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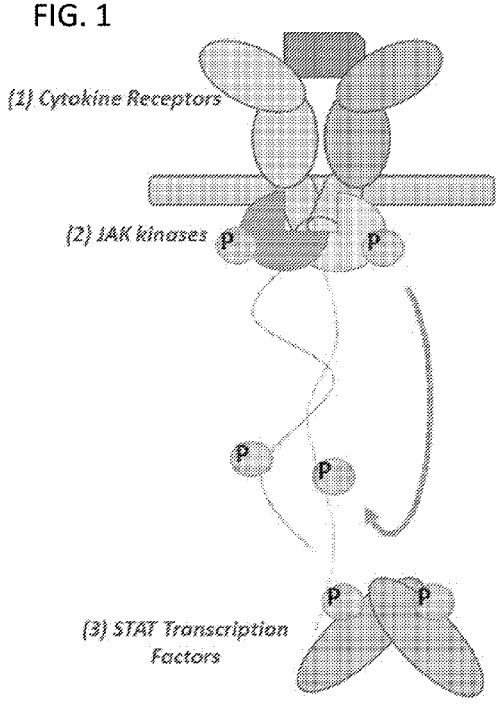
(54) Title: INDUCIBLE CHIMERIC CYTOKINE RECEPTORS

FIG. 1



(57) Abstract: The present invention provides inducible chimeric cytokine receptors responsive to a ligand, e.g., a small molecule or protein, uses of such receptors for improving the functional activities of genetically modified immune cells, such as T cells, comprising the inducible chimeric cytokine receptors, and compositions comprising such cells.

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[Continued on next page]

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INDUCIBLE CHIMERIC CYTOKINE RECEPTORS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims the benefit of priority to U.S. Provisional Application No. 62/637,600, filed on March 2, 2018, the contents of which are hereby incorporated by reference in their entirety.

REFERENCE TO SEQUENCE LISTING

[0002] This application is being filed electronically via EFS-Web and includes an electronically submitted sequence listing in .txt format. The .txt file contains a sequence listing entitled "ALGN_016_01WO_SeqList_ST25" created on February 27, 2019, and having a size of ~814 KB. The sequence listing contained in this .txt file is part of the specification and is incorporated herein by reference in its entirety.

FIELD

[0003] The present invention relates generally to inducible chimeric cytokine receptors for use with immune cells (e.g., T cells) to treat disease.

BACKGROUND

[0004] Chimeric antigen receptor T (CAR-T) cells have entered the clinic and have demonstrated very promising results (Maus, M. et al., 2014, Blood 123, 2625-35). Although the majority of subjects have been treated with autologous CAR-T cells which are derived from the subject's own T cells, allogeneic CAR-T cells derived from healthy donors offers a more commercially viable off-the-shelf option with the potential to treat a broader range of subjects.

[0005] Allogeneic CAR-T cells are generated by endowing T cells from healthy donors with CARs that are specifically activated by tumor associated antigens. Allogeneic CAR-T cells that do not express functional TCR (e.g., via knockout or knockdown) are deficient in basal TCR signaling. Basal TCR signaling increases persistence. TCR mobilizes Ca^{2+}, eventually leading to NFAT and NFkB activation. Although cytokines can increase persistence through STAT5, this does not reproduce native TCR signaling. Thus, there is a need for compositions and methods to improve allogeneic CAR-T cell persistence.

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[0005a] Any reference to or discussion of any document, act or item of knowledge in this specification is included solely for the purpose of providing a context for the present invention. It is not suggested or represented that any of these matters or any combination thereof formed at the priority date part of the common general knowledge, or was known to be relevant to an attempt to solve any problem with which this specification is concerned.

SUMMARY

[0005b] In a first aspect, the invention relates to an inducible chimeric cytokine receptor comprising:

a dimerization domain;

a tyrosine kinase activating domain that is a TPOR/MPLR, an EpoR, a GP130, a PRLR, a GCSFR, or a GHR tyrosine kinase activating domain and which comprises a transmembrane domain and a Janus Kinase (JAK)-binding domain; and

a tyrosine effector domain.

[0005c] In a second aspect, the invention relates to a polynucleotide comprising a nucleic acid sequence encoding the inducible chimeric cytokine receptor of the first aspect.

[0005d] In a third aspect, the invention relates to an expression vector comprising the polynucleotide of the second aspect.

[0005e] In a fourth aspect, the invention relates to an engineered immune cell comprising at least one inducible chimeric cytokine receptor of the first aspect or at least one polynucleotide of the second aspect.

[0005f] In a fifth aspect, the invention relates to a method of modulating an engineered immune cell in a subject, the method comprising administering a ligand to a subject that has previously been administered an engineered immune cell of the fourth aspect, wherein the dimeric ligand binds to the dimerization domain of the inducible chimeric cytokine receptor.

[0005g] In a sixth aspect, the invention relates to a method of preparing an engineered immune cell, the method comprising introducing a polynucleotide of the second aspect or an expression vector of the third aspect into an immune cell.

[0005h] In a seventh aspect, the invention relates to an isolated immune cell comprising:

(i) at least one inducible chimeric cytokine receptor comprising a dimerization domain, a tyrosine kinase activating domain, and a tyrosine effector domain, wherein the tyrosine

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kinase activating domain is a TPOR/MPLR, an EpoR, a GP130, a PRLR, a GCSFR, or a GHR tyrosine kinase activating domain and comprises a transmembrane domain and a Janus Kinase (JAK)-binding domain; and

(ii) a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain.

[0005i] In an eighth aspect, the invention relates to a method of generating an isolated immune cell comprising an inducible chimeric cytokine receptor of the first aspect, wherein the method comprises the steps of:
(a) providing an immune cell;
(b) introducing into the immune cell a polynucleotide that encodes a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain; and
(c) introducing into the immune cell a polynucleotide that encodes the inducible chimeric cytokine receptor.

[0005j] In a ninth aspect, the invention relates to a pharmaceutical composition comprising the isolated immune cell of the seventh aspect and a pharmaceutically acceptable carrier.

[0005k] In a tenth aspect, the invention relates to a method for treating a disorder in a subject, wherein the method comprises administering the isolated immune cell of the seventh aspect to the subject or administering the pharmaceutical composition of the ninth aspect to the subject, wherein the disorder is a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease.

[0005l] In an eleventh aspect, the invention relates to use of the isolated immune cell of the seventh aspect or the pharmaceutical composition of the ninth aspect in the manufacture of a medicament for treating a disorder, wherein the disorder is a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease.

[0006] The present invention provides inducible chimeric cytokine receptors responsive to a ligand, e.g., a small molecule or protein, uses of such receptors for improving the functional activities of genetically modified T cells (e.g., gene-modified antigen-specific T cells, such as chimeric antigen receptor T (CAR-T) cells), cells comprising the inducible chimeric cytokine receptors, and compositions comprising such cells. In particular, the present invention provides methods and compositions for bolstering the therapeutic efficacy of CAR-T cells.

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[0007] In one aspect, the invention provides an inducible chimeric cytokine receptor comprising: a dimerization domain; a tyrosine kinase activating domain; and a tyrosine effector domain.

[0008] In some embodiments, the tyrosine kinase activating domain comprises a Janus Kinase (JAK)-binding domain of, or derived from, a protein. In some of these embodiments, the tyrosine kinase activating domain further comprises a transmembrane domain.

[0009] In some embodiments, the tyrosine kinase activating domain comprises a tyrosine kinase domain of, or derived from, a receptor tyrosine kinase (RTK). In some of these embodiments, the tyrosine kinase activating domain further comprises a transmembrane domain.

[0010] In some embodiments, the tyrosine effector domain comprises a STAT-activation domain of, or derived from, at least one receptor. In some embodiments, the tyrosine effector domain comprises at least two STAT-activation domains of, or derived from, two receptors. In some embodiments, the tyrosine effector domain comprises STAT-activation domains of, or derived from, at least three, four, or more receptors.

[0011] In some embodiments, the tyrosine effector domain comprises a portion of the cytoplasmic tail of, or derived from, at least one receptor tyrosine kinase (RTK).

[0012] In some embodiments, the dimerization domain binds to a ligand such as AP1903, AP20187, dimeric FK506, or a dimeric FK506-like analog.

[0013] In some embodiments, the dimerization domain comprises an FKBP polypeptide. In some embodiments, the FKBP polypeptide is an FKBP12 polypeptide. In some embodiments, the FKBP12 polypeptide contains the amino acid substitution F36V (SEQ ID NO.: 218).

[0014] In some embodiments, the dimerization domain comprises an amino acid sequence selected from the group consisting of: (i) a FKBP polypeptide containing one

or more amino acid substitutions, (ii) two or three tandem repeats of an unmodified FKBP polypeptide, and (iii) two or three tandem repeats of a FKBP polypeptide containing one or more amino acid substitutions.

[0015] In some embodiments, the dimerization domain comprises a dimerization domain sequence selected from SEQ ID NOs.: 69-87.

[0016] In some embodiments, the dimerization domain comprises an FKBP dimerization domain sequence selected from SEQ ID NOs.: 69-73.

[0017] In some embodiments, the dimerization domain comprises an amino acid sequence of, or derived from, a polypeptide selected from the group consisting of: FKBP12, FKBP12(F36V), an extracellular domain of OX-40, and an extracellular domain of a TNFR2 superfamily receptors. In exemplary embodiments, the TNFR2 superfamily receptor is BCMA, TACI, or BAFFR.

[0018] In some embodiments, the dimerization domain binds a small molecule. In exemplary embodiments, a small molecule is AP1903, AP20187, dimeric FK506, or a dimeric FK506-like analog. In some embodiments, the dimerization domain binds a protein.

[0019] In some embodiments, the dimerization domain comprises an amino acid sequence of, or derived from, a protein selected from the group consisting of: FKBP, cyclophilin, steroid binding protein, estrogen binding protein, glucocorticoid binding protein, vitamin D binding protein, tetracycline binding protein, extracellular domain of a cytokine receptor, receptor tyrosine kinase, TNFR-family receptor, and immune co-receptor.

[0020] In some embodiments, the immune co-receptor, from which the dimerization domain is derived from, is selected from the group consisting of: erythropoietin receptor, prolactin receptor, growth hormone receptor, thrombopoietin receptor, granulocyte colony-stimulating factor receptor, GP130, common gamma chain receptor, common beta chain receptor, IFN alpha receptor, IFN gamma receptor, IFN lambda receptor, IL2/IL15 receptor, IL3 receptor, IL4 receptor, IL5 receptor, IL7 receptor, IL9 receptor, IL10 receptor, IL12 receptor, IL13 receptor, IL20 receptor, IL21 receptor, IL22 receptor, IL23 receptor, IL27 receptor, TSLP Receptor, G-CSF receptor, GM-CSF receptor, CNTF receptor, OSM receptor, LIF receptor, CT-1 receptor, TGFBR1/ALKL5, TGFBR2, EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1,

EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, RTK106, TNFR1, Fas, TRAILR1, TRAILR2, NGFR, DR3, DR6, EDAR, TNFR2, LTbR, OX40, CD40, CD27, CD30, 4-1BB, RANK, Fn14, TACI, BAFFR, HVEM, BCMA, GITR, TROY, RELT, XEDAR, TRAILR3, TRAILR4, OPG, DcR3, PD-1, CD80, CD86, ICOS-L, ICOS, CTLA-4, BTLA, CD160, LAG3, and TIM3.

[0021] In some embodiments, the tyrosine kinase activating domain comprises a JAK-binding domain of, or derived from, a receptor. In an exemplary embodiment, the receptor is a hormone receptor.

[0022] In some embodiments, the tyrosine kinase activating domain comprises a JAK-binding domain of, or derived from, a protein or a receptor selected from the group consisting of EPOR, GP130, PRLR, GHR, GCSFR, and TPOR/MPLR.

[0023] In some embodiments, the tyrosine kinase activating domain comprises a tyrosine kinase domain of, or derived from, a RTK, wherein the RTK is selected from the group consisting of: EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, and RTK106. In an exemplary embodiment, the RTK is EGFR.

[0024] In some embodiments, the tyrosine kinase activating domain comprises a tyrosine kinase activating domain sequence selected from SEQ ID NOs.: 88-133.

[0025] In some embodiments, the transmembrane domain present in the tyrosine kinase activating domain comprises a transmembrane domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, PD-1, and TPOR/MPLR.

[0026] In some embodiments, the transmembrane domain comprises a transmembrane domain derived from TPOR/MPLR. In some embodiments, the transmembrane domain is derived from amino acids 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID NO.: 64.

[0027] In some embodiments, the transmembrane domain comprises a deletion variant of the amino acid region 478-582 of the naturally occurring TPOR/MPLR

sequence of SEQ ID NO.: 64. In some embodiments, the deletion variant comprises a deletion of 1 to 18 amino acids from the region 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID NO.: 64. In some embodiments, the deletion variant comprises a deletion of 1 to 18 amino acids from the region 489-510 of the naturally occurring TPOR/MPLR sequence of SEQ ID NO.: 64.

[0028] In some embodiments, the transmembrane domain comprises an insertion variant of the amino acid region 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID NO.: 64. In some embodiments, the insertion variant comprises an insertion of 1 to 8 amino acids in the region 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID NO.: 64. In some embodiments, the insertion variant comprises an insertion of 1 to 8 amino acids in the region 489-510 of the naturally occurring TPOR/MPLR sequence of SEQ ID NO.: 64. In exemplary embodiments, the amino acids inserted in the insertion variant are selected from the group consisting of: leucine, valine, and isoleucine.

[0029] In some embodiments, the tyrosine effector domain comprises at least one STAT-activation domain of, or derived from, a receptor. In some embodiments, the tyrosine effector domain comprises at least two STAT-activation domains of, or derived from, two receptors. In some embodiments, the tyrosine effector domain comprises STAT-activation domains of, or derived from, at least three, four, or more receptors. In some embodiments, the receptors are hormone receptors and/or cytokine receptors.

[0030] In some embodiments, the tyrosine effector domain comprises STAT-activation domains of, or derived from, at least one, two, three, four, or more receptors, wherein the receptors are selected from the group consisting of: BLNK, IL2RG, EGFR, EpoR, GHR, IFNAR1, IFNAR2, IFNAR1/2, IFNLR1, IL10R1, IL12Rb1, IL12Rb2, IL21R, IL2Rb, IL2small, IL7R, IL7Ra, IL9R, IL15R, and IL21R.

[0031] In some embodiments, the tyrosine effector domain comprises a cytotail (a portion of the cytoplasmic tail of a receptor comprising one or more tyrosine residues that can be phosphorylated) of, or derived from, at least one, two, three, four, or more receptors, wherein the receptor is a cytokine receptor, hormone receptor, and/or a RTK.

