Leu Asp Gly Val Val Tyr Tyr Asn Ser Ile Val Ile Gln Val Pro
515 520 525

Ala Leu Gly Asp Ser Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu Glu
530 535 540

Ser Gly Asp Asn Gly Phe Pro Gly Asp Met Asp Glu Gly Asp Ala Ser
545 550 555 560

Leu Phe Thr Arg Pro Glu Ile Val Val Phe Asn Cys Ser Leu Gln Gln
565 570 575

Val Arg Asn Pro Ser Ser Phe Gln Glu Gln Pro His Gly Asn Ile Thr
580 585 590

Phe Asn Met Glu Leu Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln
595 600 605

Gly Val Phe Ser Val Pro Glu Asn Gly His Val Tyr Val Glu Val Ser
610 615 620

Val Thr Lys Ala Glu Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe
625 630 635 640

Ile Ser Pro Tyr Ser Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile
645 650 655

Glu Asn Ile Cys Pro Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys
660 665 670

Arg Val His Phe Pro Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe
675 680 685

Ser Phe Val Phe Lys Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln
690 695 700

Cys Glu Leu Thr Leu Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu
705 710 715 720

Pro Lys Cys Val Pro Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser
725 730 735

Ile Ile Trp Ala Met Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu
740 745 750

Ala Val Ile His His Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met
755 760 765

Lys Glu Pro Asn Pro Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr
770 775 780