[0032] In some embodiments, an inducible chimeric cytokine receptor comprises a dimerization domain; a tyrosine kinase activating domain comprising a transmembrane domain and a JAK-binding domain; and a tyrosine effector domain comprising at least one STAT-activation domain of, or derived from, a receptor. In some of these

embodiments, the tyrosine effector domain may comprise STAT-activation domains of, or derived from, at least two, three, four, or more receptors.

[0033] In some embodiments, an inducible chimeric cytokine receptor comprises a dimerization domain; a tyrosine kinase activating domain comprising a transmembrane domain and a JAK-binding domain; and a tyrosine effector domain comprising at least one cytotail of, or derived from, a receptor. In some of these embodiments, the tyrosine effector domain may comprise cytotails of, or derived from, at least two, three, four, or more receptors.

[0034] In some embodiments, an inducible chimeric cytokine receptor comprises a dimerization domain comprising an FKBP polypeptide; a tyrosine kinase activating domain comprising a transmembrane domain and a JAK-binding domain, wherein the transmembrane domain comprises a transmembrane domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, PD-1, and TPOR, and the JAK-binding domain comprises a JAK-binding domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, and TPOR; and a tyrosine effector domain comprising at least one STAT-activation domain of, or derived from, a receptor selected from the group consisting of: BLNK, IL2RG, EGFR, EpoR, GHR, IFNAR1, IFNAR2, IFNAR1/2, IFNLR1, IL10R1, IL12Rb1, IL12Rb2, IL21R, IL2Rb, IL2small, IL7R, IL7Ra, IL9R, IL15R, and IL21R. In some of these embodiments, the tyrosine effector domain comprises STAT-activation domains of, or derived from, at least two, three, four, or more receptors.

[0035] In some embodiments, the tyrosine effector domain comprises a tyrosine effector domain sequence selected from SEQ ID NOs.: 134-176.

[0036] In some embodiments, the dimerization domain is located at the N-terminus of the inducible chimeric cytokine receptor.

[0037] In some embodiments, the dimerization domain is located at the C-terminus of the inducible chimeric cytokine receptor.

[0038] In some embodiments, the inducible chimeric cytokine receptor provided herein comprises a membrane-targeting motif. In exemplary embodiments, the membrane-targeting motif comprises a myristoylation motif.

[0039] In some embodiments, the inducible chimeric cytokine receptor provided herein is myristoylated.

[0040] In some embodiments, the inducible chimeric cytokine receptor comprises a sequence disclosed in Tables 2A or 2B. In some embodiments, the inducible chimeric

cytokine receptor comprises a sequence selected from SEQ ID NOs.: 1-58, 187-215, and 225-311.

[0041] In another aspect, the present disclosure provides polynucleotides comprising a nucleic acid sequence encoding the inducible chimeric cytokine receptors described herein. In another aspect, the present disclosure provides an expression vector comprising the polynucleotides.

[0042] In another aspect, the present disclosure provides an engineered immune cell comprising at least one inducible chimeric cytokine receptor disclosed herein. In some embodiments, the engineered immune cell comprises at least two inducible chimeric cytokine receptors. In some embodiments, the engineered immune cell comprises at least three or four inducible chimeric cytokine receptors disclosed herein. When more than one inducible chimeric cytokine receptor is present in the immune cells, the dimerization domain, the tyrosine kinase activating domain, and the tyrosine effector domain of each receptor can be the same or different.

[0043] In another aspect, the present disclosure provides an engineered immune cell comprising at least one polynucleotide encoding inducible chimeric cytokine receptor disclosed herein.

[0044] In some embodiments, the engineered immune cell further comprises a chimeric antigen receptor (CAR) or a polynucleotide encoding a CAR.

[0045] In some embodiments, the immune cell is selected from the group consisting of: T cell, dendritic cell, killer dendritic cell, mast cell, NK-cell, macrophage, monocyte, and B-cell.

[0046] In some embodiments, the immune cell is derived from a stem cell. In exemplary embodiments, the immune cell is derived from adult stem cells, non-human stem cells, cord blood stem cells, progenitor cells, bone marrow stem cells, induced pluripotent stem cells, totipotent stem cells or hematopoietic stem cells.

[0047] In some embodiments, the immune cell is a T cell. In some embodiments, the immune cell is an autologous T cell. In some embodiments, the immune cell is an allogeneic T cell.

[0048] In another aspect, the present disclosure provides a method of modulating an engineered immune cell in a subject, the method comprising administering a ligand to a subject that has previously been administered an engineered immune cell described herein, wherein the dimeric ligand binds to the dimerization domain of the inducible chimeric cytokine receptor. In an exemplary embodiment, the ligand is AP1903.

[0049] In another aspect, provided herein is a method of preparing an engineered immune cell, the method comprising introducing a polynucleotide or an expression vector comprising a polynucleotide encoding an inducible chimeric cytokine receptor into an immune cell. In an exemplary embodiment, the immune cell is selected from the group consisting of: T cell, dendritic cell, killer dendritic cell, mast cell, NK-cell, macrophage, monocyte, B-cell, and an immune cell derived from a stem cell. In an exemplary embodiment, the immune cell is a T cell.

[0050] In another aspect, the disclosure provides an isolated immune cell comprising: (i) at least one inducible chimeric cytokine receptor comprising a dimerization domain, a tyrosine kinase activating domain, and a tyrosine effector domain as disclosed herein; and (ii) a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain.

[0051] In some embodiments, the isolated immune cell comprises at least two inducible chimeric cytokine receptors. In some other embodiments, the isolated immune cell comprises three or four inducible chimeric cytokine receptors.

[0052] In some embodiments, the isolated immune cell of the present disclosure exhibits improved persistence upon contact with a ligand that binds to the dimerization domain relative to persistence of an isolated immune cell that does not express the inducible chimeric cytokine receptor.

[0053] In some embodiments, the isolated immune cell of the present disclosure exhibits increased activation of STAT upon contact with a ligand that binds to the dimerization domain relative to activation of STAT shown by an isolated immune cell that does not express the inducible chimeric cytokine receptor. The STAT activated in the cell can be STAT1, STAT2, STAT3, STAT4, STAT5, STAT6, or combinations thereof.

[0054] In some embodiments, the activation of STAT by the isolated immune cell of the present disclosure, upon contact with a ligand that binds to the dimerization domain, increases with the dose of the ligand compared to activation of STAT shown by the isolated immune cell that does not express the inducible chimeric cytokine receptor.

[0055] In some embodiments, the isolated immune cell of the present disclosure exhibits increased cytotoxicity upon contact with a ligand that binds to the dimerization domain compared to cytotoxicity exhibited by an isolated immune cell that does not express the inducible chimeric cytokine receptor.

[0056] In some embodiments, the isolated immune cell of the present disclosure expands (proliferates) upon contact with a ligand that binds to the dimerization domain compared to an isolated immune cell that does not express the inducible chimeric cytokine receptor.

[0057] In some embodiments, the level of cell markers for stem cell memory (Tscm) and/or central memory (Tcm) on the isolated immune cell of the present disclosure are increased or maintained upon contact with a ligand that binds to the dimerization domain compared to the level of these markers on an isolated immune cell that does not express the inducible chimeric cytokine receptor.

[0058] In one aspect, provided herein is a method of generating an isolated immune cell comprising an inducible chimeric cytokine receptor disclosed herein, the method comprising the steps of: (a) providing an immune cell; (b) introducing into the immune cell a polynucleotide that encodes a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain; and (c) introducing into the immune cell a polynucleotide that encodes the inducible chimeric cytokine receptor.

[0059] In some embodiments, step c) of the above method comprises stably expressing the inducible chimeric cytokine receptor into the cell.

[0060] In some embodiments, in step c) of the above method, the polynucleotide that encodes the inducible chimeric cytokine receptor is introduced into the cell by a transposon/transposase system, a viral-based gene transfer system, or electroporation.

[0061] In some embodiments, in step b) of the above method, the polynucleotide that encodes the chimeric antigen receptor is introduced into the cell by a transposon/transposase system or a viral-based gene transfer system.

[0062] In some embodiments, the viral-based gene transfer system comprises recombinant retrovirus or lentivirus.

[0063] In some embodiments of the above method, step (b) occurs prior to step (c) or step (c) occurs prior to step (b).

[0064] In one aspect, the present disclosure provides a pharmaceutical composition comprising the isolated immune cell described herein.

[0065] In one aspect, the present disclosure provides a method for treating a disorder in a subject, wherein the method comprises administering the isolated immune cell comprising an inducible cytokine receptor disclosed herein or administering the pharmaceutical composition comprising such immune cells.

[0066] In another aspect, the present disclosure provides use of the isolated immune cell disclosed herein or a pharmaceutical composition comprising the isolated immune cell for treating a disorder.

[0067] In some embodiments, the cells or the pharmaceutical composition are provided to the subject more than once.

[0068] In some embodiments, the cells or the pharmaceutical composition are provided to the subject at least about 1, 2, 3, 4, 5, 6, 7, or more days apart

[0069] In some embodiments, the subject has been previously treated with a therapeutic agent prior to administration of the isolated immune cell or the pharmaceutical composition. In an exemplary embodiment, the therapeutic agent is an antibody or chemotherapeutic agent.

[0070] In some embodiments, the disorder treated using the methods of the present disclosure is a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease. The cancer can be a hematological malignancy or a solid cancer.

[0071] In some embodiments, the hematological malignancy treated using the present methods is selected from acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), chronic eosinophilic leukemia (CEL), myelodysplasia syndrome (MDS), non-Hodgkin's lymphoma (NHL), or multiple myeloma (MM).

[0072] In some embodiments, the solid cancer treated using the present methods is selected from biliary cancer, bladder cancer, bone and soft tissue carcinoma, brain tumor, breast cancer, cervical cancer, colon cancer, colorectal adenocarcinoma, colorectal cancer, desmoid tumor, embryonal cancer, endometrial cancer, esophageal cancer, gastric cancer, gastric adenocarcinoma, glioblastoma multiforme, gynecological tumor, head and neck squamous cell carcinoma, hepatic cancer, lung cancer, malignant melanoma, osteosarcoma, ovarian cancer, pancreatic cancer, pancreatic ductal adenocarcinoma, primary astrocytic tumor, primary thyroid cancer, prostate cancer, renal cancer, renal cell carcinoma, rhabdomyosarcoma, skin cancer, soft tissue sarcoma, testicular germ- cell tumor, urothelial cancer, uterine sarcoma, or uterine cancer.

Brief Description of the Drawings

[0073] FIG. 1 depicts a schematic diagram of an exemplary inducible chimeric cytokine receptor.

[0074] FIG. 2A depicts a schematic diagram of FKBP binding rapamycin to inhibit mTOR.

[0075] FIG. 2B depicts a schematic diagram of $FKBP^{F36V}$ binding to rapamycin-like compounds.

[0076] FIG. 2C depicts a schematic diagram of AP1903 dimerizing $FKBP^{F36V}$.

[0077] FIG. 3 depicts a schematic diagram of an exemplary inducible chimeric cytokine receptor.

[0078] FIG. 4 depicts a bar graph summarizing results of a STAT5 assay testing function of the indicated inducible chimeric cytokine receptors.

[0079] FIG. 5A depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0080] FIG. 5B depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0081] FIG. 6 depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0082] FIG. 7 depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0083] FIG. 8 depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptor.

[0084] FIG. 9 depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0085] FIG. 10A depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0086] FIG. 10B depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0087] FIG. 10C depicts a schematic showing the traditional approach of engineering chimeric cytokine receptors.

[0088] FIG. 10D depicts a schematic showing the approach used in the present disclosure for engineering chimeric cytokine receptors.

[0089] FIG. 10E depicts a schematic of the chimeric receptors tested in a cell-based reporter assay in Example 5C.

[0090] FIG. 10F depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0091] FIG. 11 depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0092] FIG. 12 depicts a schematic illustration of NFAT with AP-1binding to a promoter sequence.

[0093] FIG. 13 depicts a schematic diagram of the MEK/ERK pathway leading to upregulation of Fos through Myc/Max.

[0094] FIG. 14 depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0095] FIG. 15 depicts a schematic diagram of the BTK pathway.

[0096] FIG. 16 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cell growth.

[0097] FIG. 17 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cell survival.

[0098] FIG. 18 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cell phenotype.

[0099] FIG. 19 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cell phenotype.

[0100] FIG. 20 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release.

[0101] FIG. 21 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release.

[0102] FIG. 22 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on proliferation in the absence of signaling.

[0103] FIG. 23 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release in the absence of signaling.

[0104] FIG. 24 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release in the absence of signaling.

[0105] FIG. 25 depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cell growth.

[0106] FIG. 26 depicts a schematic of exemplary inducible cytokine receptors with dual tyrosine effector domains.

[0107] FIG. 27A depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0108] FIG. 27B depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0109] FIG. 28A depicts a schematic of an exemplary construct comprising a CAR and an inducible cytokine receptor.

[0110] FIG. 28B shows transduction efficiencies of T cells transduced with a vector comprising the construct shown in FIG. 28A.

[0111] FIG. 28C depicts a graph summarizing results of a FACS analysis testing function of the indicated inducible chimeric cytokine receptors.

[0112] FIG. 29 depicts a graph summarizing results of a FACS analysis testing function of the indicated inducible chimeric cytokine receptors.

[0113] FIG. 30A depicts a schematic of an exemplary construct comprising a CAR and an inducible cytokine receptor.

[0114] FIG. 30B depicts a graph summarizing results of an *in vitro* assay testing cytotoxicity of the indicated CAR-T cells.

[0115] FIG. 30C depicts a graph summarizing results of an *in vitro* assay testing cytotoxicity of the indicated CAR-T cells.

[0116] FIG. 30D depicts a graph summarizing results of an *in vitro* assay testing cytotoxicity of the indicated CAR-T cells.

[0117] FIG. 30E depicts a graph summarizing results of an *in vitro* assay testing cytotoxicity of the indicated CAR-T cells.

[0118] FIG. 31A depicts a graph summarizing results of a tumor volume assay for the indicated treatment groups.

[0119] FIG. 31B depicts a graph summarizing results of a tumor volume assay for the indicated treatment group.

[0120] FIG. 31C depicts a graph summarizing results of a tumor volume assay for the indicated treatment group.

[0121] FIG. 31D depicts a graph summarizing results of a tumor volume assay for the indicated treatment group.

[0122] FIG. 31E depicts a graph summarizing results of a tumor volume assay for the indicated treatment group.

[0123] FIG. 31F depicts a graph summarizing results of a tumor volume assay for the indicated treatment group.

[0124] FIG. 31G depicts a graph summarizing results of a tumor volume assay for the indicated treatment group.

[0125] FIG. 31H depicts a graph summarizing overall survival for the indicated treatment groups.

[0126] FIG. 32A depicts a graph summarizing expansion of the indicated CAR-T cells.

[0127] FIG. 32B depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cell phenotype.

[0128] FIG. 33A depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0129] FIG. 33B depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0130] FIG. 33C depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0131] FIG. 33D depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0132] FIG. 34 A depicts a schematic of exemplary constructs comprising a CAR and an inducible cytokine receptor.

[0133] FIG. 34B depicts a graph summarizing results of an *in vitro* assay testing cytotoxicity of the indicated CAR-T cells.

[0134] FIG. 34C depicts a graph summarizing results of an *in vitro* assay testing cytotoxicity of the indicated CAR-T cells.

[0135] FIG. 34D depicts a graph summarizing results of an *in vitro* assay testing cytotoxicity of the indicated CAR-T cells.

[0136] FIG. 34E depicts a graph summarizing results of an assay testing expansion of the indicated CAR-T cells.

[0137] FIG. 34F depicts a graph summarizing results of an assay testing expansion of the indicated CAR-T cells.

[0138] FIG. 35A depicts a schematic of exemplary constructs comprising a CAR and an inducible chimeric cytokine receptor.

[0139] FIG. 35B depicts a graph showing expansion of control CAR-T cells comprising the indicated inducible chimeric cytokine receptors.

[0140] FIG. 35C depicts a graph showing expansion of CAR-T cells comprising the indicated inducible chimeric cytokine receptors.

[0141] FIG. 35D depicts a graph showing expansion of CAR-T cells comprising the indicated inducible chimeric cytokine receptors.

[0142] FIG. 35E depicts a graph showing expansion of CAR-T cells comprising the indicated inducible chimeric cytokine receptors.

[0143] FIG. 36A depicts a schematic of an exemplary inducible chimeric cytokine receptor.

[0144] FIG. 36B depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0145] FIG. 36C depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0146] FIG. 37A depicts a schematic of exemplary inducible chimeric cytokine receptors.

[0147] FIG. 37B is a schematic of the interactions between the receptors BCMA, TACI, and BAFFR with their ligands BAFF and APRIL.

[0148] FIG. 37C depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0149] FIG. 37D depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0150] FIG. 38A shows the amino acid sequences for the wildtype TpoR and various transmembrane deletion variants.

[0151] FIG. 38B shows the amino acid sequences for the wildtype TpoR and various transmembrane insertion variants.

[0152] FIG. 38C depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0153] FIG. 39A depicts a schematic of an exemplary inducible chimeric cytokine receptor.

[0154] FIG. 39B depicts a graph summarizing results of a cell-based reporter assay testing function of the indicated inducible chimeric cytokine receptors.

[0155] FIG. 40A depicts a graph summarizing results of an *in vitro* cytotoxicity assay of CAR-T cells comprising the indicated inducible chimeric cytokine receptor.

[0156] FIG. 40B depicts a graph summarizing results of an *in vitro* cytotoxicity assay of CAR-T cells comprising the indicated inducible chimeric cytokine receptor.

[0157] FIG. 40C depicts a graph summarizing results of an *in vitro* cytotoxicity assay of CAR-T cells comprising the indicated inducible chimeric cytokine receptor.

[0158] FIG. 40D depicts a graph summarizing results of an *in vitro* cytotoxicity assay of CAR-T cells comprising the indicated inducible chimeric cytokine receptor.

[0159] FIG. 40E depicts a graph summarizing results of an *in vitro* cytotoxicity assay of CAR-T cells comprising the indicated inducible chimeric cytokine receptor.

[0160] FIG. 40F depicts a graph summarizing results of an *in vitro* cytotoxicity assay of CAR-T cells comprising the indicated chimeric receptor.

[0161] FIG. 41A depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release.

[0162] FIG. 41B depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release.

[0163] FIG. 42A depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release.

[0164] FIG. 42B depicts a graph summarizing the effects of the indicated inducible chimeric cytokine receptors on cytokine release.

[0165] FIG. 43 depicts a graph summarizing enrichment of CAR-T cells comprising the indicated chimeric cytokine receptors.

[0166] FIG. 44A depicts a graph summarizing the memory subset distribution of CAR-T cells comprising the indicated chimeric cytokine receptor.

[0167] FIG. 44B depicts a graph summarizing the memory subset distribution of CAR-T cells comprising the indicated chimeric cytokine receptor.

[0168] FIG. 44C depicts a graph summarizing the memory subset distribution of CAR-T cells comprising the indicated chimeric cytokine receptor.

[0169] FIG. 44D depicts a graph summarizing the memory subset distribution of CAR-T cells comprising the indicated chimeric cytokine receptor.

[0170] FIG. 44E depicts a graph summarizing the memory subset distribution of CAR-T cells comprising the indicated chimeric cytokine receptor.

[0171] FIG. 44F depicts a graph summarizing the memory subset distribution of CAR-T cells comprising the indicated chimeric cytokine receptor.

[0172] FIG. 44G depicts a graph summarizing the memory subset distribution of CAR-T cells comprising the indicated chimeric cytokine receptor.

[0173] FIG. 45A depicts a graph summarizing the effect of the indicated inducible chimeric cytokine receptor on cell phenotype.

[0174] FIG. 45B depicts a graph summarizing the effect of the indicated inducible chimeric cytokine receptor on cell phenotype.

[0175] FIG. 45C depicts a graph summarizing the effect of the indicated inducible chimeric cytokine receptor on cell phenotype.

[0176] FIG. 45D depicts a graph summarizing the effect of the indicated inducible chimeric cytokine receptor on cell phenotype.

[0177] FIG. 45E depicts a graph summarizing the effect of the indicated inducible chimeric cytokine receptor on cell phenotype.

[0178] FIG. 45F depicts a graph summarizing the effect of the indicated inducible chimeric cytokine receptor on cell phenotype.

[0179] FIG. 45G depicts a graph summarizing the effect of the indicated inducible chimeric cytokine receptor on cell phenotype.

Detailed Description

[0180] The present invention provides chimeric receptors and uses thereof for improving in vivo persistence and therapeutic efficacy of immune cells. Receptors responsive to a ligand, such as a small molecule (e.g., AP1903) or protein (e.g., Epo, Tpo, or PD-L1) are provided herein. Also provided are cells comprising such inducible chimeric cytokine receptors, compositions comprising such cells, and methods for improving the functional activities of isolated T cells, such as CAR-T cells. Also provided herein are CAR-T cells having improved persistence, and methods of using such CAR-T cells for treating a disorder.

General Techniques

[0181] The practice of the invention will employ, unless otherwise indicated, conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, biochemistry and immunology, which are within the skill of the art. Such techniques are explained fully in the literature, such as, Molecular Cloning: A Laboratory Manual, second edition (Sambrook et al., 1989) Cold Spring Harbor Press; Oligonucleotide Synthesis (M.J. Gait, ed., 1984); Methods in Molecular Biology, Humana Press; Cell Biology: A Laboratory Notebook (J.E. Cellis, ed., 1998) Academic Press; Animal Cell Culture (R.I. Freshney, ed., 1987); Introduction to Cell and Tissue Culture (J.P. Mather and P.E. Roberts, 1998) Plenum Press; Cell and Tissue Culture: Laboratory Procedures (A. Doyle, J.B. Griffiths, and D.G. Newell, eds., 1993-1998) J. Wiley and Sons; Methods in Enzymology (Academic Press, Inc.); Handbook of Experimental Immunology (D.M. Weir and C.C. Blackwell, eds.); Gene Transfer Vectors

for Mammalian Cells (J.M. Miller and M.P. Calos, eds., 1987); Current Protocols in Molecular Biology (F.M. Ausubel et al., eds., 1987); PCR: The Polymerase Chain Reaction, (Mullis et al., eds., 1994); Current Protocols in Immunology (J.E. Coligan et al., eds., 1991); Short Protocols in Molecular Biology (Wiley and Sons, 1999); Immunobiology (C.A. Janeway and P. Travers, 1997); Antibodies (P. Finch, 1997); Antibodies: a practical approach (D. Catty., ed., IRL Press, 1988-1989); Monoclonal antibodies: a practical approach (P. Shepherd and C. Dean, eds., Oxford University Press, 2000); Using antibodies: a laboratory manual (E. Harlow and D. Lane (Cold Spring Harbor Laboratory Press, 1999); The Antibodies (M. Zanetti and J.D. Capra, eds., Harwood Academic Publishers, 1995).

Definitions

[0182] As used herein "autologous" means that cells, a cell line, or population of cells used for treating subjects are originating from said subject or from a Human Leucocyte Antigen (HLA) compatible donor.

[0183] As used herein "allogeneic" means that cells or population of cells used for treating subjects are not originating from said subject but from a donor.

[0184] As used herein, the term "endogenous" refers to any material from or produced inside an organism, cell, tissue or system.

[0185] As used herein, the term "exogenous" refers to any material introduced from or produced outside an organism, cell, tissue or system.

[0186] As used herein, "immune cell" refers to a cell of hematopoietic origin functionally involved in the initiation and/or execution of innate and/or adaptative immune response. Examples of immune cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, invariant NKT cells, mast cells, myeloic-derived phagocytes, dendritic cells, killer dendritic cells, macrophages, and monocytes. The term "immune cell" as used herein also refers to cells derived from, for example without limitation, a stem cell. The stem cells can be adult stem cells, non-human embryonic stem cells, more particularly non-human stem cells, cord blood stem cells, progenitor cells, bone marrow stem cells, induced pluripotent stem cells, totipotent stem cells or hematopoietic stem cells.

[0187] The terms "polypeptide", "oligopeptide", "peptide" and "protein" are used interchangeably herein to refer to chains of amino acids of any length, preferably, relatively short chains (e.g., 10-100 amino acids) as well as longer chains containing

about 10-250, 10-500, 10-1000, 50-200, 50-500, or 50-1000 amino acids. The chain may be linear or branched, it may comprise modified amino acids, and/or may be interrupted by non-amino acids. The terms also encompass an amino acid chain that has been modified naturally or by intervention; for example, disulfide bond formation, glycosylation, lipidation, acetylation, phosphorylation, or any other manipulation or modification, such as conjugation with a labeling component. Also included within the definition are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, etc.), as well as other modifications known in the art. It is understood that the polypeptides can occur as single chains or associated chains.

[0188] As used herein, the term "expression" refers to the transcription and/or translation of a particular nucleotide sequence driven by a promoter.

[0189] As used herein, "expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. Expression vectors include all those known in the art, including cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno- associated viruses) that incorporate the recombinant polynucleotide.

[0190] As used herein, “operably linked” refers to the association of nucleic acid sequences on a single nucleic acid fragment so that the function of one is affected by the other. For example, a promoter is operably linked with a coding sequence when it is capable of affecting the expression of that coding sequence (i.e., that the coding sequence is under the transcriptional control of the promoter).

[0191] As used herein, "expression control sequence" means a nucleic acid sequence that directs transcription of a nucleic acid. An expression control sequence can be a promoter, such as a constitutive or an inducible promoter, or an enhancer. The expression control sequence is operably linked to the nucleic acid sequence to be transcribed.

[0192] “Promoter” and “promoter sequence” are used interchangeably and refer to a DNA sequence capable of controlling the expression of a coding sequence or functional RNA. In general, a coding sequence is located 3′ to a promoter sequence. It is understood by those skilled in the art that different promoters may direct the expression of a gene in different tissues or cell types, or at different stages of development, or in response to different environmental or physiological conditions.

[0193] In any of the vectors of the present invention, the vector optionally comprises a promoter disclosed herein.

[0194] A "host cell" includes an individual cell or cell culture that can be or has been a recipient for vector(s) for incorporation of polynucleotide inserts. Host cells include progeny of a single host cell, and the progeny may not necessarily be completely identical (in morphology or in genomic DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation. A host cell includes cells transfected in vivo with a polynucleotide(s) of this invention.

[0195] The term "extracellular ligand-binding domain" as used herein refers to an oligo- or polypeptide that is capable of binding a ligand. Preferably, the domain will be capable of interacting with a cell surface molecule. For example, the extracellular ligand-binding domain may be chosen to recognize a ligand that acts as a cell surface marker on target cells associated with a particular disease state.

[0196] The term "stalk domain" or "hinge domain" are used interchangeably herein to refer to any oligo- or polypeptide that functions to link the transmembrane domain to the extracellular ligand- binding domain. In particular, stalk domains are used to provide more flexibility and accessibility for the extracellular ligand-binding domain.

[0197] The term "intracellular signaling domain" refers to the portion of a protein which transduces the effector signal function signal and directs the cell to perform a specialized function.

[0198] A "co-stimulatory molecule" as used herein refers to the cognate binding partner on a T cell that specifically binds with a co-stimulatory ligand, thereby mediating a co-stimulatory response by the cell, such as, but not limited to proliferation. Co-stimulatory molecules include, but are not limited to an MHC class I molecule, BTLA and Toll ligand receptor. Examples of costimulatory molecules include CD27, CD28, CD8, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3 and a ligand that specifically binds with CD83 and the like.

[0199] A "co-stimulatory ligand" refers to a molecule on an antigen presenting cell that specifically binds a cognate co-stimulatory signal molecule 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 an MHC molecule loaded with peptide, mediates a T cell response, including, but not limited to, proliferation activation, differentiation and the like. A co-stimulatory ligand can include but is not limited to CD7, B7-1 (CD80), B7-2 (CD86),

PD-L1, PD-L2, 4-1BBL, OX40L, inducible costimulatory ligand (ICOS-L), intercellular adhesion molecule (ICAM, CD30L, CD40, CD70, CD83, HLA-G, MICA, M1CB, HVEM, lymphotoxin β receptor, 3/TR6, ILT3, ILT4, an agonist or antibody that binds Toll ligand receptor and a ligand that specifically binds with B7-H3. A co-stimulatory ligand also encompasses, inter alia, an antibody that specifically binds with a co-stimulatory molecule present on a T cell, such as but not limited to, CD27, CD28, 4-1BB, OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LTGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83.