Leu Thr Val Met Gly Ile Ala Phe Ala Ala Phe Val Ile Gly Ala Leu
785 790 795 800

Leu Thr Gly Ala Leu Trp Tyr Ile Tyr Ser His Thr Gly Glu Thr Ala
805 810 815

Gly Arg Gln Gln Val Pro Thr Ser Pro Pro Ala Ser Glu Asn Ser Ser
820 825 830

Ala Ala His Ser Ile Gly Ser Thr Gln Ser Thr Pro Cys Ser Ser Ser
835 840 845

Ser Thr Ala
850

<210> 152
<211> 750
<212> PRT
<213> Homo sapiens

<400> 152

Cys Glu Leu Ser Pro Val Ser Ala Ser His Pro Val Gln Ala Leu Met
1 5 10 15

Glu Ser Phe Thr Val Leu Ser Gly Cys Ala Ser Arg Gly Thr Thr Gly
20 25 30

Leu Pro Gln Glu Val His Val Leu Asn Leu Arg Thr Ala Gly Gln Gly
35 40 45

Pro Gly Gln Leu Gln Arg Glu Val Thr Leu His Leu Asn Pro Ile Ser
50 55 60

Ser Val His Ile His His Lys Ser Val Val Phe Leu Leu Asn Ser Pro
65 70 75 80

His Pro Leu Val Trp His Leu Lys Thr Glu Arg Leu Ala Thr Gly Val
85 90 95

Ser Arg Leu Phe Leu Val Ser Glu Gly Ser Val Val Gln Phe Ser Ser
100 105 110

Ala Asn Phe Ser Leu Thr Ala Glu Thr Glu Glu Arg Asn Phe Pro His
115 120 125

Gly Asn Glu His Leu Leu Asn Trp Ala Arg Lys Glu Tyr Gly Ala Val
130 135 140

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

Gly Glu Asp Gln Val Phe Pro Pro Lys Cys Asn Ile Gly Lys Asn Phe
165 170 175

Leu Ser Leu Asn Tyr Leu Ala Glu Tyr Leu Gln Pro Lys Ala Ala Glu
180 185 190

Gly Cys Val Met Ser Ser Gln Pro Gln Asn Glu Glu Val His Ile Ile
195 200 205

Glu Leu Ile Thr Pro Asn Ser Asn Pro Tyr Ser Ala Phe Gln Val Asp
210 215 220

Ile Thr Ile Asp Ile Arg Pro Ser Gln Glu Asp Leu Glu Val Val Lys
225 230 235 240

Asn Leu Ile Leu Ile Leu Lys Cys Lys Lys Ser Val Asn Trp Val Ile
245 250 255

Lys Ser Phe Asp Val Lys Gly Ser Leu Lys Ile Ile Ala Pro Asn Ser
260 265 270

Ile Gly Phe Gly Lys Glu Ser Glu Arg Ser Met Thr Met Thr Lys Ser
275 280 285

Ile Arg Asp Asp Ile Pro Ser Thr Gln Gly Asn Leu Val Lys Trp Ala
290 295 300

Leu Asp Asn Gly Tyr Ser Pro Ile Thr Ser Tyr Thr Met Ala Pro Val
305 310 315 320

Ala Asn Arg Phe His Leu Arg Leu Glu Asn Asn Ala Glu Glu Met Gly

325

330

335

Asp Glu Glu Val His Thr Ile Pro Pro Glu Leu Arg Ile Leu Leu Asp
 340 345 350

Pro Gly Ala Leu Pro Ala Leu Gln Asn Pro Pro Ile Arg Gly Gly Glu
 355 360 365

Gly Gln Asn Gly Gly Leu Pro Phe Pro Phe Pro Asp Ile Ser Arg Arg
 370 375 380

Val Trp Asn Glu Glu Gly Glu Asp Gly Leu Pro Arg Pro Lys Asp Pro
 385 390 395 400

Val Ile Pro Ser Ile Gln Leu Phe Pro Gly Leu Arg Glu Pro Glu Glu
 405 410 415

Val Gln Gly Ser Val Asp Ile Ala Leu Ser Val Lys Cys Asp Asn Glu
 420 425 430

Lys Met Ile Val Ala Val Glu Lys Asp Ser Phe Gln Ala Ser Gly Tyr
 435 440 445

Ser Gly Met Asp Val Thr Leu Leu Asp Pro Thr Cys Lys Ala Lys Met
 450 455 460

Asn Gly Thr His Phe Val Leu Glu Ser Pro Leu Asn Gly Cys Gly Thr
 465 470 475 480

Arg Pro Arg Trp Ser Ala Leu Asp Gly Val Val Tyr Tyr Asn Ser Ile
 485 490 495

Val Ile Gln Val Pro Ala Leu Gly Asp Ser Ser Gly Trp Pro Asp Gly
 500 505 510

Tyr Glu Asp Leu Glu Ser Gly Asp Asn Gly Phe Pro Gly Asp Met Asp
 515 520 525

Glu Gly Asp Ala Ser Leu Phe Thr Arg Pro Glu Ile Val Val Phe Asn
530 535 540

Cys Ser Leu Gln Gln Val Arg Asn Pro Ser Ser Phe Gln Glu Gln Pro
545 550 555 560

His Gly Asn Ile Thr Phe Asn Met Glu Leu Tyr Asn Thr Asp Leu Phe
565 570 575

Leu Val Pro Ser Gln Gly Val Phe Ser Val Pro Glu Asn Gly His Val
580 585 590

Tyr Val Glu Val Ser Val Thr Lys Ala Glu Gln Glu Leu Gly Phe Ala
595 600 605

Ile Gln Thr Cys Phe Ile Ser Pro Tyr Ser Asn Pro Asp Arg Met Ser
610 615 620

His Tyr Thr Ile Ile Glu Asn Ile Cys Pro Lys Asp Glu Ser Val Lys
625 630 635 640

Phe Tyr Ser Pro Lys Arg Val His Phe Pro Ile Pro Gln Ala Asp Met
645 650 655

Asp Lys Lys Arg Phe Ser Phe Val Phe Lys Pro Val Phe Asn Thr Ser
660 665 670

Leu Leu Phe Leu Gln Cys Glu Leu Thr Leu Cys Thr Lys Met Glu Lys
675 680 685

His Pro Gln Lys Leu Pro Lys Cys Val Pro Pro Asp Glu Ala Cys Thr
690 695 700

Ser Leu Asp Ala Ser Ile Ile Trp Ala Met Met Gln Asn Lys Lys Thr
705 710 715 720

Phe Thr Lys Pro Leu Ala Val Ile His His Glu Ala Glu Ser Lys Glu

725

730

735

Lys Gly Pro Ser Met Lys Glu Pro Asn Pro Ile Ser Pro Pro
 740 745 750

<210> 153

<211> 850

<212> PRT

<213> Homo sapiens

<400> 153

Met Thr Ser His Tyr Val Ile Ala Ile Phe Ala Leu Met Ser Ser Cys
 1 5 10 15

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

Val Ser Ala Ser His Pro Val Gln Ala Leu Met Glu Ser Phe Thr Val
 35 40 45

Leu Ser Gly Cys Ala Ser Arg Gly Thr Thr Gly Leu Pro Gln Glu Val
 50 55 60

His Val Leu Asn Leu Arg Thr Ala Gly Gln Gly Pro Gly Gln Leu Gln
 65 70 75 80

Arg Glu Val Thr Leu His Leu Asn Pro Ile Ser Ser Val His Ile His
 85 90 95

His Lys Ser Val Val Phe Leu Leu Asn Ser Pro His Pro Leu Val Trp
 100 105 110

His Leu Lys Thr Glu Arg Leu Ala Thr Gly Val Ser Arg Leu Phe Leu
 115 120 125

Val Ser Glu Gly Ser Val Val Gln Phe Ser Ser Ala Asn Phe Ser Leu
 130 135 140

Thr Ala Glu Thr Glu Glu Arg Asn Phe Pro His Gly Asn Glu His Leu
145 150 155 160

Leu Asn Trp Ala Arg Lys Glu Tyr Gly Ala Val Thr Ser Phe Thr Glu
165 170 175

Leu Lys Ile Ala Arg Asn Ile Tyr Ile Lys Val Gly Glu Asp Gln Val
180 185 190

Phe Pro Pro Lys Cys Asn Ile Gly Lys Asn Phe Leu Ser Leu Asn Tyr
195 200 205

Leu Ala Glu Tyr Leu Gln Pro Lys Ala Ala Glu Gly Cys Val Met Ser
210 215 220

Ser Gln Pro Gln Asn Glu Glu Val His Ile Ile Glu Leu Ile Thr Pro
225 230 235 240

Asn Ser Asn Pro Tyr Ser Ala Phe Gln Val Asp Ile Thr Ile Asp Ile
245 250 255

Arg Pro Ser Gln Glu Asp Leu Glu Val Val Lys Asn Leu Ile Leu Ile
260 265 270

Leu Lys Cys Lys Lys Ser Val Asn Trp Val Ile Lys Ser Phe Asp Val
275 280 285

Lys Gly Ser Leu Lys Ile Ile Ala Pro Asn Ser Ile Gly Phe Gly Lys
290 295 300

Glu Ser Glu Arg Ser Met Thr Met Thr Lys Ser Ile Arg Asp Asp Ile
305 310 315 320

Pro Ser Thr Gln Gly Asn Leu Val Lys Trp Ala Leu Asp Asn Gly Tyr
325 330 335

Ser Pro Ile Thr Ser Tyr Thr Met Ala Pro Val Ala Asn Arg Phe His
340 345 350

Leu Arg Leu Glu Asn Asn Glu Glu Met Gly Asp Glu Glu Val His Thr
355 360 365

Ile Pro Pro Glu Leu Arg Ile Leu Leu Asp Pro Gly Ala Leu Pro Ala
370 375 380

Leu Gln Asn Pro Pro Ile Arg Gly Gly Glu Gly Gln Asn Gly Gly Leu
385 390 395 400

Pro Phe Pro Phe Pro Asp Ile Ser Arg Arg Val Trp Asn Glu Glu Gly
405 410 415

Glu Asp Gly Leu Pro Arg Pro Lys Asp Pro Val Ile Pro Ser Ile Gln
420 425 430

Leu Phe Pro Gly Leu Arg Glu Pro Glu Glu Val Gln Gly Ser Val Asp
435 440 445

Ile Ala Leu Ser Val Lys Cys Asp Asn Glu Lys Met Ile Val Ala Val
450 455 460

Glu Lys Asp Ser Phe Gln Ala Ser Gly Tyr Ser Gly Met Asp Val Thr
465 470 475 480

Leu Leu Asp Pro Thr Cys Lys Ala Lys Met Asn Gly Thr His Phe Val
485 490 495

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

Leu Asp Gly Val Val Tyr Tyr Asn Ser Ile Val Ile Gln Val Pro Ala
515 520 525

Leu Gly Asp Ser Ser Gly Trp Pro Asp Gly Tyr Glu Asp Leu Glu Ser
530 535 540

Gly Asp Asn Gly Phe Pro Gly Asp Met Asp Glu Gly Asp Ala Ser Leu
545 550 555 560

Phe Thr Arg Pro Glu Ile Val Val Phe Asn Cys Ser Leu Gln Gln Val
565 570 575

Arg Asn Pro Ser Ser Phe Gln Glu Gln Pro His Gly Asn Ile Thr Phe
580 585 590

Asn Met Glu Leu Tyr Asn Thr Asp Leu Phe Leu Val Pro Ser Gln Gly
595 600 605

Val Phe Ser Val Pro Glu Asn Gly His Val Tyr Val Glu Val Ser Val
610 615 620

Thr Lys Ala Glu Gln Glu Leu Gly Phe Ala Ile Gln Thr Cys Phe Ile
625 630 635 640

Ser Pro Tyr Ser Asn Pro Asp Arg Met Ser His Tyr Thr Ile Ile Glu
645 650 655

Asn Ile Cys Pro Lys Asp Glu Ser Val Lys Phe Tyr Ser Pro Lys Arg
660 665 670

Val His Phe Pro Ile Pro Gln Ala Asp Met Asp Lys Lys Arg Phe Ser
675 680 685

Phe Val Phe Lys Pro Val Phe Asn Thr Ser Leu Leu Phe Leu Gln Cys
690 695 700

Glu Leu Thr Leu Cys Thr Lys Met Glu Lys His Pro Gln Lys Leu Pro
705 710 715 720

Lys Cys Val Pro Pro Asp Glu Ala Cys Thr Ser Leu Asp Ala Ser Ile
725 730 735

Ile Trp Ala Met Met Gln Asn Lys Lys Thr Phe Thr Lys Pro Leu Ala
740 745 750

Val Ile His His Glu Ala Glu Ser Lys Glu Lys Gly Pro Ser Met Lys
755 760 765

Glu Pro Asn Pro Ile Ser Pro Pro Ile Phe His Gly Leu Asp Thr Leu
770 775 780

Thr Val Met Gly Ile Ala Phe Ala Ala Phe Val Ile Gly Ala Leu Leu
785 790 795 800

Thr Gly Ala Leu Trp Tyr Ile Tyr Ser His Thr Gly Glu Thr Ala Gly
805 810 815

Arg Gln Gln Val Pro Thr Ser Pro Pro Ala Ser Glu Asn Ser Ser Ala
820 825 830

Ala His Ser Ile Gly Ser Thr Gln Ser Thr Pro Cys Ser Ser Ser Ser
835 840 845

Thr Ala
850

<210> 154
<211> 761
<212> PRT
<213> Homo sapiens

<400> 154

Leu Cys Glu Leu Ser Pro Val Ser Ala Ser His Pro Val Gln Ala Leu
1 5 10 15

Met Glu Ser Phe Thr Val Leu Ser Gly Cys Ala Ser Arg Gly Thr Thr
20 25 30

Gly Leu Pro Gln Glu Val His Val Leu Asn Leu Arg Thr Ala Gly Gln
35 40 45

Gly Pro Gly Gln Leu Gln Arg Glu Val Thr Leu His Leu Asn Pro Ile

50

55

60

Ser Ser Val His Ile His His Lys Ser Val Val Phe Leu Leu Asn Ser
65 70 75 80

Pro His Pro Leu Val Trp His Leu Lys Thr Glu Arg Leu Ala Thr Gly
85 90 95

Val Ser Arg Leu Phe Leu Val Ser Glu Gly Ser Val Val Gln Phe Ser
100 105 110

Ser Ala Asn Phe Ser Leu Thr Ala Glu Thr Glu Glu Arg Asn Phe Pro
115 120 125

His Gly Asn Glu His Leu Leu Asn Trp Ala Arg Lys Glu Tyr Gly Ala
130 135 140

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

Val Gly Glu Asp Gln Val Phe Pro Pro Lys Cys Asn Ile Gly Lys Asn
165 170 175

Phe Leu Ser Leu Asn Tyr Leu Ala Glu Tyr Leu Gln Pro Lys Ala Ala
180 185 190

Glu Gly Cys Val Met Ser Ser Gln Pro Gln Asn Glu Glu Val His Ile
195 200 205

Ile Glu Leu Ile Thr Pro Asn Ser Asn Pro Tyr Ser Ala Phe Gln Val
210 215 220

Asp Ile Thr Ile Asp Ile Arg Pro Ser Gln Glu Asp Leu Glu Val Val
225 230 235 240

Lys Asn Leu Ile Leu Ile Leu Lys Cys Lys Lys Ser Val Asn Trp Val
245 250 255

Ile Lys Ser Phe Asp Val Lys Gly Ser Leu Lys Ile Ile Ala Pro Asn
260 265 270

Ser Ile Gly Phe Gly Lys Glu Ser Glu Arg Ser Met Thr Met Thr Lys
275 280 285

Ser Ile Arg Asp Asp Ile Pro Ser Thr Gln Gly Asn Leu Val Lys Trp
290 295 300

Ala Leu Asp Asn Gly Tyr Ser Pro Ile Thr Ser Tyr Thr Met Ala Pro
305 310 315 320

Val Ala Asn Arg Phe His Leu Arg Leu Glu Asn Asn Glu Glu Met Gly
325 330 335

Asp Glu Glu Val His Thr Ile Pro Pro Glu Leu Arg Ile Leu Leu Asp
340 345 350

Pro Gly Ala Leu Pro Ala Leu Gln Asn Pro Pro Ile Arg Gly Gly Glu
355 360 365

Gly Gln Asn Gly Gly Leu Pro Phe Pro Phe Pro Asp Ile Ser Arg Arg
370 375 380

Val Trp Asn Glu Glu Gly Glu Asp Gly Leu Pro Arg Pro Lys Asp Pro
385 390 395 400

Val Ile Pro Ser Ile Gln Leu Phe Pro Gly Leu Arg Glu Pro Glu Glu
405 410 415

Val Gln Gly Ser Val Asp Ile Ala Leu Ser Val Lys Cys Asp Asn Glu
420 425 430

Lys Met Ile Val Ala Val Glu Lys Asp Ser Phe Gln Ala Ser Gly Tyr
435 440 445

Ser Gly Met Asp Val Thr Leu Leu Asp Pro Thr Cys Lys Ala Lys Met

450

455

460

Asn Gly Thr His Phe Val Leu Glu Ser Pro Leu Asn Gly Cys Gly Thr
 465 470 475 480

Arg Pro Arg Trp Ser Ala Leu Asp Gly Val Val Tyr Tyr Asn Ser Ile
 485 490 495

Val Ile Gln Val Pro Ala Leu Gly Asp Ser Ser Gly Trp Pro Asp Gly
 500 505 510

Tyr Glu Asp Leu Glu Ser Gly Asp Asn Gly Phe Pro Gly Asp Met Asp
 515 520 525

Glu Gly Asp Ala Ser Leu Phe Thr Arg Pro Glu Ile Val Val Phe Asn
 530 535 540

Cys Ser Leu Gln Gln Val Arg Asn Pro Ser Ser Phe Gln Glu Gln Pro
 545 550 555 560

His Gly Asn Ile Thr Phe Asn Met Glu Leu Tyr Asn Thr Asp Leu Phe
 565 570 575

Leu Val Pro Ser Gln Gly Val Phe Ser Val Pro Glu Asn Gly His Val
 580 585 590

Tyr Val Glu Val Ser Val Thr Lys Ala Glu Gln Glu Leu Gly Phe Ala
 595 600 605

Ile Gln Thr Cys Phe Ile Ser Pro Tyr Ser Asn Pro Asp Arg Met Ser
 610 615 620

His Tyr Thr Ile Ile Glu Asn Ile Cys Pro Lys Asp Glu Ser Val Lys
 625 630 635 640

Phe Tyr Ser Pro Lys Arg Val His Phe Pro Ile Pro Gln Ala Asp Met
 645 650 655

Asp Lys Lys Arg Phe Ser Phe Val Phe Lys Pro Val Phe Asn Thr Ser
660 665 670

Leu Leu Phe Leu Gln Cys Glu Leu Thr Leu Cys Thr Lys Met Glu Lys
675 680 685

His Pro Gln Lys Leu Pro Lys Cys Val Pro Pro Asp Glu Ala Cys Thr
690 695 700

Ser Leu Asp Ala Ser Ile Ile Trp Ala Met Met Gln Asn Lys Lys Thr
705 710 715 720

Phe Thr Lys Pro Leu Ala Val Ile His His Glu Ala Glu Ser Lys Glu
725 730 735

Lys Gly Pro Ser Met Lys Glu Pro Asn Pro Ile Ser Pro Pro Ile Phe
740 745 750

His Gly Leu Asp Thr Leu Thr Val Met
755 760

<210> 155
<211> 814
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 155

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
20 25 30

Thr Arg Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe
35 40 45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val
65 70 75 80

Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp
85 90 95

Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn
100 105 110

Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu
115 120 125

Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu
130 135 140

Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg
145 150 155 160

Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly
165 170 175

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

Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro
195 200 205

Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser
210 215 220

Ala Gln Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
225 230 235 240

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys

245

250

255

Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln
 260 265 270

Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val
 275 280 285

Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg
 290 295 300

Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp
 305 310 315 320

Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr Cys Ile
 325 330 335

Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu
 340 345 350

Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro
 355 360 365

Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr
 370 375 380

Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg
 385 390 395 400

Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp
 405 410 415

Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp
 420 425 430

Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala
 435 440 445

Ala Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
450 455 460

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
465 470 475 480

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
485 490 495

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
500 505 510

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
515 520 525

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
530 535 540

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
545 550 555 560

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
565 570 575

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn
580 585 590

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
595 600 605

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
610 615 620

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
625 630 635 640

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys

645

650

655

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
 660 665 670

Ser Leu Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 675 680 685

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Leu
 690 695 700

Asp Thr Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg
 705 710 715 720

Pro Leu Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His
 725 730 735

Glu Pro Lys Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr
 740 745 750

Leu Arg Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn
 755 760 765

Thr Leu Asn Pro Glu Ala Ser Ala Ser Pro Ser Cys Val Pro Gln Asp
 770 775 780

Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val
 785 790 795 800

Glu Gln Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser
 805 810

<210> 156

<211> 956

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 156

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
20 25 30

Thr Arg Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe
35 40 45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val
65 70 75 80

Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp
85 90 95

Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn
100 105 110

Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu
115 120 125

Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu
130 135 140

Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg
145 150 155 160

Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly
165 170 175

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

Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro
195 200 205

Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser
210 215 220

Ala Gln Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
225 230 235 240

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys
245 250 255

Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln
260 265 270

Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val
275 280 285

Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg
290 295 300

Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp
305 310 315 320

Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr Cys Ile
325 330 335

Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu
340 345 350

Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro
355 360 365

Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr
370 375 380

Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg

385 390 395 400

Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp
405 410 415

Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp
420 425 430

Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala
435 440 445

Ala Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
450 455 460

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
465 470 475 480

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
485 490 495

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
500 505 510

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
515 520 525

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
530 535 540

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
545 550 555 560

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
565 570 575

Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
580 585 590

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
595 600 605

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
610 615 620

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
625 630 635 640

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
645 650 655

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
660 665 670

Ser Leu Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
675 680 685

Gly Gly Gly Ser Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr
690 695 700

Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile
705 710 715 720

Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp
725 730 735

Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr
740 745 750

His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys
755 760 765

Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser
770 775 780

Ala Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser

785 790 795 800

Asn Pro Asp Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
805 810 815

Gly Ser Gly Gly Gly Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys
820 825 830

Thr Gln Leu Gln Leu Glu Ala Leu Leu Leu Asp Leu Gln Met Ile Leu
835 840 845

Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr
850 855 860

Ala Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln
865 870 875 880

Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala
885 890 895

Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile
900 905 910

Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys
915 920 925

Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp
930 935 940

Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
945 950 955

<210> 157
<211> 812
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 157

Asn Phe Ile Arg Met Val Ile Ser Asn Pro Ala Ala Thr Gly Gly Gly
1 5 10 15

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Asp Thr Arg
20 25 30

Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe Asn Gly
35 40 45

Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu Glu
50 55 60

Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr Glu
65 70 75 80

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

Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr Gly
100 105 110

Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu Val Thr
115 120 125

Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu Val
130 135 140

Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg Trp Phe
145 150 155 160

Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly Leu Ile
165 170 175

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

Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser Leu
195 200 205

Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala Gln
210 215 220

Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys Glu Glu
245 250 255

His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly
260 265 270

Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met
275 280 285

Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala
290 295 300

Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala
305 310 315 320

Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr Cys Ile Thr Asn
325 330 335

Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg
340 345 350

Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val
355 360 365

Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val
370 375 380

Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe

385		390		395		400
His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg						
		405		410		415
Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe						
		420		425		430
Asp Ala Pro Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly						
		435		440		445
Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala						
		450		455		460
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu						
465		470		475		480
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser						
		485		490		495
His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu						
		500		505		510
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr						
		515		520		525
Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn						
		530		535		540
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro						
545		550		555		560
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln						
		565		570		575
Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val						
		580		585		590

Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
595 600 605

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
610 615 620

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
625 630 635 640

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
645 650 655

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
660 665 670

Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
675 680 685

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Leu Asp Thr
690 695 700

Asn Tyr Cys Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu
705 710 715 720

Tyr Ile Asp Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro
725 730 735

Lys Gly Tyr Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg
740 745 750

Ser Ala Asp Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu
755 760 765

Asn Pro Glu Ala Ser Ala Ser Pro Ser Cys Val Pro Gln Asp Leu Glu
770 775 780

Pro Leu Thr Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln

785 790 795 800

Leu Ser Asn Met Val Val Lys Ser Cys Lys Cys Ser
 805 810

<210> 158
<211> 954
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 158

Asn Phe Ile Arg Met Val Ile Ser Asn Pro Ala Ala Thr Gly Gly Gly
1 5 10 15

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Asp Thr Arg
 20 25 30

Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe Asn Gly
 35 40 45

Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu Glu
50 55 60

Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr Glu
65 70 75 80

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

Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr Gly
 100 105 110

Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu Val Thr
115 120 125

Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu Val

130

135

140

Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg Trp Phe
 145 150 155 160

Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly Leu Ile
 165 170 175

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

Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser Leu
 195 200 205

Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala Gln
 210 215 220

Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys Glu Glu
 245 250 255

His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly
 260 265 270

Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met
 275 280 285

Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala
 290 295 300

Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala
 305 310 315 320

Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr Cys Ile Thr Asn
 325 330 335

Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg
340 345 350

Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val
355 360 365

Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val
370 375 380

Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe
385 390 395 400

His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg
405 410 415

Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe
420 425 430

Asp Ala Pro Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly
435 440 445

Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
450 455 460

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
465 470 475 480

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
485 490 495

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
500 505 510

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
515 520 525

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn

530

535

540

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
 545 550 555 560

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
 565 570 575

Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
 580 585 590

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 595 600 605

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 610 615 620

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
 625 630 635 640

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 645 650 655

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 660 665 670

Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 675 680 685

Gly Ser Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp
 690 695 700

Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu
 705 710 715 720

Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn
 725 730 735

Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp
740 745 750

Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys
755 760 765

Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Ala Glu
770 775 780

Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro
785 790 795 800

Asp Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
805 810 815

Gly Gly Gly Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln
820 825 830

Leu Gln Leu Glu Ala Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly
835 840 845

Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Ala Lys
850 855 860

Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu
865 870 875 880

Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser
885 890 895

Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val
900 905 910

Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr
915 920 925

Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr

930

935

940

Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
945 950

<210> 159
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 159

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly
1 5 10 15

<210> 160
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 160

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 161
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 161

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser

20

25

<210> 162
<211> 8
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 162

Gly Gly Ser Ala Ala Ala Gly Gly
1 5

<210> 163
<211> 13
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 163

Asn Phe Ile Arg Met Val Ile Ser Asn Pro Ala Ala Thr
1 5 10

<210> 164
<211> 803
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 164

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
20 25 30

Thr Arg Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe

35

40

45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
 50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val
 65 70 75 80

Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp
 85 90 95

Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn
 100 105 110

Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu
 115 120 125

Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu
 130 135 140

Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg
 145 150 155 160

Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly
 165 170 175

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

Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro
 195 200 205

Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser
 210 215 220

Ala Gln Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 225 230 235 240

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys
245 250 255

Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln
260 265 270

Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val
275 280 285

Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg
290 295 300

Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp
305 310 315 320

Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr Cys Ile
325 330 335

Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu
340 345 350

Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro
355 360 365

Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr
370 375 380

Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg
385 390 395 400

Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp
405 410 415

Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp
420 425 430

Glu Phe Asp Ala Pro Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala

435

440

445

Ala Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
 450 455 460

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
 465 470 475 480

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
 485 490 495

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
 500 505 510

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
 515 520 525

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
 530 535 540

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
 545 550 555 560

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
 565 570 575

Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
 580 585 590

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
 595 600 605

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
 610 615 620

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
 625 630 635 640

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
645 650 655

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
660 665 670

Ser Leu Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
675 680 685

Gly Gly Gly Ser Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr
690 695 700

Cys Asp Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile
705 710 715 720

Cys Glu Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp
725 730 735

Glu Asn Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr
740 745 750

His Asp Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys
755 760 765

Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser
770 775 780

Ala Glu Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser
785 790 795 800

Asn Pro Asp

<210> 165

<211> 801

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 165

Asn Phe Ile Arg Met Val Ile Ser Asn Pro Ala Ala Thr Gly Gly Gly
1 5 10 15

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp Thr Arg
20 25 30

Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe Asn Gly
35 40 45

Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln Glu Glu
50 55 60

Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val Thr Glu
65 70 75 80

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

Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn Tyr Gly
100 105 110

Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu Val Thr
115 120 125

Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu Leu Val
130 135 140

Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg Trp Phe
145 150 155 160

Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly Leu Ile
165 170 175

Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu Glu Thr Val

180

185

190

Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro Ser Leu
 195 200 205

Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser Ala Gln
 210 215 220

Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 225 230 235 240

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys Glu Glu
 245 250 255

His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly
 260 265 270

Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met
 275 280 285

Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala
 290 295 300

Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala
 305 310 315 320

Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr Cys Ile Thr Asn
 325 330 335

Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg
 340 345 350

Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val
 355 360 365

Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val
 370 375 380

Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe
385 390 395 400

His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg
405 410 415

Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe
420 425 430

Asp Ala Pro Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly
435 440 445

Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala
450 455 460

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
465 470 475 480

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
485 490 495

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
500 505 510

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
515 520 525

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
530 535 540

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
545 550 555 560

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
565 570 575

Val Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val

580

585

590

Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
 595 600 605

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
 610 615 620

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr
 625 630 635 640

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
 645 650 655

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
 660 665 670

Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 675 680 685

Gly Ser Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp
 690 695 700

Asn Gln Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu
 705 710 715 720

Lys Pro Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn
 725 730 735

Ile Thr Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp
 740 745 750

Phe Ile Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys
 755 760 765

Lys Lys Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Ala Glu
 770 775 780

Cys Asn Asp Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro
785 790 795 800

Asp

<210> 166
<211> 809
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 166

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
20 25 30

Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe
35 40 45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val
65 70 75 80

Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp
85 90 95

Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn
100 105 110

Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu
115 120 125

Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu
130 135 140

Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg
145 150 155 160

Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly
165 170 175

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

Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro
195 200 205

Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser
210 215 220

Ala Gln Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
225 230 235 240

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys Glu Glu His Val Ile
245 250 255

Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met
260 265 270

Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys
275 280 285

Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu
290 295 300

Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu
305 310 315 320

Ile Met Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro

325

330

335

Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn
 340 345 350

Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val
 355 360 365

Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val Ser Glu Thr
 370 375 380

Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu
 385 390 395 400

Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His
 405 410 415

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe Asp Ala Pro
 420 425 430

Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly Gly Asp Lys
 435 440 445

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
 450 455 460

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 465 470 475 480

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
 485 490 495

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 500 505 510

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
 515 520 525

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
530 535 540

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
545 550 555 560

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

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
580 585 590

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
595 600 605

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
610 615 620

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
625 630 635 640

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
645 650 655

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
660 665 670

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
675 680 685

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Leu Asp Thr Asn Tyr Cys
690 695 700

Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp
705 710 715 720

Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr

725

730

735

Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp
 740 745 750

Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu
 755 760 765

Ala Ser Ala Ser Pro Ser Cys Val Pro Gln Asp Leu Glu Pro Leu Thr
 770 775 780

Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu Ser Asn
 785 790 795 800

Met Val Val Lys Ser Cys Lys Cys Ser
 805

<210> 167

<211> 798

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 167

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
 1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
 20 25 30

Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe
 35 40 45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
 50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val

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

Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys
275 280 285

Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu
290 295 300

Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu
305 310 315 320

Ile Met Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro
325 330 335

Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn
340 345 350

Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val
355 360 365

Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val Ser Glu Thr
370 375 380

Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu
385 390 395 400

Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His
405 410 415

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe Asp Ala Pro
420 425 430

Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly Gly Asp Lys
435 440 445

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
450 455 460

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser

465		470		475		480
Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp						
		485		490		495
Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn						
		500		505		510
Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val						
		515		520		525
Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu						
		530		535		540
Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys						
545		550		555		560
Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr						
		565		570		575
Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser						
		580		585		590
Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu						
		595		600		605
Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu						
		610		615		620
Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys						
625		630		635		640
Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu						
		645		650		655
Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly						
		660		665		670

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
675 680 685

Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln Lys
690 695 700

Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln
705 710 715 720

Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu
725 730 735

Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile Leu
740 745 750

Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys Pro
755 760 765

Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Ala Glu Cys Asn Asp
770 775 780

Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp
785 790 795

<210> 168
<211> 951
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 168

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
20 25 30

Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe
35 40 45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val
65 70 75 80

Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp
85 90 95

Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn
100 105 110

Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu
115 120 125

Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu
130 135 140

Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg
145 150 155 160

Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly
165 170 175

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

Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro
195 200 205

Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser
210 215 220

Ala Gln Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

225		230		235		240									
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ile	Lys	Glu	Glu	His	Val	Ile
				245					250					255	
Ile	Gln	Ala	Glu	Phe	Tyr	Leu	Asn	Pro	Asp	Gln	Ser	Gly	Glu	Phe	Met
			260					265					270		
Phe	Asp	Phe	Asp	Gly	Asp	Glu	Ile	Phe	His	Val	Asp	Met	Ala	Lys	Lys
		275					280					285			
Glu	Thr	Val	Trp	Arg	Leu	Glu	Glu	Phe	Gly	Arg	Phe	Ala	Ser	Phe	Glu
	290					295					300				
Ala	Gln	Gly	Ala	Leu	Ala	Asn	Ile	Ala	Val	Asp	Lys	Ala	Asn	Leu	Glu
305					310					315					320
Ile	Met	Thr	Lys	Arg	Ser	Asn	Tyr	Thr	Pro	Ile	Thr	Asn	Val	Pro	Pro
				325					330					335	
Glu	Val	Thr	Val	Leu	Thr	Asn	Ser	Pro	Val	Glu	Leu	Arg	Glu	Pro	Asn
			340					345					350		
Val	Leu	Ile	Cys	Phe	Ile	Asp	Lys	Phe	Thr	Pro	Pro	Val	Val	Asn	Val
		355					360					365			
Thr	Trp	Leu	Arg	Asn	Gly	Lys	Pro	Val	Thr	Thr	Gly	Val	Ser	Glu	Thr
	370					375					380				
Val	Phe	Leu	Pro	Arg	Glu	Asp	His	Leu	Phe	Arg	Lys	Phe	His	Tyr	Leu
385					390					395					400
Pro	Phe	Leu	Pro	Ser	Thr	Glu	Asp	Val	Tyr	Asp	Cys	Arg	Val	Glu	His
				405					410					415	
Trp	Gly	Leu	Asp	Glu	Pro	Leu	Leu	Lys	His	Trp	Glu	Phe	Asp	Ala	Pro
			420					425					430		

Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly Gly Asp Lys
435 440 445

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
450 455 460

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
465 470 475 480

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
485 490 495

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
500 505 510

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
515 520 525

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
530 535 540

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
545 550 555 560

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

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser
580 585 590

Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
595 600 605

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
610 615 620

Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys

625					630						635					640
Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	
			645						650					655		
Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu	Ser	Pro	Gly	
			660					665					670			
Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gln	
		675					680					685				
Leu	Cys	Lys	Phe	Cys	Asp	Val	Arg	Phe	Ser	Thr	Cys	Asp	Asn	Gln	Lys	
	690					695					700					
Ser	Cys	Met	Ser	Asn	Cys	Ser	Ile	Thr	Ser	Ile	Cys	Glu	Lys	Pro	Gln	
705					710					715					720	
Glu	Val	Cys	Val	Ala	Val	Trp	Arg	Lys	Asn	Asp	Glu	Asn	Ile	Thr	Leu	
				725					730					735		
Glu	Thr	Val	Cys	His	Asp	Pro	Lys	Leu	Pro	Tyr	His	Asp	Phe	Ile	Leu	
			740					745					750			
Glu	Asp	Ala	Ala	Ser	Pro	Lys	Cys	Ile	Met	Lys	Glu	Lys	Lys	Lys	Pro	
		755					760					765				
Gly	Glu	Thr	Phe	Phe	Met	Cys	Ser	Cys	Ser	Ser	Ala	Glu	Cys	Asn	Asp	
	770					775					780					
Asn	Ile	Ile	Phe	Ser	Glu	Glu	Tyr	Asn	Thr	Ser	Asn	Pro	Asp	Gly	Gly	
785					790					795					800	
Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	
			805					810						815		
Gly	Ser	Ala	Pro	Thr	Ser	Ser	Ser	Thr	Lys	Lys	Thr	Gln	Leu	Gln	Leu	
			820					825					830			

Glu Ala Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn
835 840 845

Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Ala Lys Phe Tyr Met
850 855 860

Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu
865 870 875 880

Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe
885 890 895

His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu
900 905 910

Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu
915 920 925

Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln
930 935 940

Ser Ile Ile Ser Thr Leu Thr
945 950

<210> 169
<211> 809
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 169

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
20 25 30

Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe
35 40 45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val
65 70 75 80

Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp
85 90 95

Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn
100 105 110

Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu
115 120 125

Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu
130 135 140

Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg
145 150 155 160

Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly
165 170 175

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

Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro
195 200 205

Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser
210 215 220

Ala Gln Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

225		230		235		240									
Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Ile	Lys	Glu	Glu	His	Val	Ile
				245					250					255	
Ile	Gln	Ala	Glu	Phe	Tyr	Leu	Asn	Pro	Asp	Gln	Ser	Gly	Glu	Phe	Met
			260					265					270		
Phe	Asp	Phe	Asp	Gly	Asp	Glu	Ile	Phe	His	Val	Asp	Met	Ala	Lys	Lys
		275					280					285			
Glu	Thr	Val	Trp	Arg	Leu	Glu	Glu	Phe	Gly	Arg	Phe	Ala	Ser	Phe	Glu
	290					295					300				
Ala	Gln	Gly	Ala	Leu	Ala	Asn	Ile	Ala	Val	Asp	Lys	Ala	Asn	Leu	Glu
305					310					315					320
Ile	Met	Thr	Lys	Arg	Ser	Asn	Tyr	Thr	Pro	Ile	Thr	Asn	Val	Pro	Pro
				325					330					335	
Glu	Val	Thr	Val	Leu	Thr	Asn	Ser	Pro	Val	Glu	Leu	Arg	Glu	Pro	Asn
			340					345					350		
Val	Leu	Ile	Cys	Phe	Ile	Asp	Lys	Phe	Thr	Pro	Pro	Val	Val	Asn	Val
		355					360					365			
Thr	Trp	Leu	Arg	Asn	Gly	Lys	Pro	Val	Thr	Thr	Gly	Val	Ser	Glu	Thr
	370					375					380				
Val	Phe	Leu	Pro	Arg	Glu	Asp	His	Leu	Phe	Arg	Lys	Phe	His	Tyr	Leu
385					390					395					400
Pro	Phe	Leu	Pro	Ser	Thr	Glu	Asp	Val	Tyr	Asp	Cys	Arg	Val	Glu	His
				405					410					415	
Trp	Gly	Leu	Asp	Glu	Pro	Leu	Leu	Lys	His	Trp	Glu	Phe	Asp	Ala	Pro
			420					425					430		

Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly Gly Asp Lys
435 440 445

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
450 455 460

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
465 470 475 480

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
485 490 495

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
500 505 510

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
515 520 525

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
530 535 540

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
545 550 555 560

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

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp
580 585 590

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
595 600 605

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
610 615 620

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys

625 630 635 640

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
645 650 655

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
660 665 670

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
675 680 685

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Leu Asp Thr Asn Tyr Cys
690 695 700

Phe Arg Asn Leu Glu Glu Asn Cys Cys Val Arg Pro Leu Tyr Ile Asp
705 710 715 720

Phe Arg Gln Asp Leu Gly Trp Lys Trp Val His Glu Pro Lys Gly Tyr
725 730 735

Tyr Ala Asn Phe Cys Ser Gly Pro Cys Pro Tyr Leu Arg Ser Ala Asp
740 745 750

Thr Thr His Ser Thr Val Leu Gly Leu Tyr Asn Thr Leu Asn Pro Glu
755 760 765

Ala Ser Ala Ser Pro Ser Cys Val Pro Gln Asp Leu Glu Pro Leu Thr
770 775 780

Ile Leu Tyr Tyr Val Gly Arg Thr Pro Lys Val Glu Gln Leu Ser Asn
785 790 795 800

Met Val Val Lys Ser Cys Lys Cys Ser
805

<210> 170

<211> 951

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 170

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Asp
20 25 30

Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe Phe
35 40 45

Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His Gln
50 55 60

Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala Val
65 70 75 80

Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp
85 90 95

Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His Asn
100 105 110

Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val Tyr Pro Glu
115 120 125

Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn Leu
130 135 140

Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile Glu Val Arg
145 150 155 160

Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val Ser Thr Gly
165 170 175

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

Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His Pro
195 200 205

Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg Ser Glu Ser
210 215 220

Ala Gln Ser Lys Met Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
225 230 235 240

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ile Lys Glu Glu His Val Ile
245 250 255

Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu Phe Met
260 265 270

Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala Lys Lys
275 280 285

Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser Phe Glu
290 295 300

Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn Leu Glu
305 310 315 320

Ile Met Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn Val Pro Pro
325 330 335

Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg Glu Pro Asn
340 345 350

Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val Val Asn Val
355 360 365

Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val Ser Glu Thr

370

375

380

Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe His Tyr Leu
 385 390 395 400

Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg Val Glu His
 405 410 415

Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp Glu Phe Asp Ala Pro
 420 425 430

Ser Pro Leu Pro Glu Thr Gly Gly Ser Ala Ala Ala Gly Gly Asp Lys
 435 440 445

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly Pro
 450 455 460

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 465 470 475 480

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
 485 490 495

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 500 505 510

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
 515 520 525

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 530 535 540

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 545 550 555 560

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

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser
580 585 590

Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
595 600 605

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
610 615 620

Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys
625 630 635 640

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
645 650 655

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
660 665 670

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
675 680 685

Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln Lys
690 695 700

Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln
705 710 715 720

Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu
725 730 735

Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile Leu
740 745 750

Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys Pro
755 760 765

Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Ala Glu Cys Asn Asp

770

775

780

Asn Ile Ile Phe Ser Glu Glu Tyr Asn Thr Ser Asn Pro Asp Gly Gly
 785 790 795 800

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
 805 810 815

Gly Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu
 820 825 830

Glu Ala Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn
 835 840 845

Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Ala Lys Phe Tyr Met
 850 855 860

Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu
 865 870 875 880

Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe
 885 890 895

His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu
 900 905 910

Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu
 915 920 925

Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln
 930 935 940

Ser Ile Ile Ser Thr Leu Thr
 945 950

<210> 171

<211> 20

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 171

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 172

<211> 6

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 172

Leu Leu Gly Gly Pro Ser
1 5

<210> 173

<211> 226

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 173

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly
225

<210> 174

<211> 226
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 174

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro

165

170

175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
 180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 210 215 220

Pro Gly
 225

<210> 175
 <211> 15
 <212> PRT
 <213> Artificial sequence

<220>
 <223> synthetic sequence

<400> 175

Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly
 1 5 10 15

<210> 176
 <211> 18
 <212> PRT
 <213> Artificial sequence

<220>
 <223> synthetic sequence

<400> 176

Gly Ala Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys
 1 5 10 15

Arg Gly

<210> 177
<211> 13
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 177

Asn Phe Phe Arg Met Val Ile Ser Asn Pro Ala Ala Thr
1 5 10

<210> 178
<211> 55
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> VARIANT
<222> (6)..(55)
<223> Each copy of Gly Gly Gly Gly Ser at positions 6 to 55 is either
present or absent such that the number of copies ranges from 1 to
10

<400> 178

Cys Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser Gly Gly Gly Gly Ser
50 55

<210> 179

<211> 55
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> VARIANT
<222> (6)..(55)
<223> Each copy of Gly Gly Gly Gly Ser at positions 6 to 55 is either
present or absent such that the number of copies ranges from 1 to
10

<400> 179

Gly Cys Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser Gly Gly Gly Gly Ser
50 55

<210> 180
<211> 55
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> VARIANT
<222> (6)..(55)
<223> Each copy of Gly Gly Gly Gly Ser at positions 6 to 55 is either
present or absent such that the number of copies ranges from 1 to
10

<400> 180

Gly Gly Cys Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser Gly Gly Gly Gly Ser
50 55

<210> 181

<211> 55

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<220>

<221> VARIANT

<222> (6)..(55)

<223> Each copy of Gly Gly Gly Gly Ser at positions 6 to 55 is either
present or absent such that the number of copies ranges from 1 to
10

<400> 181

Gly Gly Gly Cys Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser Gly Gly Gly Gly Ser
50 55

<210> 182
<211> 55
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> VARIANT
<222> (6)..(55)
<223> Each copy of Gly Gly Gly Gly Ser at positions 6 to 55 is either present or absent such that the number of copies ranges from 1 to 10

<400> 182

Gly Gly Gly Gly Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser Gly Gly Gly Gly Ser
50 55

<210> 183
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> VARIANT
<222> (1)..(40)
<223> Each copy of Gly Gly Gly Gly Ser is either present or absent such that the number of copies ranges from 1 to 8

<400> 183

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser
35 40

<210> 184

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 184

Ala Ala Ala Gly Gly
1 5

<210> 185

<211> 133

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 185

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Ala
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Ala Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 186
<211> 133
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 186

Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu Thr
1 5 10 15

Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys
20 25 30

Asn Pro Lys Leu Thr Arg Met Leu Thr Ala Lys Phe Tyr Met Pro Lys
35 40 45

Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys
50 55 60

Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu
65 70 75 80

Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu
85 90 95

Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala
100 105 110

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile
115 120 125

Ile Ser Thr Leu Thr
130

<210> 187
<211> 179
<212> PRT
<213> Homo sapiens

<400> 187

Gln Leu Phe His Leu Gln Lys Glu Leu Ala Glu Leu Arg Glu Ser Thr
1 5 10 15

Ser Gln Met His Thr Ala Ser Ser Leu Glu Lys Gln Ile Gly His Pro
20 25 30

Ser Pro Pro Pro Glu Lys Lys Glu Leu Arg Lys Val Ala His Leu Thr
35 40 45

Gly Lys Ser Asn Ser Arg Ser Met Pro Leu Glu Trp Glu Asp Thr Tyr
50 55 60

Gly Ile Val Leu Leu Ser Gly Val Lys Tyr Lys Lys Gly Gly Leu Val
65 70 75 80

Ile Asn Glu Thr Gly Leu Tyr Phe Val Tyr Ser Lys Val Tyr Phe Arg
85 90 95

Gly Gln Ser Cys Asn Asn Leu Pro Leu Ser His Lys Val Tyr Met Arg
100 105 110

Asn Ser Lys Tyr Pro Gln Asp Leu Val Met Met Glu Gly Lys Met Met
115 120 125

Ser Tyr Cys Thr Thr Gly Gln Met Trp Ala Arg Ser Ser Tyr Leu Gly
130 135 140

Ala Val Phe Asn Leu Thr Ser Ala Asp His Leu Tyr Val Asn Val Ser
145 150 155 160

Glu Leu Ser Leu Val Asn Phe Glu Glu Ser Gln Thr Phe Phe Gly Leu
165 170 175

Tyr Lys Leu

<210> 188
<211> 178
<212> PRT
<213> Homo sapiens

<400> 188

Ile Lys Glu Glu His Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro
1 5 10 15

Asp Gln Ser Gly Glu Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe
20 25 30

His Val Asp Met Ala Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe
35 40 45

Gly Arg Phe Ala Ser Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala
50 55 60

Val Asp Lys Ala Asn Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr
65 70 75 80

Pro Ile Thr Asn Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro
85 90 95

Val Glu Leu Arg Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe
100 105 110

Thr Pro Pro Val Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val
115 120 125

Thr Thr Gly Val Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu
130 135 140

Phe Arg Lys Phe His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val
145 150 155 160

Tyr Asp Cys Arg Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys
165 170 175