[0200] An "antibody" is an immunoglobulin molecule capable of specific binding to a target, such as a carbohydrate, polynucleotide, lipid, polypeptide, etc., through at least one antigen recognition site, located in the variable region of the immunoglobulin molecule. As used herein, the term encompasses not only intact polyclonal or monoclonal antibodies, but also antigen-binding fragments thereof (such as Fab, Fab', $F(ab')_2$, and Fv), and any other modified configuration of the immunoglobulin molecule that comprises an antigen recognition site including, for example without limitation, single chain (scFv) and domain antibodies (including, for example, shark and camelid antibodies), and fusion proteins comprising an antibody, antibody mimetic or any protein that provides specific protein-protein interaction.

[0201] The term "antigen-binding fragment" or "antigen binding portion" of an antibody, as used herein, refers to one or more fragments of an intact antibody that retain the ability to specifically bind to a given antigen. Antigen binding functions of an antibody can be performed by fragments of an intact antibody. Examples of binding fragments encompassed within the term "antigen binding fragment" of an antibody include Fab; Fab'; $F(ab')_2$; an Fd fragment consisting of the VH and CH1 domains; an Fv fragment consisting of the VL and VH domains of a single arm of an antibody; a single domain antibody (dAb) fragment (Ward et al., Nature 341:544-546, 1989), and an isolated complementarity determining region (CDR).

[0202] An antibody, an antibody conjugate, or a polypeptide that "preferentially binds" or "specifically binds" (used interchangeably herein) to a target (e.g., BCMA protein) is a term well understood in the art, and methods to determine such specific or preferential binding are also well known in the art. A molecule is said to exhibit "specific binding" or "preferential binding" if it reacts or associates more frequently, more rapidly, with greater duration and/or with greater affinity with a particular cell or substance than it does with alternative cells or substances. An antibody "specifically binds" or "preferentially binds"

to a target if it binds with greater affinity, avidity, more readily, and/or with greater duration than it binds to other substances. It is also understood that by reading this definition, for example, an antibody (or moiety or epitope) that specifically or preferentially binds to a first target may or may not specifically or preferentially bind to a second target. As such, "specific binding" or "preferential binding" does not necessarily require (although it can include) exclusive binding. Generally, but not necessarily, reference to binding means preferential binding.

[0203] As known in the art, "polynucleotide," or "nucleic acid," as used interchangeably herein, refer to chains of nucleotides of any length, and include DNA and RNA. The nucleotides can be deoxyribonucleotides, ribonucleotides, modified nucleotides or bases, and/or their analogs, or any substrate that can be incorporated into a chain by DNA or RNA polymerase. A polynucleotide may comprise modified nucleotides, such as methylated nucleotides and their analogs. If present, modification to the nucleotide structure may be imparted before or after assembly of the chain. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component. Other types of modifications include, for example, "caps", substitution of one or more of the naturally occurring nucleotides with an analog, internucleotide modifications such as, for example, those with uncharged linkages (e.g., methyl phosphonates, phosphotriesters, phosphoamidates, carbamates, etc.) and with charged linkages (e.g., phosphorothioates, phosphorodithioates, etc.), those containing pendant moieties, such as, for example, proteins (e.g., nucleases, toxins, antibodies, signal peptides, poly-L-lysine, etc.), those with intercalators (e.g., acridine, psoralen, etc.), those containing chelators (e.g., metals, radioactive metals, boron, oxidative metals, etc.), those containing alkylators, those with modified linkages (e.g., alpha anomeric nucleic acids, etc.), as well as unmodified forms of the polynucleotide(s). Further, any of the hydroxyl groups ordinarily present in the sugars may be replaced, for example, by phosphonate groups, phosphate groups, protected by standard protecting groups, or activated to prepare additional linkages to additional nucleotides, or may be conjugated to solid supports. The 5' and 3' terminal OH can be phosphorylated or substituted with amines or organic capping group moieties of from 1 to 20 carbon atoms. Other hydroxyls may also be derivatized to standard protecting groups. Polynucleotides can also contain analogous forms of ribose or deoxyribose sugars that are generally known in the art, including, for example, 2'-O-methyl-, 2'-O-allyl, 2'-fluoro- or 2'-azido-ribose,

carbocyclic sugar analogs, alpha- or beta-anomeric sugars, epimeric sugars such as arabinose, xyloses or lyxoses, pyranose sugars, furanose sugars, sedoheptuloses, acyclic analogs and abasic nucleoside analogs such as methyl riboside. One or more phosphodiester linkages may be replaced by alternative linking groups. These alternative linking groups include, but are not limited to, embodiments wherein phosphate is replaced by P(O)S("thioate"), P(S)S ("dithioate"), (O)NR_2 ("amidate"), P(O)R, P(O)OR', CO or CH_2 ("formacetal"), in which each R or R' is independently H or substituted or unsubstituted alkyl (1-20 C) optionally containing an ether (-O-) linkage, aryl, alkenyl, cycloalkyl, cycloalkenyl or araldyl. Not all linkages in a polynucleotide need be identical. The preceding description applies to all polynucleotides referred to herein, including RNA and DNA.

[0204] As used herein, "transfection" refers to the uptake of exogenous or heterologous RNA or DNA by a cell. A cell has been "transfected" by exogenous or heterologous RNA or DNA when such RNA or DNA has been introduced inside the cell. A cell has been "transformed" by exogenous or heterologous RNA or DNA when the transfected RNA or DNA effects a phenotypic change. The transforming RNA or DNA can be integrated (covalently linked) into chromosomal DNA making up the genome of the cell.

[0205] As used herein, "transformation" refers to the transfer of a nucleic acid fragment into the genome of a host organism, resulting in genetically stable inheritance. Host organisms containing the transformed nucleic acid fragments are referred to as "transgenic" or "recombinant" or "transformed" organisms.

[0206] As used herein, "substantially pure" refers to material which is at least 50% pure (i.e., free from contaminants), more preferably, at least 90% pure, more preferably, at least 95% pure, yet more preferably, at least 98% pure, and most preferably, at least 99% pure.

[0207] As used herein, "treatment" is an approach for obtaining beneficial or desired clinical results. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, one or more of the following: reducing the proliferation of (or destroying) neoplastic or cancerous cells, inhibiting metastasis of neoplastic cells, shrinking or decreasing the size of tumor, remission of a disease (e.g., cancer), decreasing symptoms resulting from a disease (e.g., cancer), increasing the quality of life of those suffering from a disease (e.g., cancer), decreasing the dose of other medications required to treat a disease (e.g., cancer), delaying the progression of a

disease (e.g., cancer), curing a disease (e.g., cancer), and/or prolong survival of subjects having a disease (e.g., cancer).

[0208] "Ameliorating" means a lessening or improvement of one or more symptoms as compared to not administering a treatment. "Ameliorating" also includes shortening or reduction in duration of a symptom.

[0209] As used herein, an "effective dosage" or "effective amount" of drug, compound, or pharmaceutical composition is an amount sufficient to effect any one or more beneficial or desired results. For prophylactic use, beneficial or desired results include eliminating or reducing the risk, lessening the severity, or delaying the outset of the disease, including biochemical, histological and/or behavioral symptoms of the disease, its complications and intermediate pathological phenotypes presenting during development of the disease. For therapeutic use, beneficial or desired results include clinical results such as reducing incidence or amelioration of one or more symptoms of various diseases or conditions (such as for example cancer), decreasing the dose of other medications required to treat the disease, enhancing the effect of another medication, and/or delaying the progression of the disease. An effective dosage can be administered in one or more administrations. For purposes of this invention, an effective dosage of drug, compound, or pharmaceutical composition is an amount sufficient to accomplish prophylactic or therapeutic treatment either directly or indirectly. As is understood in the clinical context, an effective dosage of a drug, compound, or pharmaceutical composition may or may not be achieved in conjunction with another drug, compound, or pharmaceutical composition. Thus, an "effective dosage" may be considered in the context of administering one or more therapeutic agents, and a single agent may be considered to be given in an effective amount if, in conjunction with one or more other agents, a desirable result may be or is achieved.

[0210] As used herein, the term "subject" refers to any vertebrate including, without limitation, humans and other primates (*e.g.*, chimpanzees, cynomologous monkeys, and other apes and monkey species), farm animals (*e.g.*, cattle, sheep, pigs, goats and horses), sport animals, pets including domestic mammals (*e.g.*, dogs and cats), laboratory animals (*e.g.*, rabbits, rodents such as mice, rats, and guinea pigs), and birds (*e.g.*, domestic, wild and game birds such as chickens, turkeys and other gallinaceous birds, ducks, geese, and the like). In some embodiments, the subject is a mammal. In exemplary embodiments, the subject is a human.

[0211] As used herein, "vector" means a construct, which is capable of delivering, and, preferably, expressing, one or more gene(s) or sequence(s) of interest in a host cell. Examples of vectors include, but are not limited to, viral vectors, naked DNA or RNA expression vectors, plasmid, cosmid or phage vectors, DNA or RNA expression vectors associated with cationic condensing agents, DNA or RNA expression vectors encapsulated in liposomes, and certain eukaryotic cells, such as producer cells.

[0212] As used herein, "pharmaceutically acceptable carrier" or "pharmaceutical acceptable excipient" includes any material which, when combined with an active ingredient, allows the ingredient to retain biological activity and is non-reactive with the subject's immune system. Examples include, but are not limited to, any of the standard pharmaceutical carriers such as a phosphate buffered saline solution, water, emulsions such as oil/water emulsion, and various types of wetting agents. Preferred diluents for aerosol or parenteral administration are phosphate buffered saline (PBS) or normal (0.9%) saline. Compositions comprising such carriers are formulated by well-known conventional methods (see, for example, Remington's Pharmaceutical Sciences, 18th edition, A. Gennaro, ed., Mack Publishing Co., Easton, PA, 1990; and Remington, The Science and Practice of Pharmacy 21st Ed. Mack Publishing, 2005).

[0213] Reference to “about” a value or parameter herein includes (and describes) embodiments that are directed to that value or parameter per se. For example, description referring to “about X” includes description of “X.” Numeric ranges are inclusive of the numbers defining the range.

[0214] It is understood that wherever embodiments are described herein with the language “comprising,” otherwise analogous embodiments described in terms of “consisting of” and/or “consisting essentially of” are also provided.

[0215] Where aspects or embodiments of the invention are described in terms of a Markush group or other grouping of alternatives, the invention encompasses not only the entire group listed as a whole, but each member of the group individually and all possible subgroups of the main group, but also the main group absent one or more of the group members. The invention also envisages the explicit exclusion of one or more of any of the group members in the claimed invention.

[0216] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. In case of conflict, the present specification, including definitions, will control. Throughout this specification and claims, the word "comprise," or variations

such as "comprises" or "comprising" will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers. Unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular.

[0217] Exemplary methods and materials are described herein, although methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the invention. The materials, methods, and examples are illustrative only and not intended to be limiting.

Inducible chimeric cytokine receptors and improved isolated immune cells

[0218] Inducible chimeric cytokine receptors, cells comprising such receptors, and methods comprising such cells are provided herein. Also provided are uses of such inducible chimeric cytokine receptors for improving the functional activities of isolated immune cells, e.g., isolated T cells, such as isolated T cells comprising chimeric antigenic receptor (CAR). The methods and compositions provided herein are useful for improving *in vivo* and *in vitro* persistence, cytotoxicity, memory phenotype, and/or therapeutic efficacy of immune cells comprising CARs, such as CAR-T cells.

[0219] In some embodiments, an inducible chimeric cytokine receptor provided herein comprises, in any order: a dimerization domain, a tyrosine kinase activating domain, and a tyrosine effector domain. Optionally, an inducible chimeric cytokine receptor provided herein can include a membrane-targeting motif. Ligand-mediated dimerization of an inducible chimeric cytokine receptor provided herein induces receptor-mediated signaling events in host cells containing the inducible chimeric cytokine receptor. In some embodiments, this signaling can result in improved persistence. For example, in an exemplary embodiment, dimerization of the inducible chimeric cytokine receptor provided herein by a ligand would activate the JAK-STAT pathway and mimic signaling induced by a natural cytokine receptor. By “mimic”, it is meant that the signaling cascade activated by the inducible chimeric cytokine receptor of the present disclosure would be similar to the signaling cascade activated by a natural cytokine receptor, while the magnitude of activation induced by the chimeric cytokine receptors of the present disclosure could be different from that of a natural cytokine receptor. For example, if an inducible chimeric cytokine receptor of the present disclosure and a natural cytokine receptor both activate a STAT transcription factor; it is possible that the level of activation of STAT by the two receptors can be similar or different.

[0220] The "dimerization domain" of an inducible chimeric cytokine receptor may be any amino acid sequence that can be induced to dimerize or even trimerize or multimerize by a ligand that can bind to the dimerization domain. Accordingly, the dimerization domain is a ligand binding domain. In some embodiments, the dimerization domain of an inducible chimeric cytokine receptor provided herein can be present outside the cell membrane. In some embodiments, the dimerization domain of an inducible chimeric cytokine receptor can be present inside the cell.

[0221] In some embodiments, the ligand that binds to the dimerization domain is a dimeric ligand. For example, the dimerization domain may contain the amino acid sequence of an FK506 Binding Protein ("FKBP"). The FKBP protein specifically binds to the drug FK506. Ligands that are multimeric analogs of FK506 (i.e. ligands which contain at least two copies of FK506, or derivatives thereof) can induce the dimerization of a first protein and second protein that each contain the amino acid sequence of an FKBP, by the ligand binding to both the first protein and second protein, and thereby bringing them together. The first and the second protein can be identical or different. Thus, inducible chimeric cytokine receptors provided herein may be induced to dimerize by exposure of the inducible chimeric cytokine receptor to a suitable dimeric ligand which binds to the dimerization domain of the inducible chimeric cytokine receptor.

[0222] In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor provided herein may contain amino acid sequences of or derived from, for example, FKBPs, cyclophilins, steroid binding proteins, estrogen binding proteins, glucocorticoid binding proteins, vitamin D binding proteins, or tetracycline binding proteins. As used herein, an "FKBP polypeptide", "cyclophilin polypeptide" or like refers to a polypeptide having the amino acid sequence of the respective protein, or a portion thereof or variant thereof, wherein the portion or variant thereof retains the ability to bind to the corresponding ligand (e.g. for a FKBP polypeptide, the ligand FK506 and related molecules) with high affinity.

[0223] In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor provided herein may contain amino acid sequences of, or derived from, the extracellular domains of a cytokine receptor such as, for example without limitation, erythropoietin receptor, prolactin receptor, growth hormone receptor, thrombopoietin receptor, granulocyte colony-stimulating factor receptor, GP130, the common gamma chain receptor, common beta chain receptor, IFN alpha receptor, IFN gamma receptor, IFN lambda receptor, IL2/IL15 receptor, IL3 receptor, IL4 receptor, IL5 receptor, IL7

receptor, IL9 receptor, IL10 receptor, IL12 receptor, IL13 receptor, IL20 receptor, IL21 receptor, IL22 receptor, IL23 receptor, IL27 receptor, TSLP Receptor, G-CSF receptor, GM-CSF receptor, CNTF receptor, OSM receptor, LIF receptor, CT-1 receptor, TGFBR1/ALKL5, and TGFBR2. In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor provided herein may contain amino acid sequences of or derived from the extracellular domains of receptor tyrosine kinases (RTK) such as EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, and RTK106. The extracellular domains of cytokine receptors and RTKs may be dimerized by the corresponding ligand or agonist (e.g., for a thrombopoietin receptor polypeptide, corresponding ligands included, for example, TPO, eltrombopag, and related molecules).

[0224] In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor provided herein may contain amino acid sequences of or derived from, for example, the extracellular domains of TNFR family receptors such as TNFR1, Fas, TRAILR1, TRAILR2, NGFR, DR3, DR6, EDAR, TNFR2, LTbR, OX40, CD40, CD27, CD30, 4-1BB, RANK, Fn14, TACI, BAFFR, HVEM, BCMA, GITR, TROY, RELT, XEDAR, TRAILR3, TRAILR4, OPG, DcR3. The extracellular domain of TNFR family receptors multimerize upon binding to a trimeric TNFR ligand. An exemplary dimerization domain amino acid sequence that is derived from a TNFR family receptor (containing the BCMA extracellular domain) is: MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNTPPLTCQRYCNASVTNSVKGTNA (SEQ ID NO: 216). In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor provided herein may contain amino acid sequences of or derived from, for example, the extracellular domains of immune co-receptors or ligands such as PD-1, CD80, CD86, ICOS-L, ICOS, CTLA-4, BTLA, CD160, LAG3, or TIM3. The extracellular domains of immune co-receptors cluster upon binding a cell presenting the corresponding ligand. An exemplary dimerization domain amino acid sequence that is derived from an immune co-receptor (containing the PD-1 extracellular) is: MQIPQAPWPVVWAVLQLGWRPGWFLDSPDRPWNPPTFSPALLVVTEGDNATFTCSF

SNTSESFVLNWYRMSPSNQTDKLAAFPEDRSQPGQDCRFRVTQLPNGRDFHMSVVR ARRNDSGTYLCGAISLAPKAQIKESLRAELRVTERRAEVPTAHPSPSPRPAGQFQTLV (SEQ ID NO: 217).

[0225] In some embodiments, the dimerization domain may contain an FKBP polypeptide amino acid sequence. FKBPs are a group of proteins that have prolyl isomerase activity and bind to the drug FK506 and other related drugs.

[0226] Optionally, the FKBP may be human FKBP12 (also known as FKBP1A; GenBank: CAG46965.1). Optionally, a FKBP12 polypeptide may contain the F36V mutation. FKBP12 containing the F36V mutation binds with high affinity to the dimeric ligand AP1903 (Jemal, A. et al., CA Cancer J. Clinic. 58, 71-96 (2008); Scher, H. I. and Kelly, W. K., Journal of Clinical Oncology 11, 1566-72 (1993)). In addition, FKBP12 containing the F36V mutation binds to AP1903 with much higher affinity than wild-type FKBP12 binds AP1903.

[0227] An exemplary dimerization domain amino acid sequence (containing an FKBP12 polypeptide with the F36V mutation) is: GVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIR GWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLES (SEQ ID NO: 218).

[0228] In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor may contain an amino acid sequence of an FKBP comprising a modification selected from the group consisting of: (i) a FKBP polypeptide containing one or more amino acid substitutions, (ii) two or three tandem repeats of an unmodified (naturally occurring) FKBP amino acid sequence, and (iii) two or three tandem repeats of a FKBP polypeptide containing one or more amino acid substitutions. In some embodiments, the FKBP protein is a human FKBP protein (GenBank: CAG46965.1) and the modifications to FKBP described herein are made to the human FKBP protein. In some embodiments, the one or more amino acid substitutions in FKBP include one or more of: F36V, L106P, E31G, R71G, and K105E, residues in reference to the human FKBP protein (GenBank: CAG46965.1). In the embodiments, where the dimerization domain comprises two or three tandem repeats of the dimerization domain sequences disclosed herein, each repeat may comprise a different mutation of that sequence. For example, in an exemplary embodiment, the dimerization domain comprises three tandem repeats of an FKBP sequence, where one of the repeats comprises a natural FKBP sequence, a

second repeat comprises FKBP containing F36V substitution, and a third repeat comprises FKBP containing F36V and L106P substitutions, in any order.

[0229] In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor may contain an amino acid sequence of an FKBP comprising a modification selected from the group consisting of: (i) a FKBP polypeptide containing F36V substitution, (ii) a FKBP polypeptide containing F36V and L106P substitutions, (iii) a FKBP polypeptide containing E31G, F36V, R71G, and K105E substitutions, and (iv) two or three tandem repeats of any of these FKBP polypeptides.

[0230] In some embodiments, a dimerization domain may be cyclophilin polypeptide amino acid sequence. Cyclophilins are proteins that bind to ciclosporin (cyclosporin A). Cyclophilins include, for example, cyclophilin A and cyclophilin D.

[0231] In some embodiments, a dimerization domain may have any of the characteristics of the ligand binding region disclosed in US Patent No. 9434935, which is hereby incorporated by reference for all purposes.

[0232] In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor of the present disclosure may comprise an amino acid sequence of, or derived from, a polypeptide selected from the group consisting of: FKBP12(F36V), an extracellular domain of OX-40, and an extracellular domain of a TNFR2 superfamily receptors (e.g., BCMA, TACI, BAFFR).

[0233] In some embodiments, a dimerization domain of an inducible chimeric cytokine receptor provided herein comprises a dimerization domain amino acid sequence disclosed in Table 1B.

[0234] As used herein, a "dimeric" ligand may optionally contain more than two copies of a suitable binding molecule (i.e. the ligand may be multimeric); however, such ligands may still be considered "dimeric" as used herein, based on the ability of such ligands to dimerize corresponding binding molecules. Similarly, in some embodiments, a "dimerization domain" as provided herein may be capable of supporting multimerization (e.g. in the event that multiple copies of the dimerization domain are provided in the same molecule); however, such domains may also still be considered "dimerization domains" as used herein, based on the ability of such domains to dimerize. Typically, caspase-9 signaling can be effectively induced upon dimerization of caspase-9 molecules (i.e. trimerization or other multimerization is not required). In addition, references herein to a "ligand" are to a dimeric ligand (for example, when referring to a

"ligand" which induces dimerization of a chimeric caspase-9 protein provided herein), unless the context clearly dictates otherwise.

[0235] As used herein, a tyrosine kinase activating domain of an inducible chimeric cytokine receptor provided herein may comprise a transmembrane domain followed by a Janus Kinase (JAK) binding domain or the tyrosine kinase of a RTK. JAK and RTK kinases are activated by multimerization. JAKs include JAK1, JAK2, JAK3, and TYK2, and bind to a juxtamembrane motif consisting of a Box 1 and Box 2 motif. An exemplary tyrosine kinase activating domain amino acid sequence that activates a JAK2 kinase (containing the Erythropoietin Receptor transmembrane, Box 1, and Box 2 motifs) is: SEPVSGPTPSDLDPLILTLSLILVVILVLLTVLALLSHRRALKQKIWPGIPSPESEFEGLFT THKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC (SEQ ID NO: 219). In some embodiments, the transmembrane domain may contain mutations that reduce ligand-independent dimerization.

[0236] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor provided herein comprises a JAK binding domain of, or derived from, a protein. In some embodiments, the protein is a receptor. In some embodiments, the protein is a hormone receptor or a cytokine receptor.

[0237] In some embodiments, the tyrosine kinase activating domain comprises a JAK binding domain of, or derived from, a protein selected from the prolactin receptor (PRLR), growth hormone receptor (GHR), thrombopoietin receptor/ myeloproliferative leukemia protein receptor (TPOR/MPLR), erythropoietin receptor (EPOR), granulocyte colony-stimulating factor receptor (GCSFR), or GP130. The term "derived from" means one or more modifications are made to the natural sequence. For example, only a portion of the natural sequence may be used, or the natural sequence may be modified to contain a substitution, insertion, and/or deletion mutations, or a combination of these modifications. In some embodiments, the JAK binding domain comprises a JAK binding domain of, or derived from, TPOR or EPOR.

[0238] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor provided herein comprises a transmembrane domain of, or derived from, a protein selected from the PRLR, GHR, TPOR/MPLR, EPOR, GCSFR, and GP130.

[0239] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor provided herein comprises a transmembrane domain of, or derived from, PD-1. In these embodiments, the tyrosine kinase activating domain

further comprises a JAK-binding domain or a tyrosine kinase domain of, or derived from, a receptor as described herein.

[0240] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor provided herein comprises a transmembrane domain and a JAK-binding domain or a transmembrane domain and a tyrosine kinase domain, wherein the transmembrane domain is derived from a cytokine/hormone receptor (e.g., TpoR), a monomerized cytokine/hormone receptor (e.g., EpoR L241G L242P), or monomeric receptors (e.g., PD1). "Monomerized cytokine/hormone receptor" as used herein refers to a cytokine receptor or a hormone receptor that is a homodimer or a heterodimer in natural form but is mutated to exist as a monomeric receptor.

[0241] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor provided herein comprises a transmembrane domain of, or derived from, TPOR/MPLR. An exemplary full length sequence of naturally occurring TPOR/MPLR is shown in Table 1A (SEQ ID NO.: 64). In some embodiments, the tyrosine kinase activating domain comprises a transmembrane domain of, or derived from, the TPOR/MPLR sequence shown in Table 1A. For example, in some embodiments, the tyrosine kinase activating domain comprises amino acids 478-582 of TPOR/MPLR shown in Table 1A (this sequence is also shown as "TPOR/MPLR (478-582) (wildtype sequence)" in Table 1C).

[0242] In some other embodiments, the tyrosine kinase activating domain comprises a sequence derived from amino acids 478-582 of TPOR/MPLR shown in Table 1A. In these embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor comprises a sequence derived from amino acids 478-582 of TPOR/MPLR shown in Table 1A, wherein the sequence comprises one or more mutations selected from the group consisting of substitution, deletion, insertion, and combinations thereof. In an exemplary embodiment, the tyrosine kinase activating domain comprises a deletion variant of the amino acid sequence 478-582 of TPOR/MPLR shown in Table 1A. In some embodiments, the deletion variant comprises a deletion of 1, 1 to 20, 1 to 19, 1 to 18, 1 to 17, 1 to 16, 1 to 15, 1 to 14, 1 to 13, 1 to 12, 1 to 11, 1 to 10, 1 to 9, 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, 1 to 2, amino acids from the region 478-582 of TPOR/MPLR shown in Table 1A. In some embodiments, the deletion variant comprises a deletion of 1, 1 to 20, 1 to 19, 1 to 18, 1 to 17, 1 to 16, 1 to 15, 1 to 14, 1 to 13, 1 to 12, 1 to 11, 1 to 10, 1 to 9, 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, 1 to 2, amino acids from the region 489-510 of TPOR/MPLR shown in Table 1A. In

an exemplary embodiment, the tyrosine kinase activating domain comprises a deletion variant of the amino acid sequence 478-582 of TPOR/MPLR shown in Table 1C.

[0243] In some embodiments, the tyrosine kinase activating domain comprises an insertion variant of the amino acid sequence 478-582 of TPOR/MPLR shown in Table 1A. In some embodiments, the insertion variant comprises an insertion of 1, 1 to 10, 1 to 9, 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, 1 to 2, amino acids in the region 478-582 of TPOR/MPLR shown in Table 1A. In an exemplary embodiment, the tyrosine kinase activating domain comprises an insertion variant of the amino acid sequence 478-582 of TPOR/MPLR shown in Table 1C. In some embodiments, the amino acids that are inserted into the insertion variants are selected from the group consisting of: leucine, valine, and isoleucine.

[0244] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor comprises a sequence derived from amino acids 478-582 of TPOR/MPLR shown in Table 1A, wherein the sequence comprises a combination of deletions and insertions of amino acids in this region. In an exemplary embodiment, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor comprises a sequence derived from amino acids 478-582 of TPOR/MPLR shown in Table 1A, wherein the sequence comprises a deletion of 1 to 18 amino acids from the region 478-582 and an insertion of 1 to 8 amino acids in the region 478-582. In another exemplary embodiment, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor comprises a sequence derived from amino acids 489-510 of TPOR/MPLR shown in Table 1A, wherein the sequence comprises a deletion of 1 to 18 amino acids from the region 489-510 and an insertion of 1 to 8 amino acids in the region 489-510. In some embodiments, the amino acids that are inserted into the insertion variants are selected from the group consisting of: leucine, valine, and isoleucine.

[0245] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor comprises a sequence disclosed in Table 1C.

[0246] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor comprises a deletion and/or insertion variant of the transmembrane domain of PRLR, GHR, EPOR, GCSFR, or GP130. Exemplary full length sequences of naturally occurring PRLR, GHR, EPOR, GCSFR, and GP130 are disclosed in Table 1A along with their accession numbers. From this disclosure, the transmembrane domains of PRLR, GHR, EPOR, GCSFR, and GP130 can be located

and insertion and/or deletion variants of these transmembrane domains can be prepared.

[0247] In some embodiments, the transmembrane and/or the JAK binding domain of the tyrosine kinase activating domain may be derived from, for example, the common gamma chain receptor, common beta chain receptor, IFN alpha receptor (IFNAR), IFN gamma receptor (IFNGR), IFN lambda receptor (IFNLR), IL2/IL15 receptor (IL2R/IL15R), IL3 receptor (IL3R), IL4 receptor (IL4R), IL5 receptor (IL5R), IL7 receptor (IL7R), IL9 receptor (IL9R), IL10 receptor (IL10R), IL12 receptor (IL12R), IL13 receptor (IL13R), IL20 receptor (IL20R), IL21 receptor (IL21R), IL22 receptor (IL22R), IL23 receptor (IL23R), IL27 receptor (IL27R), TSLP Receptor (TSLPR), G-CSF receptor (GCSFR), GM-CSF receptor (GMCSFR), CNTF receptor (CNTFR), OSM receptor (OSMR), LIF receptor (LIFR), or CT-1 receptor (CT1R).