His Trp

<210> 189
<211> 79
<212> PRT
<213> Homo sapiens

<400> 189

Val Ile Ile Gln Ala Glu Phe Tyr Leu Asn Pro Asp Gln Ser Gly Glu
1 5 10 15

Phe Met Phe Asp Phe Asp Gly Asp Glu Ile Phe His Val Asp Met Ala
20 25 30

Lys Lys Glu Thr Val Trp Arg Leu Glu Glu Phe Gly Arg Phe Ala Ser
35 40 45

Phe Glu Ala Gln Gly Ala Leu Ala Asn Ile Ala Val Asp Lys Ala Asn

50

55

60

Leu Glu Ile Met Thr Lys Arg Ser Asn Tyr Thr Pro Ile Thr Asn
65 70 75

<210> 190
<211> 94
<212> PRT
<213> Homo sapiens

<400> 190

Val Pro Pro Glu Val Thr Val Leu Thr Asn Ser Pro Val Glu Leu Arg
1 5 10 15

Glu Pro Asn Val Leu Ile Cys Phe Ile Asp Lys Phe Thr Pro Pro Val
20 25 30

Val Asn Val Thr Trp Leu Arg Asn Gly Lys Pro Val Thr Thr Gly Val
35 40 45

Ser Glu Thr Val Phe Leu Pro Arg Glu Asp His Leu Phe Arg Lys Phe
50 55 60

His Tyr Leu Pro Phe Leu Pro Ser Thr Glu Asp Val Tyr Asp Cys Arg
65 70 75 80

Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp
85 90

<210> 191
<211> 98
<212> PRT
<213> Homo sapiens

<400> 191

Val Pro Glu Ala Pro Thr Pro Met Trp Pro Asp Asp Leu Gln Asn His
1 5 10 15

Thr Phe Leu His Thr Val Tyr Cys Gln Asp Gly Ser Pro Ser Val Gly

20

25

30

Leu Ser Glu Ala Tyr Asp Glu Asp Gln Leu Phe Phe Phe Asp Phe Ser
 35 40 45

Gln Asn Thr Arg Val Pro Arg Leu Pro Glu Phe Ala Asp Trp Ala Gln
 50 55 60

Glu Gln Gly Asp Ala Pro Ala Ile Leu Phe Asp Lys Glu Phe Cys Glu
 65 70 75 80

Trp Met Ile Gln Gln Ile Gly Pro Lys Leu Asp Gly Lys Ile Pro Val
 85 90 95

Ser Arg

<210> 192

<211> 93

<212> PRT

<213> Homo sapiens

<400> 192

Gly Phe Pro Ile Ala Glu Val Phe Thr Leu Lys Pro Leu Glu Phe Gly
 1 5 10 15

Lys Pro Asn Thr Leu Val Cys Phe Val Ser Asn Leu Phe Pro Pro Met
 20 25 30

Leu Thr Val Asn Trp Gln His His Ser Val Pro Val Glu Gly Phe Gly
 35 40 45

Pro Thr Phe Val Ser Ala Val Asp Gly Leu Ser Phe Gln Ala Phe Ser
 50 55 60

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

Thr His Glu Ile Asp Arg Tyr Thr Ala Ile Ala Tyr Trp
85 90

<210> 193
<211> 85
<212> PRT
<213> Homo sapiens

<400> 193

Thr Lys Ala Asp His Met Gly Ser Tyr Gly Pro Ala Phe Tyr Gln Ser
1 5 10 15

Tyr Gly Ala Ser Gly Gln Phe Thr His Glu Phe Asp Glu Glu Gln Leu
20 25 30

Phe Ser Val Asp Leu Lys Lys Ser Glu Ala Val Trp Arg Leu Pro Glu
35 40 45

Phe Gly Asp Phe Ala Arg Phe Asp Pro Gln Gly Gly Leu Ala Gly Ile
50 55 60

Ala Ala Ile Lys Ala His Leu Asp Ile Leu Val Glu Arg Ser Asn Arg
65 70 75 80

Ser Arg Ala Ile Asn
85

<210> 194
<211> 94
<212> PRT
<213> Homo sapiens

<400> 194

Val Pro Pro Arg Val Thr Val Leu Pro Lys Ser Arg Val Glu Leu Gly
1 5 10 15

Gln Pro Asn Ile Leu Ile Cys Ile Val Asp Asn Ile Phe Pro Pro Val
20 25 30

Ile Asn Ile Thr Trp Leu Arg Asn Gly Gln Thr Val Thr Glu Gly Val
35 40 45

Ala Gln Thr Ser Phe Tyr Ser Gln Pro Asp His Leu Phe Arg Lys Phe
50 55 60

His Tyr Leu Pro Phe Val Pro Ser Ala Glu Asp Val Tyr Asp Cys Gln
65 70 75 80

Val Glu His Trp Gly Leu Asp Ala Pro Leu Leu Arg His Trp
85 90

<210> 195
<211> 85
<212> PRT
<213> Homo sapiens

<400> 195

Ala Ile Lys Ala Asp His Val Ser Thr Tyr Ala Ala Phe Val Gln Thr
1 5 10 15

His Arg Pro Thr Gly Glu Phe Met Phe Glu Phe Asp Glu Asp Glu Met
20 25 30

Phe Tyr Val Asp Leu Asp Lys Lys Glu Thr Val Trp His Leu Glu Glu
35 40 45

Phe Gly Gln Ala Phe Ser Phe Glu Ala Gln Gly Gly Leu Ala Asn Ile
50 55 60

Ala Ile Leu Asn Asn Asn Leu Asn Thr Leu Ile Gln Arg Ser Asn His
65 70 75 80

Thr Gln Ala Thr Asn
85

<210> 196
<211> 94
<212> PRT

<213> Homo sapiens

<400> 196

Asp Pro Pro Glu Val Thr Val Phe Pro Lys Glu Pro Val Glu Leu Gly
1 5 10 15

Gln Pro Asn Thr Leu Ile Cys His Ile Asp Lys Phe Phe Pro Pro Val
20 25 30

Leu Asn Val Thr Trp Leu Cys Asn Gly Glu Leu Val Thr Glu Gly Val
35 40 45

Ala Glu Ser Leu Phe Leu Pro Arg Thr Asp Tyr Ser Phe His Lys Phe
50 55 60

His Tyr Leu Thr Phe Val Pro Ser Ala Glu Asp Phe Tyr Asp Cys Arg
65 70 75 80

Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His Trp
85 90

<210> 197

<211> 181

<212> PRT

<213> Homo sapiens

<400> 197

Glu Asp Ile Val Ala Asp His Val Ala Ser Cys Gly Val Asn Leu Tyr
1 5 10 15

Gln Phe Tyr Gly Pro Ser Gly Gln Tyr Thr His Glu Phe Asp Gly Asp
20 25 30

Glu Gln Phe Tyr Val Asp Leu Glu Arg Lys Glu Thr Ala Trp Arg Trp
35 40 45

Pro Glu Phe Ser Lys Phe Gly Gly Phe Asp Pro Gln Gly Ala Leu Arg
50 55 60

Asn Met Ala Val Ala Lys His Asn Leu Asn Ile Met Ile Lys Arg Tyr
65 70 75 80

Asn Ser Thr Ala Ala Thr Asn Glu Val Pro Glu Val Thr Val Phe Ser
85 90 95

Lys Ser Pro Val Thr Leu Gly Gln Pro Asn Thr Leu Ile Cys Leu Val
100 105 110

Asp Asn Ile Phe Pro Pro Val Val Asn Ile Thr Trp Leu Ser Asn Gly
115 120 125

Gln Ser Val Thr Glu Gly Val Ser Glu Thr Ser Phe Leu Ser Lys Ser
130 135 140

Asp His Ser Phe Phe Lys Ile Ser Tyr Leu Thr Phe Leu Pro Ser Ala
145 150 155 160

Asp Glu Ile Tyr Asp Cys Lys Val Glu His Trp Gly Leu Asp Gln Pro
165 170 175

Leu Leu Lys His Trp
180

<210> 198

<211> 87

<212> PRT

<213> Homo sapiens

<400> 198

Glu Asp Ile Val Ala Asp His Val Ala Ser Cys Gly Val Asn Leu Tyr
1 5 10 15

Gln Phe Tyr Gly Pro Ser Gly Gln Tyr Thr His Glu Phe Asp Gly Asp
20 25 30

Glu Gln Phe Tyr Val Asp Leu Glu Arg Lys Glu Thr Ala Trp Arg Trp
35 40 45

Pro Glu Phe Ser Lys Phe Gly Gly Phe Asp Pro Gln Gly Ala Leu Arg
50 55 60

Asn Met Ala Val Ala Lys His Asn Leu Asn Ile Met Ile Lys Arg Tyr
65 70 75 80

Asn Ser Thr Ala Ala Thr Asn
85

<210> 199
<211> 94
<212> PRT
<213> Homo sapiens

<400> 199

Glu Val Pro Glu Val Thr Val Phe Ser Lys Ser Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Asn Thr Leu Ile Cys Leu Val Asp Asn Ile Phe Pro Pro Val
20 25 30

Val Asn Ile Thr Trp Leu Ser Asn Gly Gln Ser Val Thr Glu Gly Val
35 40 45

Ser Glu Thr Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile
50 55 60

Ser Tyr Leu Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys
65 70 75 80

Val Glu His Trp Gly Leu Asp Gln Pro Leu Leu Lys His Trp
85 90

<210> 200
<211> 181
<212> PRT
<213> Homo sapiens

<400> 200

Glu Asp Ile Val Ala Asp His Val Ala Ser Tyr Gly Val Asn Phe Tyr
1 5 10 15

Gln Ser His Gly Pro Ser Gly Gln Tyr Thr His Glu Phe Asp Gly Asp
20 25 30

Glu Glu Phe Tyr Val Asp Leu Glu Thr Lys Glu Thr Val Trp Gln Leu
35 40 45

Pro Met Phe Ser Lys Phe Ile Ser Phe Asp Pro Gln Ser Ala Leu Arg
50 55 60

Asn Met Ala Val Gly Lys His Thr Leu Glu Phe Met Met Arg Gln Ser
65 70 75 80

Asn Ser Thr Ala Ala Thr Asn Glu Val Pro Glu Val Thr Val Phe Ser
85 90 95

Lys Phe Pro Val Thr Leu Gly Gln Pro Asn Thr Leu Ile Cys Leu Val
100 105 110

Asp Asn Ile Phe Pro Pro Val Val Asn Ile Thr Trp Leu Ser Asn Gly
115 120 125

His Ser Val Thr Glu Gly Val Ser Glu Thr Ser Phe Leu Ser Lys Ser
130 135 140

Asp His Ser Phe Phe Lys Ile Ser Tyr Leu Thr Phe Leu Pro Ser Ala
145 150 155 160

Asp Glu Ile Tyr Asp Cys Lys Val Glu His Trp Gly Leu Asp Glu Pro
165 170 175

Leu Leu Lys His Trp
180

<210> 201
<211> 87
<212> PRT
<213> Homo sapiens

<400> 201

Glu Asp Ile Val Ala Asp His Val Ala Ser Tyr Gly Val Asn Phe Tyr
1 5 10 15

Gln Ser His Gly Pro Ser Gly Gln Tyr Thr His Glu Phe Asp Gly Asp
20 25 30

Glu Glu Phe Tyr Val Asp Leu Glu Thr Lys Glu Thr Val Trp Gln Leu
35 40 45

Pro Met Phe Ser Lys Phe Ile Ser Phe Asp Pro Gln Ser Ala Leu Arg
50 55 60

Asn Met Ala Val Gly Lys His Thr Leu Glu Phe Met Met Arg Gln Ser
65 70 75 80

Asn Ser Thr Ala Ala Thr Asn
85

<210> 202
<211> 94
<212> PRT
<213> Homo sapiens

<400> 202

Glu Val Pro Glu Val Thr Val Phe Ser Lys Phe Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Asn Thr Leu Ile Cys Leu Val Asp Asn Ile Phe Pro Pro Val
20 25 30

Val Asn Ile Thr Trp Leu Ser Asn Gly His Ser Val Thr Glu Gly Val
35 40 45

Ser Glu Thr Ser Phe Leu Ser Lys Ser Asp His Ser Phe Phe Lys Ile
50 55 60

Ser Tyr Leu Thr Phe Leu Pro Ser Ala Asp Glu Ile Tyr Asp Cys Lys
65 70 75 80

Val Glu His Trp Gly Leu Asp Glu Pro Leu Leu Lys His Trp
85 90

<210> 203
<211> 29
<212> PRT
<213> Homo sapiens

<400> 203

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Ser Leu Ala Ala Leu Thr
1 5 10 15

Val Thr Leu Met Val Leu Ser Ser Arg Leu Ala Phe Ala
20 25

<210> 204
<211> 19
<212> PRT
<213> Homo sapiens

<400> 204

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Cys Met Ala Ala Leu Thr
1 5 10 15

Val Thr Leu

<210> 205
<211> 19
<212> PRT
<213> Homo sapiens

<400> 205

Met Val Cys Leu Lys Leu Pro Gly Gly Ser Tyr Met Ala Lys Leu Thr

1 5 10 15

Val Thr Leu

<210> 206
<211> 94
<212> PRT
<213> Homo sapiens

<400> 206

Asp Thr Arg Pro Arg Phe Leu Glu Gln Val Lys His Glu Cys His Phe
1 5 10 15

Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr His
20 25 30

Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala
35 40 45

Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys
50 55 60

Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg His
65 70 75 80

Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val
85 90

<210> 207
<211> 95
<212> PRT
<213> Homo sapiens

<400> 207

Gly Asp Thr Arg Cys Arg Phe Leu Glu Gln Val Lys His Glu Cys His
1 5 10 15

Phe Phe Asn Gly Thr Glu Arg Val Arg Phe Leu Asp Arg Tyr Phe Tyr

20

25

30

His Gln Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg
 35 40 45

Ala Val Thr Glu Leu Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
 50 55 60

Lys Asp Leu Leu Glu Gln Lys Arg Ala Ala Val Asp Thr Tyr Cys Arg
 65 70 75 80

His Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val
 85 90 95

<210> 208

<211> 103

<212> PRT

<213> Homo sapiens

<400> 208

Tyr Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His
 1 5 10 15

His Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile
 20 25 30

Glu Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val
 35 40 45

Ser Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val
 50 55 60

Met Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val
 65 70 75 80

Glu His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg
 85 90 95

Ser Glu Ser Ala Gln Ser Lys
100

<210> 209
<211> 104
<212> PRT
<213> Homo sapiens

<400> 209

Tyr Pro Glu Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His
1 5 10 15

His Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Ala Ser Ile
20 25 30

Glu Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Thr Gly Val Val
35 40 45

Ser Thr Gly Leu Ile Gln Asn Gly Asp Cys Thr Phe Gln Thr Leu Val
50 55 60

Met Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val
65 70 75 80

Glu His Pro Ser Leu Thr Ser Pro Leu Thr Val Glu Trp Arg Ala Arg
85 90 95

Ser Glu Ser Ala Gln Ser Lys Met
100

<210> 210
<211> 197
<212> PRT
<213> Homo sapiens

<400> 210

Asp Thr Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe
1 5 10 15

Phe Asn Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn
20 25 30

Gln Glu Glu Phe Leu Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala
35 40 45

Val Thr Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys
50 55 60

Asp Leu Leu Glu Gln Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His
65 70 75 80

Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val His Pro
85 90 95

Gln Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His His Asn
100 105 110

Leu Leu Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile Glu Val
115 120 125

Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val Ser Thr
130 135 140

Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val Met Leu
145 150 155 160

Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val Glu His
165 170 175

Pro Ser Val Thr Ser Ala Leu Thr Val Glu Trp Arg Ala Arg Ser Glu
180 185 190

Ser Ala Gln Ser Lys
195

<210> 211

<211> 94

<212> PRT
<213> Homo sapiens

<400> 211

Asp Thr Arg Pro Arg Phe Leu Glu Leu Arg Lys Ser Glu Cys His Phe
1 5 10 15

Phe Asn Gly Thr Glu Arg Val Arg Tyr Leu Asp Arg Tyr Phe His Asn
20 25 30

Gln Glu Glu Phe Leu Arg Phe Asp Ser Asp Val Gly Glu Tyr Arg Ala
35 40 45

Val Thr Glu Leu Gly Arg Pro Val Ala Glu Ser Trp Asn Ser Gln Lys
50 55 60

Asp Leu Leu Glu Gln Lys Arg Gly Arg Val Asp Asn Tyr Cys Arg His
65 70 75 80

Asn Tyr Gly Val Gly Glu Ser Phe Thr Val Gln Arg Arg Val
85 90

<210> 212
<211> 103
<212> PRT
<213> Homo sapiens

<400> 212

His Pro Gln Val Thr Val Tyr Pro Ala Lys Thr Gln Pro Leu Gln His
1 5 10 15

His Asn Leu Leu Val Cys Ser Val Ser Gly Phe Tyr Pro Gly Ser Ile
20 25 30

Glu Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val
35 40 45

Ser Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val
50 55 60

Met Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val
65 70 75 80

Glu His Pro Ser Val Thr Ser Ala Leu Thr Val Glu Trp Arg Ala Arg
85 90 95

Ser Glu Ser Ala Gln Ser Lys
100

<210> 213
<211> 105
<212> PRT
<213> Homo sapiens

<400> 213

Thr Val Leu Ser Ser Pro Leu Ala Leu Ala Gly Asp Thr Gln Pro Arg
1 5 10 15

Phe Leu Glu Gln Ala Lys Cys Glu Cys His Phe Leu Asn Gly Thr Glu
20 25 30

Arg Val Trp Asn Leu Ile Arg Tyr Ile Tyr Asn Gln Glu Glu Tyr Ala
35 40 45

Arg Tyr Asn Ser Asp Leu Gly Glu Tyr Gln Ala Val Thr Glu Leu Gly
50 55 60

Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln Lys Asp Leu Leu Glu Arg
65 70 75 80