[0248] In some embodiments, the tyrosine kinase activating domain of an inducible chimeric cytokine receptor provided herein comprises a tyrosine kinase domain of, or derived from, a receptor tyrosine kinase (RTK). An exemplary tyrosine kinase activating domain from a RTK that activates a RTK kinase (containing the Epidermal Growth Factor Receptor transmembrane and kinase domains) is: GLEGCPTNGPKIPSIATGMVGALLLLLVVALGIGLFMRRRHIVRKRTLRRLLQERELVEP LTPSGEAPNQALLRILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREATS PKANKEILDEAYVMASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLDYVREHKDNIGS QYLLNWCVQIAKGMNYLEDRRLVHRDLAARNVLVKTPQHVKITDFGLAKLLGAEEKEY HAEGGKVPIKWMALESILHRIYTHQSDVWSYGVTVWELMTFGSKPYDGIPASEISSILE KGERLPQPPICTIDVYMIMVKCWMIDADSRPKFRELIIEFSKMARDPQRYL (SEQ ID NO: 220). In some embodiments, the tyrosine kinase activating domain comprises a transmembrane domain and a tyrosine kinase domain derived from other RTKs such as, for example, EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, or RTK106.

[0249] In some embodiments, the tyrosine kinase activating domain comprises a tyrosine kinase domain of, or derived from, EGFR.

[0250] In some embodiments, the tyrosine kinase activating domain comprises a tyrosine kinase activating domain sequence disclosed in Table 1B.

[0251] In some embodiments, a tyrosine effector domain may contain a portion of the cytoplasmic tail (cytotail) of at least one receptor such as a cytokine receptor, hormone receptor, or RTK, or a tyrosine kinase adaptor protein. The "cytotail" as used herein is the portion that contains one or more tyrosine residues that are capable of being phosphorylated by a kinase upon activation. Tyrosines within the cytotail or adaptor protein become phosphorylated by an activated tyrosine kinase. The phosphorylated tyrosine motifs recruit signal transduction factors. An exemplary tyrosine effector domain amino acid sequence from a cytokine receptor (containing the IL2Rb distal cytotail) is: VTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQVYFTYDPYSEED PDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSLLGGPSPPSTAPGGS GAGEERMPPSLQERVPRDWDPQPLGPPTPGVPDLVDFQPPPELVLREAGEEVPDAG PREGVSFPWSRPPGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV (SEQ ID NO: 221).

[0252] The cytotails of certain receptors, such as cytokine receptors and hormone receptors, comprise STAT-activation domains (can also be referred to herein as STAT-binding domains). In some embodiments, the tyrosine effector domain of the inducible chimeric cytokine receptors provided herein comprises at least one STAT-activation domain of, or derived from, a receptor. In some embodiments, the tyrosine effector domain of the inducible chimeric cytokine receptors provided herein comprises at least two, three, four, or more STAT-activation domains of, or derived from, two, three, four, or more receptors. The receptors can be cytokine receptors and/or hormone receptors.

[0253] In some embodiments, the tyrosine effector domain of an inducible chimeric cytokine receptor comprises a cytotail (a portion of the cytoplasmic tail that contains one or more tyrosine residues that are capable of being phosphorylated by a kinase) of, or derived from, at least one, two, three, four, or more receptors (e.g., cytokine receptor, hormone receptor, or RTK) or tyrosine kinase adaptor proteins. In an exemplary embodiment, the tyrosine effector domain of an inducible chimeric cytokine receptor comprises a cytotail of, or derived from, a cytokine receptor and a cytotail of, or derived from, a hormone receptor. In another exemplary embodiment, the tyrosine effector domain of an inducible chimeric cytokine receptor comprises a cytotail of, or derived from, a cytokine receptor and a cytotail of, or derived from, a RTK. In yet another exemplary embodiment, the tyrosine effector domain of an inducible chimeric cytokine

receptor comprises a cytotail of, or derived from, a hormone receptor and a cytotail of, or derived from, a RTK. In yet another exemplary embodiment, the tyrosine effector domain of an inducible chimeric cytokine receptor comprises a cytotail of, or derived from, a hormone receptor; a cytotail of, or derived from, a RTK; and a cytotail of, or derived from, a cytokine receptor. Similar combinations of cytotails where at least one of the cytotails comprises a phosphorylatable tyrosine-containing portion of a tyrosine kinase adaptor protein are contemplated. When the tyrosine effector domain of an inducible chimeric cytokine receptor comprises more than one cytotail, the cytotails can be present in any order.

[0254] In some embodiments, the tyrosine effector domain of the inducible chimeric cytokine receptors comprises a STAT-activation domain of, or derived from, two cytokine receptors. In some embodiments, the tyrosine effector domain of the inducible chimeric cytokine receptors comprises a STAT-activation domain of, or derived from, at least one receptor selected from the group consisting of: BLNK (B-cell linker protein), IL2RG, EGFR, EpoR, GHR, IFNAR1, IFNAR2, IFNAR1/2, IFNLR1, IL10R1, IL12Rb1, IL12Rb2, IL21R, IL2Rb, IL2small, IL7R, IL7Ra, IL9R, IL15R, and IL21R. When the tyrosine effector domain comprises more than one STAT-activation domain, the STAT-activation domains are in tandem with one domain being membrane-proximal and the other domain(s) being membrane-distal.

[0255] In some embodiments, the tyrosine effector domain of an inducible chimeric cytokine receptor comprises a cyotail of, or derived from, a first receptor selected from the group consisting of: BLNK, IL2RG, EGFR, EpoR, GHR, IFNAR1, IFNAR2, IFNAR1/2, IFNLR1, IL10R1, IL12Rb1, IL12Rb2, IL21R, IL2Rb, IL2small, IL7R, IL7Ra, IL9R, IL15R, and IL21R, and a cytotail of, or derived from, a second receptor selected from the group consisting of: BLNK, IL2RG, EGFR, EpoR, GHR, IFNAR1, IFNAR2, IFNAR1/2, IFNLR1, IL10R1, IL12Rb1, IL12Rb2, IL21R, IL2Rb, IL2small, IL7R, IL7Ra, IL9R, IL15R, and IL21R. In these embodiments, the cyotail from the first receptor can be membrane-proximal and the cyotail from the second receptor can be membrane-distal or vice versa. Similar embodiments, where the tyrosine effector domain of an inducible chimeric cytokine receptor comprises more than two, such as three, four, or more, cytotails from the receptors described in this paragraph are encompassed by the present disclosure.

[0256] In some embodiments, the tyrosine effector domain of the inducible chimeric cytokine receptors comprises at least one tyrosine effector domain sequences disclosed

in Table 1B. In some embodiments, the tyrosine effector domain comprises at least two tyrosine effector domain sequences disclosed in Table 1B. When more than one tyrosine effector domain sequence disclosed in Table 1B is present, any of the sequence can be membrane-proximal and the other sequence(s) can be membrane-distal.

[0257] In some embodiments the tyrosine effector domain contains sequences from the cytotail of cytokine receptors such as the common gamma chain receptor, common beta chain receptor, IFN alpha receptor, IFN gamma receptor, IFN lambda receptor, IL2/IL15 receptor, IL3 receptor, IL4 receptor, IL5 receptor, IL7 receptor, IL9 receptor, IL10 receptor, IL12 receptor, IL13 receptor, IL20 receptor, IL21 receptor, IL22 receptor, IL23 receptor, IL27 receptor, TSLP Receptor, G-CSF receptor, GM-CSF receptor, CNTF receptor, OSM receptor, LIF receptor, CT-1 receptor, Erythropoietin Receptor, Growth Hormone Receptor, Prolactin Receptor, Thrombopoietin receptor, or GP130. An exemplary tyrosine effector domain amino acid sequence from a RTK (containing the EGFR distal cytotail) is: VIQGDERMHLPSPTDSNFYRALMDEEDMDDVVDADEYLIPQQGFFSSPSTSRTPLLSS LSATSNNSTVACIDRNGLQSCPIKEDSFLQRYSSDPTGALTEDSIDDTFLPVPEYINQSV PKRPAGSVQNPVYHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQPTCVNSTFDSP AHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA (SEQ ID NO: 222). In some embodiments the tyrosine effector domain contains sequences from the cytotail of RTK such as EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, or RTK106. An exemplary tyrosine effector domain amino acid sequence from a tyrosine kinase adaptor protein (containing the BLNK tyrosine domain) is: ASESPADEEEQWSDDFDSDYENPDEHSDSEMYVMPAEENADDSYEPPPVEQETRPV HPALPFARGEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARLTSTLPALTALQKPQVPP KPKGLLEDEADYVVPVEDNDENYIHPTESSSPPPEKAPMVNR (SEQ ID NO: 223). In some embodiments the tyrosine effector domain contains sequences from or bind to adaptor proteins such as ALX, BLNK, Grb7, Nsp, SLP-76, SOCS, TSAd, APS, Bam32,

Crk, Gads, Grb2, Nck, SLAP, Shc, FRS2, Dab, Dok, IRS, eps8, AFAP110, Gab, ADAP, Carma1, Cas, CIN85, Cortactin, E3B1, Vinexin, SKAP-55, BANK, BCAP, Dof, Paxillin, LAT, LAX, LIME, NTAL, PAG, SIT, or TRIM.

[0258] In some embodiments, the tyrosine effector domain of an inducible chimeric cytokine receptor provided herein may contain sequences from one or more cytokine receptors, RTKs, and/or adaptor proteins. In some embodiments, the sequences may be in tandem. In some embodiments, the tyrosine effect domain may contain, for example, shorter tyrosine-containing peptides from the cytokine receptor, RTK, or tyrosine kinase adaptor protein. In some embodiments, the tyrosine effector domain can be a synthetic sequence capable of binding one or more proteins comprising, for example, phosphor-tyrosine binding protein (PTB) domains, Src homology 2 (SH2) domains, C2 domains, and/or Src homology 3 (SH3) domains.

[0259] In some embodiments, an inducible chimeric cytokine receptor provided herein comprises a dimerization domain; a tyrosine kinase activating domain comprising a transmembrane domain and a JAK-binding domain; and a tyrosine effector domain comprising a STAT-activation domain of, or derived from, at least one receptor. In some of these embodiments, the dimerization domain comprises an FKBP polypeptide; the transmembrane domain comprises a transmembrane domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, PD-1, and TPOR; the JAK-binding domain comprises a JAK-binding domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, and TPOR; and the STAT-activation domain comprises a STAT-activation domain of, or derived from, at least one receptor selected from the group consisting of: BLNK, IL2RG, EGFR, EpoR, GHR, IFNAR1, IFNAR2, IFNAR1/2, IFNLR1, IL10R1, IL12Rb1, IL12Rb2, IL21R, IL2Rb, IL2small, IL7R, IL7Ra, IL9R, IL15R, and IL21R.

[0260] In some embodiments, an inducible chimeric cytokine receptor provided herein comprises a dimerization domain selected from Table 1B, a tyrosine kinase activating domain selected from Table 1B or Table 1C, and a tyrosine effector domain selected from Table 1B.

[0261] In some embodiments, an inducible chimeric cytokine receptor provided herein comprises a sequence selected from Table 2A or Table 2B. In some embodiments, the inducible chimeric cytokine receptor comprises a sequence selected from SEQ ID NOs.: 1-58, 187-215, and 225-311.

[0262] Table 1A provides exemplary full length sequences of naturally occurring receptors provided in the disclosure, from which the transmembrane proteins are derived. The sequences provided in Table 1A are reference sequences, in relation to which later mutations are expressed, for example in Tables 1B and 1C.

Table 1A: Exemplary Naturally Occurring Receptors

>AAI12154.1 Erythropoietin receptor [Homo sapiens]	**SEQ ID**
MDHLGASLWPQVGSLCLLLAGAAWAPPPNLPDPKFESKAALLAARGPEELLCFTERL EDLVCFWEEAASAGVGPGNYSFSYQLEDEPWKLCRLHQAPTARGAVRFWCSLPTA DTSSFVPLELRVTAASGAPRYHRVIHINEVVLLDAPVGLVARLADESGHVVLRWLPPP ETPMTSHIRYEVDVSAGNGAGSVQRVEILEGRTECVLSNLRGRTRYTFAVRARMAEP SFGGFWSAWSEPVSLLTPSDLDPLILTLSLILVVILVLLTVLALLSHRRALKQKIWPGIPS PESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERCWGTMQ AVEPGTDDEGPLLEPVGSEHAQDTYLVLDKWLLPRNPPSEDLPGPGGSVDIVAMDE GSEASSCSSALASKPSPEGASAASFEYTILDPSSQLLRPWTLCPELPPTPPHLKYLYL VVSDSGISTDYSSGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPPSYVACS	59
>AAI17403.1 Interleukin 6 signal transducer (GP130, oncostatin M receptor) [Homo sapiens]	**60**
MLTLQTWLVQALFIFLTTESTGELLDPCGYISPESPVVQLHSNFTAVCVLKEKCMDYF HVNANYIVWKTNHFTIPKEQYTIINRTASSVTFTDIASLNIQLTCNILTFGQLEQNVYGITI ISGLPPEKPKNLSCIVNEGKKMRCEWDRGRETHLETNFTLKSEWATHKFADCKAKRD TPTSCTVDYSTVYFVNIEVWVEAENALGKVTSDHINFDPVYKVKPNPPHNLSVINSEEL SSILKLTWTNPSIKSVIILKYNIQYRTKDASTWSQIPPEDTASTRSSFTVQDLKPFTEYV FRIRCMKEDGKGYWSDWSEEASGITYEDRPSKAPSFWYKIDPSHTQGYRTVQLVWK TLPPFEANGKILDYEVTLTRWKSHLQNYTVNATKLTVNLTNDRYVATLTVRNLVGKSD AAVLTIPACDFQATHPVMDLKAFPKDNMLWVEWTTPRESVKKYILEWCVLSDKAPCIT DWQQEDGTVHRTYLRGNLAESKCYLITVTPVYADGPGSPESIKAYLKQAPPSKGPTV RTKKVGKNEAVLEWDQLPVDVQNGFIRNYTIFYRTIIGNETAVNVDSSHTEYTLSSLTS DTLYMVRMAAYTDEGGKDGPEFTFTTPKFAQGEIEAIVVPVCLAFLLTTLLGVLFCFNK RDLIKKHIWPNVPDPSKSHIAQWSPHTPPRHNFNSKDQMYSDGNFTDVSVVEIEAND KKPFPEDLKSLDLFKKEKINTEGHSSGIGGSSCMSSSRPSISSSDENESSQNTSSTVQ YSTVVHSGYRHQVPSVQVFSRSESTQPLLDSEERPEDLQLVDHVDGGDGILPRQQY FKQNCSQHESSPDISHFERSKQVSSVNEEDFVRLKQQISDHISQSCGSGQMKMFQE VSAADAFGPGTEGQVERFETVGMEAATDEGMPKSYLPQTVRQGGYMPQ	
>XP_011512371.1 prolactin receptor isoform X2 [Homo sapiens]	**61**

MKENVASATVFTLLLFLNTCLLNGQLPPGKPEIFKCRSPNKETFTCWWRPGTDGGLP TNYSLTYHREGETLMHECPDYITGGPNSCHFGKQYTSMWRTYIMMVNATNQMGSSF SDELYVDVTYIVQPDPPLELAVEVKQPEDRKPYLWIKWSPPTLIDLKTGWFTLLYEIRL KPEKAAEWEIHFAGQQTEFKILSLHPGQKYLVQVRCKPDHGYWSAWSPATFIQIPSD FTMNDTTVWISVAVLSAVICLIIVWAVALKGYSMVTCIFPPVPGPKIKGFDAHLLEKGKS EELLSALGCQDFPPTSDYEDLLVEYLEVDDSEDQHLMSVHSKEHPSQGMKPTYLDPD TDSGRGSCDSPSLLSEKCEEPQANPSTFYDPEVIEKPENPETTHTWDPQCISMEGKI PYFHAGGSKCSTWPLPQPSQHNPRSSYHNITDVCELAVGPAGAPATLLNEAGKDALK SSQTIKSREEGKATQQREVESFHSETDQDTPWLLPQEKTPFGSAKPLDYVEIHKVNK DGALSLLPKQRENSGKPKKPGTPENNKEYAKVSGVMDNNILVLVPDPHAKNVACFEE SAKEAPPSLEQNQAEKALANFTATSSKCRLQLGGLDYLDPACFTHSFH	
>NP_000154.1 growth hormone receptor isoform 1 precursor [Homo sapiens]	**62**
MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTNSSKEPKFTKCR SPERETFSCHWTDEVHHGTKNLGPIQLFYTRRNTQEWTQEWKECPDYVSAGENSC YFNSSFTSIWIPYCIKLTSNGGTVDEKCFSVDEIVQPDPPIALNWTLLNVSLTGIHADIQ VRWEAPRNADIQKGWMVLEYELQYKEVNETKWKMMDPILTTSVPVYSLKVDKEYEV RVRSKQRNSGNYGEFSEVLYVTLPQMSQFTCEEDFYFPWLLIIIFGIFGLTVMLFVFLF SKQQRIKMLILPPVPVPKIKGIDPDLLKEGKLEEVNTILAIHDSYKPEFHSDDSWVEFIEL DIDEPDEKTEESDTDRLLSSDHEKSHSNLGVKDGDSGRTSCCEPDILETDFNANDIHE GTSEVAQPQRLKGEADLLCLDQKNQNNSPYHDACPATQQPSVIQAEKNKPQPLPTE GAESTHQAAHIQLSNPSSLSNIDFYAQVSDITPAGSVVLSPGQKNKAGMSQCDMHPE MVSLCQENFLMDNAYFCEADAKKCIPVAPHIKVESHIQPSLNQEDIYITTESLTTAAGR PGTGEHVPGSEMPVPDYTSIHIVQSPQGLILNATALPLPDKEFLSSCGYVSTDQLNKIM P	
>XP_016855859.1 granulocyte colony-stimulating factor receptor isoform X1 [Homo sapiens]	**63**
MARLGNCSLTWAALIILLLPGSLEECGHISVSAPIVHLGDPITASCIIKQNCSHLDPEPQI LWRLGAELQPGGRQQRLSDGTQESIITLPHLNHTQAFLSCCLNWGNSLQILDQVELR AGYPPAIPHNLSCLMNLTTSSLICQWEPGPETHLPTSFTLKSFKSRGNCQTQGDSILD CVPKDGQSHCCIPRKHLLLYQNMGIWVQAENALGTSMSPQLCLDPMDVVKLEPPML RTMDPSPEAAPPQAGCLQLCWEPWQPGLHINQKCELRHKPQRGEASWALVGPLPL EALQYELCGLLPATAYTLQIRCIRWPLPGHWSDWSPSLELRTTERAPTVRLDTWWRQ RQLDPRTVQLFWKPVPLEEDSGRIQGYVVSWRPSGQAGAILPLCNTTELSCTFHLPS EAQEVALVAYNSAGTSRPTPVVFSESRGPALTRLHAMARDPHSLWVGWEPPNPWP QGYVIEWGLGPPSASNSNKTWRMEQNGRATGFLLKENIRPFQLYEIIVTPLYQDTMG PSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPEPPELGKSPLTHYTIFWTNAQ NQSFSAILNASSRGFVLHGLEPASLYHIHLMAASQAGATNSTVLTLMTLTPEGSELHIIL GLFGLLLLLTCLCGTAWLCCSPNRKNPLWPSVPDPAHSSLGSWVPTIMEELPGPRQG QWLGQTSEMSRALTPHPCVQDAFQLPGLGTPPITKLTVLEEDEKKPVPWESHNSSET CGLPTLVQTYVLQGDPRAVSTQPQSQSGTSDQVLYGQLLGSPTSPGPGHYLRCDST QPLLAGLTPSPKSYENLWFQASPLGTLVTPAPSQEDDCVFGPLLNFPLLQGIRVHGM EALGSF	
>NP_005364.1 thrombopoietin receptor precursor [Homo sapiens]	**64**
MPSWALFMVTSCLLLAPQNLAQVSSQDVSLLASDSEPLKCFSRTFEDLTCFWDEEEA APSGTYQLLYAYPREKPRACPLSSQSMPHFGTRYVCQFPDQEEVRLFFPLHLWVKN VFLNQTRTQRVLFVDSVGLPAPPSIIKAMGGSQPGELQISWEEPAPEISDFLRYELRY GPRDPKNSTGPTVIQLIATETCCPALQRPHSASALDQSPCAQPTMPWQDGPKQTSP SREASALTAEGGSCLISGLQPGNSYWLQLRSEPDGISLGGSWGSWSLPVTVDLPGD	

AVALGLQCFTLDLKNVTCQWQQQDHASSQGFFYHSRARCCPRDRYPIWENCEEEE KTNPGLQTPQFSRCHFKSRNDSIIHILVEVTTAPGTVHSYLGSPFWIHQAVRLPTPNLH WREISSGHLELEWQHPSSWAAQETCYQLRYTGEGHQDWKVLEPPLGARGGTLELR PRSRYRLQLRARLNGPTYQGPWSSWSDPTRVETATETAWISLVTALHLVLGLSAVLG LLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPS LLEILPKSSERTPLPLCSSQAQMDYRRLQPSCLGTMPLSVCPPMAESGSCCTTHIANH SYLPLSYWQQP	

[0263] Exemplary amino acid sequences useful in the inducible chimeric cytokine receptors provided herein are shown in Table 1B.

Table 1B

N-terminal membrane targeting motif	**Amino acid sequence**	**SEQ ID**
CD8 signal peptide	MALPVTALLLPLALLLHAARP	65
Myristoylation Motif	MGSSKSKPKDPSQR	66
Epitope tag	**Amino acid sequence**	**SEQ ID**
Myc	EQKLISEEDL	67
V5	IPNPLLGLDST	68
Dimerization domain	**Amino acid sequence**	**SEQ ID**
FKBP(F36V)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE	69
FKBP(F36V)-FKBP(F36V)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLGVQVETISPGDGRTFPKRGQTCVV HYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVI RGWEEGVAQMSVGQRAKLTISPDYAYGATGHP GIIPPHATLVFDVELLKLE	70
FKBP(F36V,L106P)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKP	71
FKBP(F36V,L106P)-FKBP(F36V,L106P)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKPGVQVETISPGDGRTFPKRGQTCVV HYTGMLEDKKVDSSRDRNKPFKFMLGKQEVIR GWEEGVAQMSVGQRAKLTISPDYAYGATGHPG IIPPHATLVFDVELLKPE	72
FKBP(E31G,36V,R71G,K105E)-	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLG DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV	73

FKBP(E31G,36V,R71G ,K105E)	AQMSVGQGAKLTISPDYAYGATGHPGIIPPHATL VFDVELLELGVQVETISPGDGRTFPKRGQTCVV HYTGMLGDGKKVDSSRDRNKPFKFMLGKQEVI RGWEEGVAQMSVGQGAKLTISPDYAYGATGHP GIIPPHATLVFDVELLELE	
ALK5/TGFBR1(1-126)	MEAAVAAPRPRLLLLVLAAAAAAAAALLPGATAL QCFCHLCTKDNFTCVTDGLCFVSVTETTDKVIH NSMCIAEIDLIPRDRPFVCAPSSKTGSVTTTYCC NQDHCNKIELPTTVKSSPGLGPVEL	74
TGFBR2(1-166)	MGRGLLRGLWPLHIVLWTRIASTIPPHVQKSVN NDMIVTDNNGAVKFPQLCKFCDVRFSTCDNQK SCMSNCSITSICEKPQEVCVAVWRKNDENITLET VCHDPKLPYHDFILEDAASPKCIMKEKKKPGETF FMCSCSSDECNDNIIFSEEYNTSNPDLLLVIFQ	75
EpoR(1-236)	MDHLGASLWPQVGSLCLLLAGAAWAPPPNLPD PKFESKAALLAARGPEELLCFTERLEDLVCFWE EAASAGVGPGNYSFSYQLEDEPWKLCRLHQAP TARGAVRFWCSLPTADTSSFVPLELRVTAASGA PRYHRVIHINEVVLLDAPVGLVARLADESGHVVL RWLPPPETPMTSHIRYEVDVSAGNGAGSVQRV EILEGRTECVLSNLRGRTRYTFAVRARMAEPSF GGFWSAW	76
PrlR(1-220)	MKENVASATVFTLLLFLNTCLLNGQLPPGKPEIF KCRSPNKETFTCWWRPGTDGGLPTNYSLTYHR EGETLMHECPDYITGGPNSCHFGKQYTSMWRT YIMMVNATNQMGSSFSDELYVDVTYIVQPDPPL ELAVEVKQPEDRKPYLWIKWSPPTLIDLKTGWF TLLYEIRLKPEKAAEWEIHFAGQQTEFKILSLHPG QKYLVQVRCKPDHGYWSAWSP	77
GHR(1-250)	MDLWQLLLTLALAGSSDAFSGSEATAAILSRAP WSLQSVNPGLKTNSSKEPKFTKCRSPERETFSC HWTDEVHHGTKNLGPIQLFYTRRNTQEWTQEW KECPDYVSAGENSCYFNSSFTSIWIPYCIKLTSN GGTVDEKCFSVDEIVQPDPPIALNWTLLNVSLTG IHADIQVRWEAPRNADIQKGWMVLEYELQYKEV NETKWKMMDPILTTSVPVYSLKVDKEYEVRVRS KQRNSGNYGEFSEVLYVT	78
TPOR/MPLR(1-478)	MPSWALFMVTSCLLLAPQNLAQVSSQDVSLLAS DSEPLKCFSRTFEDLTCFWDEEEAAPSGTYQLL YAYPREKPRACPLSSQSMPHFGTRYVCQFPDQ EEVRLFFPLHLWVKNVFLNQTRTQRVLFVDSVG LPAPPSIIKAMGGSQPGELQISWEEPAPEISDFL RYELRYGPRDPKNSTGPTVIQLIATETCCPALQR PHSASALDQSPCAQPTMPWQDGPKQTSPSRE ASALTAEGGSCLISGLQPGNSYWLQLRSEPDGI SLGGSWGSWSLPVTVDLPGDAVALGLQCFTLD LKNVTCQWQQQDHASSQGFFYHSRARCCPRD RYPIWENCEEEEKTNPGLQTPQFSRCHFKSRN DSIIHILVEVTTAPGTVHSYLGSPFWIHQAVRLPT PNLHWREISSGHLELEWQHPSSWAAQETCYQL RYTGEGHQDWKVLEPPLGARGGTLELRPRSRY	79

	RLQLRARLNGPTYQGPWSSW	
EGFR(1-631)	MRPSGTAGAALLALLAALCPASRALEEKKVCQG TSNKLTQLGTFEDHFLSLQRMFNNCEVVLGNLEI TYVQRNYDLSFLKTIQEVAGYVLIALNTVERIPLE NLQIIRGNMYYENSYALAVLSNYDANKTGLKELP MRNLQEILHGAVRFSNNPALCNVESIQWRDIVS SDFLSNMSMDFQNHLGSCQKCDPSCPNGSCW GAGEENCQKLTKIICAQQCSGRCRGKSPSDCC HNQCAAGCTGPRESDCLVCRKFRDEATCKDTC PPLMLYNPTTYQMDVNPEGKYSFGATCVKKCP RNYVVTDHGSCVRACGADSYEMEEDGVRKCK KCEGPCRKVCNGIGIGEFKDSLSINATNIKHFKN CTSISGDLHILPVAFRGDSFTHTPPLDPQELDILK TVKEITGFLLIQAWPENRTDLHAFENLEIIRGRTK QHGQFSLAVVSLNITSLGLRSLKEISDGDVIISGN KNLCYANTINWKKLFGTSGQKTKIISNRGENSCK ATGQVCHALCSPEGCWGPEPRDCVSCRNVSR GRECVDKCNLLEGEPREFVENSECIQCHPECLP QAMNITCTGRGPDNCIQCAHYIDGPHCVKTCPA GVMGENNTLVWKYADAGHVCHLCHPNCTYGC TGP	80
FGFR1(1-362)	MWSWKCLLFWAVLVTATLCTARPSPTLPEQAQ PWGAPVEVESFLVHPGDLLQLRCRLRDDVQSIN WLRDGVQLAESNRTRITGEEVEVQDSVPADSG LYACVTSSPSGSDTTYFSVNVSDALPSSEDDDD DDDSSSEEKETDNTKPNRMPVAPYWTSPEKME KKLHAVPAAKTVKFKCPSSGTPNPTLRWLKNGK EFKPDHRIGGYKVRYATWSIIMDSVVPSDKGNY TCIVENEYGSINHTYQLDVVERSPHRPILQAGLP ANKTVALGSNVEFMCKVYSDPQPHIQWLKHIEV NGSKIGPDNLPYVQILKTAGVNTTDKEMEVLHLR NVSFEDAGEYTCLAGNSIGLSHHSAWLTVLEAL	81
PDGFRA(1-514)	MGTSHPAFLVLGCLLTGLSLILCQLSLPSILPNEN EKVVQLNSSFSLRCFGESEVSWQYPMSEEESS DVEIRNEENNSGLFVTVLEVSSASAAHTGLYTCY YNHTQTEENELEGRHIYIYVPDPDVAFVPLGMT DYLVIVEDDDSAIIPCRTTDPETPVTLHNSEGVVP ASYDSRQGFNGTFTVGPYICEATVKGKKFQTIPF NVYALKATSELDLEMEALKTVYKSGETIVVTCAV FNNEVVDLQWTYPGEVKGKGITMLEEIKVPSIKL VYTLTVPEATVKDSGDYECAARQATREVKEMKK VTISVHEKGFIEIKPTFSQLEAVNLHEVKHFVVEV RAYPPPRISWLKNNLTLIENLTEITTDVEKIQEIRY RSKLKLIRAKEEDSGHYTIVAQNEDAVKSYTFEL LTQVPSSILDLVDDHHGSTGGQTVRCTAEGTPL PDIEWMICKDIKKCNNETSWTILANNVSNIITEIHS RDRSTVEGRVTFAKVEETIAVRCLAKNLLGAEN REL	82
PDGFRB(1-518)	MRLPGAMPALALKGELLLLSLLLLLEPQISQGLV VTPPGPELVLNVSSTFVLTCSGSAPVVWERMS QEPPQEMAKAQDGTFSSVLTLTNLTGLDTGEYF	83