Arg Arg Ala Glu Val Asp Thr Tyr Cys Arg Tyr Asn Tyr Gly Val Val
85 90 95

Glu Ser Phe Thr Val Gln Arg Arg Val
100 105

<210> 214

<211> 103
<212> PRT
<213> Homo sapiens

<400> 214

Gln Pro Lys Val Thr Val Tyr Pro Ser Lys Thr Gln Pro Leu Gln His
1 5 10 15

His Asn Leu Leu Val Cys Ser Val Asn Gly Phe Tyr Pro Gly Ser Ile
20 25 30

Glu Val Arg Trp Phe Arg Asn Gly Gln Glu Glu Lys Ala Gly Val Val
35 40 45

Ser Thr Gly Leu Ile Gln Asn Gly Asp Trp Thr Phe Gln Thr Leu Val
50 55 60

Met Leu Glu Thr Val Pro Arg Ser Gly Glu Val Tyr Thr Cys Gln Val
65 70 75 80

Glu His Pro Ser Met Met Ser Pro Leu Thr Val Gln Trp Ser Ala Arg
85 90 95

Ser Glu Ser Ala Gln Ser Lys
100

<210> 215
<211> 94
<212> PRT
<213> Homo sapiens

<400> 215

Gly Gly Phe Val Ala His Val Glu Ser Thr Cys Leu Leu Asp Asp Ala
1 5 10 15

Gly Thr Pro Lys Asp Phe Thr Tyr Cys Ile Ser Phe Asn Lys Asp Leu
20 25 30

Leu Thr Cys Trp Asp Pro Glu Glu Asn Lys Met Ala Pro Cys Glu Phe

35

40

45

Gly Val Leu Asn Ser Leu Ala Asn Val Leu Ser Gln His Leu Asn Gln
 50 55 60

Lys Asp Thr Leu Met Gln Arg Leu Arg Asn Gly Leu Gln Asn Cys Ala
 65 70 75 80

Thr His Thr Gln Pro Phe Trp Gly Ser Leu Thr Asn Arg Thr
 85 90

<210> 216

<211> 95

<212> PRT

<213> Homo sapiens

<400> 216

Arg Pro Pro Ser Val Gln Val Ala Lys Thr Thr Pro Phe Asn Thr Arg
 1 5 10 15

Glu Pro Val Met Leu Ala Cys Tyr Val Trp Gly Phe Tyr Pro Ala Glu
 20 25 30

Val Thr Ile Thr Trp Arg Lys Asn Gly Lys Leu Val Met Pro His Ser
 35 40 45

Ser Ala His Lys Thr Ala Gln Pro Asn Gly Asp Trp Thr Tyr Gln Thr
 50 55 60

Leu Ser His Leu Ala Leu Thr Pro Ser Tyr Gly Asp Thr Tyr Thr Cys
 65 70 75 80

Val Val Glu His Thr Gly Ala Pro Glu Pro Ile Leu Arg Asp Trp
 85 90 95

<210> 217

<211> 94

<212> PRT

<213> Homo sapiens

<400> 217

Thr Asp Ser Pro Glu Asp Phe Val Ile Gln Ala Lys Ala Asp Cys Tyr
1 5 10 15

Phe Thr Asn Gly Thr Glu Lys Val Gln Phe Val Val Arg Phe Ile Phe
20 25 30

Asn Leu Glu Glu Tyr Val Arg Phe Asp Ser Asp Val Gly Met Phe Val
35 40 45

Ala Leu Thr Lys Leu Gly Gln Pro Asp Ala Glu Gln Trp Asn Ser Arg
50 55 60

Leu Asp Leu Leu Glu Arg Ser Arg Gln Ala Val Asp Gly Val Cys Arg
65 70 75 80

His Asn Tyr Arg Leu Gly Ala Pro Phe Thr Val Gly Arg Lys
85 90

<210> 218

<211> 94

<212> PRT

<213> Homo sapiens

<400> 218

Val Gln Pro Glu Val Thr Val Tyr Pro Glu Arg Thr Pro Leu Leu His
1 5 10 15

Gln His Asn Leu Leu His Cys Ser Val Thr Gly Phe Tyr Pro Gly Asp
20 25 30

Ile Lys Ile Lys Trp Phe Leu Asn Gly Gln Glu Glu Arg Ala Gly Val
35 40 45

Met Ser Thr Gly Pro Ile Arg Asn Gly Asp Trp Thr Phe Gln Thr Val
50 55 60

Val Met Leu Glu Met Thr Pro Glu Leu Gly His Val Tyr Thr Cys Leu
65 70 75 80

Val Asp His Ser Ser Leu Leu Ser Pro Val Ser Val Glu Trp
85 90

<210> 219
<211> 186
<212> PRT
<213> Homo sapiens

<400> 219

Arg Ala Thr Pro Glu Asn Tyr Leu Phe Gln Gly Arg Gln Glu Cys Tyr
1 5 10 15

Ala Phe Asn Gly Thr Gln Arg Phe Leu Glu Arg Tyr Ile Tyr Asn Arg
20 25 30

Glu Glu Phe Ala Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val
35 40 45

Thr Glu Leu Gly Arg Pro Ala Ala Glu Tyr Trp Asn Ser Gln Lys Asp
50 55 60

Ile Leu Glu Glu Lys Arg Ala Val Pro Asp Arg Met Cys Arg His Asn
65 70 75 80

Tyr Glu Leu Gly Gly Pro Met Thr Leu Gln Arg Arg Val Gln Pro Arg
85 90 95

Val Asn Val Ser Pro Ser Lys Lys Gly Pro Leu Gln His His Asn Leu
100 105 110

Leu Val Cys His Val Thr Asp Phe Tyr Pro Gly Ser Ile Gln Val Arg
115 120 125

Trp Phe Leu Asn Gly Gln Glu Glu Thr Ala Gly Val Val Ser Thr Asn
130 135 140

Leu Ile Arg Asn Gly Asp Trp Thr Phe Gln Ile Leu Val Met Leu Glu
145 150 155 160

Met Thr Pro Gln Gln Gly Asp Val Tyr Thr Cys Gln Val Glu His Thr
165 170 175

Ser Leu Asp Ser Pro Val Thr Val Glu Trp
180 185

<210> 220

<211> 92

<212> PRT

<213> Homo sapiens

<400> 220

Arg Ala Thr Pro Glu Asn Tyr Leu Phe Gln Gly Arg Gln Glu Cys Tyr
1 5 10 15

Ala Phe Asn Gly Thr Gln Arg Phe Leu Glu Arg Tyr Ile Tyr Asn Arg
20 25 30

Glu Glu Phe Ala Arg Phe Asp Ser Asp Val Gly Glu Phe Arg Ala Val
35 40 45

Thr Glu Leu Gly Arg Pro Ala Ala Glu Tyr Trp Asn Ser Gln Lys Asp
50 55 60

Ile Leu Glu Glu Lys Arg Ala Val Pro Asp Arg Met Cys Arg His Asn
65 70 75 80

Tyr Glu Leu Gly Gly Pro Met Thr Leu Gln Arg Arg
85 90

<210> 221

<211> 94

<212> PRT

<213> Homo sapiens

<400> 221

Val Gln Pro Arg Val Asn Val Ser Pro Ser Lys Lys Gly Pro Leu Gln
1 5 10 15

His His Asn Leu Leu Val Cys His Val Thr Asp Phe Tyr Pro Gly Ser
20 25 30

Ile Gln Val Arg Trp Phe Leu Asn Gly Gln Glu Glu Thr Ala Gly Val
35 40 45

Val Ser Thr Asn Leu Ile Arg Asn Gly Asp Trp Thr Phe Gln Ile Leu
50 55 60

Val Met Leu Glu Met Thr Pro Gln Gln Gly Asp Val Tyr Thr Cys Gln
65 70 75 80

Val Glu His Thr Ser Leu Asp Ser Pro Val Thr Val Glu Trp
85 90

<210> 222

<211> 94

<212> PRT

<213> Homo sapiens

<400> 222

Arg Asp Ser Pro Glu Asp Phe Val Phe Gln Phe Lys Gly Met Cys Tyr
1 5 10 15

Phe Thr Asn Gly Thr Glu Arg Val Arg Leu Val Thr Arg Tyr Ile Tyr
20 25 30

Asn Arg Glu Glu Tyr Ala Arg Phe Asp Ser Asp Val Gly Val Tyr Arg
35 40 45

Ala Val Thr Pro Gln Gly Arg Pro Asp Ala Glu Tyr Trp Asn Ser Gln
50 55 60

Lys Glu Val Leu Glu Gly Thr Arg Ala Glu Leu Asp Thr Val Cys Arg
65 70 75 80

His Asn Tyr Glu Val Ala Phe Arg Gly Ile Leu Gln Arg Arg
85 90

<210> 223
<211> 94
<212> PRT
<213> Homo sapiens

<400> 223

Val Glu Pro Thr Val Thr Ile Ser Pro Ser Arg Thr Glu Ala Leu Asn
1 5 10 15

His His Asn Leu Leu Val Cys Ser Val Thr Asp Phe Tyr Pro Gly Gln
20 25 30

Ile Lys Val Arg Trp Phe Arg Asn Asp Gln Glu Glu Thr Ala Gly Val
35 40 45

Val Ser Thr Pro Leu Ile Arg Asn Gly Asp Trp Thr Phe Gln Ile Leu
50 55 60

Val Met Leu Glu Met Thr Pro Gln Arg Gly Asp Val Tyr Thr Cys His
65 70 75 80

Val Glu His Pro Ser Leu Gln Ser Pro Ile Thr Val Glu Trp
85 90

<210> 224
<211> 182
<212> PRT
<213> Homo sapiens

<400> 224

Asp Phe Leu Val Gln Phe Lys Gly Met Cys Tyr Phe Thr Asn Gly Thr
1 5 10 15

Glu Arg Val Arg Gly Val Ala Arg Tyr Ile Tyr Asn Arg Glu Glu Tyr
20 25 30

Gly Arg Phe Asp Ser Asp Val Gly Glu Phe Gln Ala Val Thr Glu Leu
35 40 45

Gly Arg Ser Ile Glu Asp Trp Asn Asn Tyr Lys Asp Phe Leu Glu Gln
50 55 60

Glu Arg Ala Ala Val Asp Lys Val Cys Arg His Asn Tyr Glu Ala Glu
65 70 75 80

Leu Arg Thr Thr Leu Gln Arg Gln Val Glu Pro Thr Val Thr Ile Ser
85 90 95

Pro Ser Arg Thr Glu Ala Leu Asn His His Asn Leu Leu Val Cys Ser
100 105 110

Val Thr Asp Phe Tyr Pro Ala Gln Ile Lys Val Arg Trp Phe Arg Asn
115 120 125

Asp Gln Glu Glu Thr Ala Gly Val Val Ser Thr Ser Leu Ile Arg Asn
130 135 140

Gly Asp Trp Thr Phe Gln Ile Leu Val Met Leu Glu Ile Thr Pro Gln
145 150 155 160

Arg Gly Asp Ile Tyr Thr Cys Gln Val Glu His Pro Ser Leu Gln Ser
165 170 175

Pro Ile Thr Val Glu Trp
180

<210> 225

<211> 93

<212> PRT

<213> Homo sapiens

<400> 225

Asp Phe Leu Val Gln Phe Lys Gly Met Cys Tyr Phe Thr Asn Gly Thr

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

<210> 226
 <211> 89
 <212> PRT
 <213> Homo sapiens

<400> 226

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

Leu Gln Ser Pro Ile Thr Val Glu Trp
85

<210> 227
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> VARIANT
<222> (4)..(4)
<223> Xaa is any amino acid other than Pro

<400> 227

Val Pro Gly Xaa Gly
1 5

<210> 228
<211> 223
<212> PRT
<213> Homo sapiens

<400> 228

Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly Gly Pro Ser
1 5 10 15

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
20 25 30

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln Glu Asp Pro
35 40 45

Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
50 55 60

Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val
65 70 75 80

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
85 90 95

Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile Glu Lys Thr
100 105 110

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
115 120 125

Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
130 135 140

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
145 150 155 160

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
165 170 175

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val Asp Lys Ser
180 185 190

Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
195 200 205

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
210 215 220

<210> 229
<211> 112
<212> PRT
<213> Homo sapiens

<400> 229

Ala Leu Asp Thr Asn Tyr Cys Phe Ser Ser Thr Glu Lys Asn Cys Cys
1 5 10 15

Val Arg Gln Leu Tyr Ile Asp Phe Arg Lys Asp Leu Gly Trp Lys Trp
20 25 30

Ile His Glu Pro Lys Gly Tyr His Ala Asn Phe Cys Leu Gly Pro Cys
35 40 45

Pro Tyr Ile Trp Ser Leu Asp Thr Gln Tyr Ser Lys Val Leu Ala Leu
50 55 60

Tyr Asn Gln His Asn Pro Gly Ala Ser Ala Ala Pro Ser Cys Val Pro
65 70 75 80

Gln Ala Leu Glu Pro Leu Pro Ile Val Tyr Tyr Val Gly Arg Lys Pro
85 90 95

Lys Val Glu Gln Leu Ser Asn Met Ile Val Arg Ser Cys Lys Cys Ser
100 105 110

<210> 230
<211> 112
<212> PRT
<213> Homo sapiens

<400> 230

Ala Leu Asp Ala Ala Tyr Cys Phe Arg Asn Val Gln Asp Asn Cys Cys
1 5 10 15

Leu Arg Pro Leu Tyr Ile Asp Phe Lys Arg Asp Leu Gly Trp Lys Trp
20 25 30

Ile His Glu Pro Lys Gly Tyr Asn Ala Asn Phe Cys Ala Gly Ala Cys
35 40 45

Pro Tyr Leu Trp Ser Ser Asp Thr Gln His Ser Arg Val Leu Ser Leu
50 55 60

Tyr Asn Thr Ile Asn Pro Glu Ala Ser Ala Ser Pro Ser Cys Val Ser
65 70 75 80

Gln Asp Leu Glu Pro Leu Thr Ile Leu Tyr Tyr Ile Gly Lys Thr Pro

85

90

95

Lys Ile Glu Gln Leu Ser Asn Met Ile Val Lys Ser Cys Lys Cys Ser
 100 105 110

<210> 231

<211> 114

<212> PRT

<213> Homo sapiens

<400> 231

Thr Asp Asn Asn Gly Ala Val Lys Phe Pro Gln Leu Cys Lys Phe Cys
 1 5 10 15

Asp Val Arg Phe Ser Thr Cys Asp Asn Gln Lys Ser Cys Met Ser Asn
 20 25 30

Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro Gln Glu Val Cys Val Ala
 35 40 45

Val Trp Arg Lys Asn Asp Glu Asn Ile Thr Leu Glu Thr Val Cys His
 50 55 60

Asp Pro Lys Leu Pro Tyr His Asp Phe Ile Leu Glu Asp Ala Ala Ser
 65 70 75 80

Pro Lys Cys Ile Met Lys Glu Lys Lys Lys Pro Gly Glu Thr Phe Phe
 85 90 95

Met Cys Ser Cys Ser Ser Asp Glu Cys Asn Asp Asn Ile Ile Phe Ser
 100 105 110

Glu Glu

<210> 232

<211> 104

<212> PRT

<213> Homo sapiens

<400> 232

Gln Leu Cys Lys Phe Cys Asp Val Arg Phe Ser Thr Cys Asp Asn Gln
1 5 10 15

Lys Ser Cys Met Ser Asn Cys Ser Ile Thr Ser Ile Cys Glu Lys Pro
20 25 30

Gln Glu Val Cys Val Ala Val Trp Arg Lys Asn Asp Glu Asn Ile Thr
35 40 45

Leu Glu Thr Val Cys His Asp Pro Lys Leu Pro Tyr His Asp Phe Ile
50 55 60

Leu Glu Asp Ala Ala Ser Pro Lys Cys Ile Met Lys Glu Lys Lys Lys
65 70 75 80

Pro Gly Glu Thr Phe Phe Met Cys Ser Cys Ser Ser Asp Glu Cys Asn
85 90 95

Asp Asn Ile Ile Phe Ser Glu Glu
100

<210> 233

<211> 5

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 233

Gly Ser Gly Gly Ser
1 5

<210> 234

<211> 4

<212> PRT

<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 234

Gly Gly Gly Ser
1

<210> 235
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 235

Gly Gly Ser Gly
1

<210> 236
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 236

Gly Gly Ser Gly Gly
1 5

<210> 237
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 237

Gly Ser Gly Ser Gly
1 5

<210> 238
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 238

Gly Ser Gly Gly Gly
1 5

<210> 239
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 239

Gly Gly Gly Ser Gly
1 5

<210> 240
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 240

Gly Ser Ser Ser Gly
1 5

<210> 241
<211> 41
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<220>
<221> VARIANT
<222> (2)..(41)
<223> Each copy of Ser Ser Ser Ser at positions 2 to 41 is either present or absent such that the number of copies ranges from 1 to 10

<400> 241

Gly Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
1 5 10 15

Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
20 25 30

Ser Ser Ser Ser Ser Ser Ser Ser Ser Ser
35 40

<210> 242
<211> 20
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 242

Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly
1 5 10 15

Ser Ser Ser Ser
20

<210> 243
<211> 25
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 243

Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly
1 5 10 15

Ser Ser Ser Ser Gly Ser Ser Ser Ser
20 25

<210> 244
<211> 50
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 244

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser
50

<210> 245
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 245

Gly Gly Gly Gly Ser
1 5

<210> 246

<211> 10
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 246

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 247
<211> 30
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 247

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25 30

<210> 248
<211> 35
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 248

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser

35

<210> 249
<211> 40
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 249

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser
35 40

<210> 250
<211> 45
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 250

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
35 40 45

<210> 251
<211> 17
<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 251

Gly	Ala	Gly	Ser	Leu	Gln	Pro	Leu	Ala	Leu	Glu	Gly	Ser	Leu	Gln	Lys
1				5					10					15	

Arg

<210> 252

<211> 15

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 252

Gly	Ile	Val	Asp	Gln	Cys	Cys	Thr	Ser	Ile	Cys	Ser	Leu	Tyr	Gln
1				5					10					15

<210> 253

<211> 15

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 253

Gly	Ile	Val	Glu	Gln	Cys	Cys	Thr	Ser	Ile	Cys	Ser	Leu	Tyr	Gln
1				5					10					15

<210> 254

<211> 20

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 254

Ser Phe Tyr Leu Lys Asn Val Gln Thr Gln Glu Thr Arg Thr Leu Thr
1 5 10 15

Gln Phe His Phe
20

<210> 255

<211> 18

<212> PRT

<213> Artificial sequence

<220>

<223> synthetic sequence

<400> 255

Gly Ser Leu Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly
1 5 10 15

Ile Val

<210> 256

<211> 110

<212> PRT

<213> Homo sapiens

<400> 256

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu
1 5 10 15

Trp Gly Pro Asp Pro Ala Ala Ala Phe Val Asn Gln His Leu Cys Gly
20 25 30

Ser His Leu Val Glu Ala Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe
35 40 45

Phe Tyr Thr Pro Lys Thr Arg Arg Glu Ala Glu Asp Leu Gln Val Gly
50 55 60

Gln Val Glu Leu Gly Gly Gly Pro Gly Ala Gly Ser Leu Gln Pro Leu
65 70 75 80

Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly Ile Val Glu Gln Cys Cys
85 90 95

Thr Ser Ile Cys Ser Leu Tyr Gln Leu Glu Asn Tyr Cys Asn
100 105 110

<210> 257
<211> 13
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 257

Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Lys Arg Gly
1 5 10

<210> 258
<211> 13
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 258

Gln Pro Leu Ala Leu Glu Gly Ser Leu Gln Ser Arg Gly
1 5 10

<210> 259
<211> 50
<212> PRT
<213> Artificial sequence

<220>
<223> synthetic sequence

<400> 259

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser
50