	CTHNDSRGLETDERKRLYIFVPDPTVGFLPNDA EELFIFLTEITEITIPCRVTDPQLVVTLHEKKGDVA LPVPYDHQRGFSGIFEDRSYICKTTIGDREVDSD AYYVYRLQVSSINVSVNAVQTVVRQGENITLMCI VIGNEVVNFEWTYPRKESGRLVEPVTDFLLDMP YHIRSILHIPSAELEDSGTYTCNVTESVNDHQDE KAINITVVESGYVRLLGEVGTLQFAELHRSRTLQ VVFEAYPPPTVLWFKDNRTLGDSSAGEIALSTR NVSETRYVSELTLVRVKVAEAGHYTMRAFHEDA EVQLSFQLQINVPVRVLELSESHPDSGEQTVRC RGRGMPQPNIIWSACRDLKRCPRELPPTLLGNS SEEESQLETNVTYWEEEQEFEVVSTLRLQHVDR PLSVRCTLRNAVGQDT	
BCMA (1-54)	MLQMAGQCSQNEYFDSLLHACIPCQLRCSSNT PPLTCQRYCNASVTNSVKGTNA	84
BAFF-R (1-78)	MRRGPRSLRGRDAPAPTPCVPAECFDLLVRHC VACGLLRTPRPKPAGASSPAPRTALQPQESVGA GAGEAALPLPGLL	85
TACI (1-165)	MSGLGRSRRGGRSRVDQEERFPQGLWTGVAM RSCPEEQYWDPLLGTCMSCKTICNHQSQRTCA AFCRSLSCRKEQGKFYDHLLRDCISCASICGQH PKQCAYFCENKLRSPVNLPPELRRQRSGEVEN NSDNSGRYQGLEHRGSEASPALPGLKLSADQV ALVYS	86
OX40 (1-214)	MCVGARRLGRGPCAALLLLGLGLSTVTGLHCVG DTYPSNDRCCHECRPGNGMVSRCSRSQNTVC RPCGPGFYNDVVSSKPCKPCTWCNLRSGSERK QLCTATQDTVCRCRAGTQPLDSYKPGVDCAPC PPGHFSPGDNQACKPWTNCTLAGKHTLQPASN SSDAICEDRDPPATQPQETQGPPARPITVQPTE AWPRTSQGPSTRPVEVPGGRA	87
Tyrosine kinase activating domain	**Amino acid sequence**	**SEQ ID**
CD8(138-206)	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC	88
EpoR(237-338;L241G,L242P)	SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C	89
EpoR(237-338)	SEPVSGPTPSDLDPLILTLSLILVVILVLLTVLALLS HRRALKQKIWPGIPSPESEFEGLFTTHKGNFQL WLYQNDGCLWWSPCTPFTEDPPASLEVLSERC	90
EpoR(237-282;L241G,L242P)	SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKI	91
GP130(609-700)	TTPKFAQGEIEAIVVPVCLAFLLTTLLGVLFCFNK RDLIKKHIWPNVPDPSKSHIAQWSPHTPPRHNF NSKDQMYSDGNFTDVSVVEIEAND	92
PrlR(221-319)	ATFIQIPSDFTMNDTTVWISVAVLSAVICLIIVWAV ALKGYSMVTCIFPPVPGPKIKGFDAHLLEKGKSE ELLSALGCQDFPPTSDYEDLLVEYLEVDD	93

GHR(251-352)	LPQMSQFTCEEDFYFPWLLIIIFGIFGLTVMLFVF LFSKQQRIKMLILPPVPVPKIKGIDPDLLKEGKLE EVNTILAIHDSYKPEFHSDDSWVEFIELDIDE	94
GCSFR(614-710)	LTLMTLTPEGSELHIILGLFGLLLLLTCLCGTAWL CCSPNRKNPLWPSVPDPAHSSLGSWVPTIMEE DAFQLPGLGTPPITKLTVLEEDEKKPVPWE	95
TPOR/MPLR(478-582)	SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL	96
TPOR/MPLR(478-528)	SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHAL	97
EGFR(632-979)	GLEGCPTNGPKIPSIATGMVGALLLLLVVALGIGL FMRRRHIVRKRTLRRLLQERELVEPLTPSGEAP NQALLRILKETEFKKIKVLGSGAFGTVYKGLWIPE GEKVKIPVAIKELREATSPKANKEILDEAYVMASV DNPHVCRLLGICLTSTVQLITQLMPFGCLLDYVR EHKDNIGSQYLLNWCVQIAKGMNYLEDRRLVHR DLAARNVLVKTPQHVKITDFGLAKLLGAEEKEYH AEGGKVPIKWMALESILHRIYTHQSDVWSYGVT VWELMTFGSKPYDGIPASEISSILEKGERLPQPPI CTIDVYMIMVKCWMIDADSRPKFRELIIEFSKMA RDPQRYL	98
FGFR1(363-767)	EERPAVMTSPLYLEIIIYCTGAFLISCMVGSVIVYK MKSGTKKSDFHSQMAVHKLAKSIPLRRQVTVSA DSSASMNSGVLLVRPSRLSSSGTPMLAGVSEY ELPEDPRWELPRDRLVLGKPLGEGCFGQVVLA EAIGLDKDKPNRVTKVAVKMLKSDATEKDLSDLI SEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEY ASKGNLREYLQARRPPGLEYCYNPSHNPEEQL SSKDLVSCAYQVARGMEYLASKKCIHRDLAARN VLVTEDNVMKIADFGLARDIHHIDYYKKTTNGRL PVKWMAPEALFDRIYTHQSDVWSFGVLLWEIFT LGGSPYPGVPVEELFKLLKEGHRMDKPSNCTN ELYMMMRDCWHAVPSQRPTFKQLVEDLDRIVA LTSNQEYL	99
PDGFRA(515-954)	KLVAPTLRSELTVAAAVLVLLVIVIISLIVLVVIWKQ KPRYEIRWRVIESISPDGHEYIYVDPMQLPYDSR WEFPRDGLVLGRVLGSGAFGKVVEGTAYGLSR SQPVMKVAVKMLKPTARSSEKQALMSELKIMTH LGPHLNIVNLLGACTKSGPIYIITEYCFYGDLVNY LHKNRDSFLSHHPEKPKKELDIFGLNPADESTRS YVILSFENNGDYMDMKQADTTQYVPMLERKEV SKYSDIQRSLYDRPASYKKKSMLDSEVKNLLSD DNSEGLTLLDLLSFTYQVARGMEFLASKNCVHR DLAARNVLLAQGKIVKICDFGLARDIMHDSNYVS KGSTFLPVKWMAPESIFDNLYTTLSDVWSYGILL WEIFSLGGTPYPGMMVDSTFYNKIKSGYRMAKP DHATSEVYEIMVKCWNSEPEKRPSFYHLSEIVE NLL	100
PDGFRB(519-962)	QEVIVVPHSLPFKVVVISAILALVVLTIISLIILIMLW	101

	QKKPRYEIRWKVIESVSSDGHEYIYVDPMQLPY DSTWELPRDQLVLGRTLGSGAFGQVVEATAHG LSHSQATMKVAVKMLKSTARSSEKQALMSELKI MSHLGPHLNVVNLLGACTKGGPIYIITEYCRYGD LVDYLHRNKHTFLQHHSDKRRPPSAELYSNALP VGLPLPSHVSLTGESDGGYMDMSKDESVDYVP MLDMKGDVKYADIESSNYMAPYDNYVPSAPER TCRATLINESPVLSYMDLVGFSYQVANGMEFLA SKNCVHRDLAARNVLICEGKLVKICDFGLARDIM RDSNYISKGSTFLPLKWMAPESIFNSLYTTLSDV WSFGILLWEIFTLGGTPYPELPMNEQFYNAIKRG YRMAQPAHASDEIYEIMQKCWEEKFEIRPPFSQ LVLLLERLL	
murine EpoR(236-337;L264G,L265P)	SEPASLLTASDLDPLILTLSLILVLISLGPTVLALLS HRRTLQQKIWPGIPSPESEFEGLFTTHKGNFQL WLLQRDGCLWWSPGSSFPEDPPAHLEVLSEPR	102
EpoR(273-508)	SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER CWGTMQAVEPGTDDEGPLLEPVGSEHAQDTYL VLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGS EASSCSSALASKPSPEGASAASFEYTILDPSSQL LRPWTLCPELPPTPPHLKYLYLVVSDSGISTDYS SGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPP SYVACS	103
Tyrosine effector domains	**Amino acid sequence**	**SEQ ID**
IL7R(316-459)	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	134
IL2Rb(333-551)	VTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYF FFHLPDALEIEACQVYFTYDPYSEEDPDEGVAG APTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFS PSLLGGPSPPSTAPGGSGAGEERMPPSLQERV PRDWDPQPLGPPTPGVPDLVDFQPPPELVLRE AGEEVPDAGPREGVSFPWSRPPGQGEFRALNA RLPLNTDAYLSLQELQGQDPTHLV	135
IFNAR1(508-557)	ISTIATVEETNQTDEDHKKYSSQTSQDSGNYSN EDESESKTSEELQQDFV	136
IFNAR2(310-515)	KKKVWDYNYDDESDSDTEAAPRTSGGGYTMH GLTVRPLGQASATSTESQLIDPESEEEPDLPEVD VELPTMPKDSPQQLELLSGPCERRKSPLQDPFP EEDYSSTEGSGGRITFNVDLNSVFLRVLDDEDS DDLEAPLMLSSHLEEMVDPEDPDNVQSNHLLAS GEGTQPTFPSPSSEGLWSEDAPSDQSDTSESD VDLGDGYIMR	137
IFNAR1/2(IFNAR1 residues 508-557-IFNAR2 residues 310-	ISTIATVEETNQTDEDHKKYSSQTSQDSGNYSN EDESESKTSEELQQDFVKKKVWDYNYDDESDS DTEAAPRTSGGGYTMHGLTVRPLGQASATSTE	138

515)	SQLIDPESEEEPDLPEVDVELPTMPKDSPQQLE LLSGPCERRKSPLQDPFPEEDYSSTEGSGGRIT FNVDLNSVFLRVLDDEDSDDLEAPLMLSSHLEE MVDPEDPDNVQSNHLLASGEGTQPTFPSPSSE GLWSEDAPSDQSDTSESDVDLGDGYIMR	
IFNLR1(300-520)	RGVRPTPRVRAPATQQTRWKKDLAEDEEEEDE EDTEDGVSFQPYIEPPSFLGQEHQAPGHSEAG GVDSGRPRAPLVPSEGSSAWDSSDRSWASTV DSSWDRAGSSGYLAEKGPGQGPGGDGHQESL PPPEFSKDSGFLEELPEDNLSSWATWGTLPPEP NLVPGGPPVSLQTLTFCWESSPEEEEEARESEI EDSDAGSWGAESTQRTEDRGRTLGHYMAR	139
Common Gamma Chain(335-369)	IPPKGGALGEGPGASPCNQHSPYWAPPCYTLK PET	140
IL9R(356-521)	TALLTCGPARPWKSVALEEEQEGPGTRLPGNLS SEDVLPAGCTEWRVQTLAYLPQEDWAPTSLTR PAPPDSEGSRSSSSSSSSNNNNYCALGCYGG WHLSALPGNTQSSGPIPALACGLSCDHQGLETQ QGVAWVLAGHCQRPGLHEDLQGMLLPSVLSKA RSWTF	141
IL21R(322-538)	PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	142
GHR(353-638)	PDEKTEESDTDRLLSSDHEKSHSNLGVKDGDS GRTSCCEPDILETDFNANDIHEGTSEVAQPQRL KGEADLLCLDQKNQNNSPYHDACPATQQPSVI QAEKNKPQPLPTEGAESTHQAAHIQLSNPSSLS NIDFYAQVSDITPAGSVVLSPGQKNKAGMSQCD MHPEMVSLCQENFLMDNAYFCEADAKKCIPVAP HIKVESHIQPSLNQEDIYITTESLTTAAGRPGTGE HVPGSEMPVPDYTSIHIVQSPQGLILNATALPLP DKEFLSSCGYVSTDQLNKIMP	143
EpoR(339-508)	WGTMQAVEPGTDDEGPLLEPVGSEHAQDTYLV LDKWLLPRNPPSEDLPGPGGSVDIVAMDEGSE ASSCSSALASKPSPEGASAASFEYTILDPSSQLL RPWTLCPELPPTPPHLKYLYLVVSDSGISTDYSS GDSQGAQGGLSDGPYSNPYENSLIPAAEPLPPS YVACS	144
murine IL2Rb(337-539)	AVQLLLLQKDSAPLPSPSGHSQASCFTNQGYFF FHLPNALEIESCQVYFTYDPCVEEEVEEDGSRL PEGSPHPPLLPLAGEQDDYCAFPPRDDLLLFSP SLSTPNTAYGGSRAPEERSPLSLHEGLPSLASR DLMGLQRPLERMPEGDGEGLSANSSGEQASVP EGNLHGQDQDRGQGPILTLNTDAYLSLQELQAQ DSVHLI	145
murine IL7Ra(316-459)	ARDEVESFLPNDLPAQPEELETQGHRAAVHSAN RSPETSVSPPETVRRESPLRCLARNLSTCNAPP	146

	LLSSRSPDYRDGDRNRPPVYQDLLPNSGNTNV PVPVPQPLPFQSGILIPVSQRQPISTSSVLNQEE AYVTMSSFYQNK	
EGFR(955-1186)	VIQGDERMHLPSPTDSNFYRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNS TVACIDRNGLQSCPIKEDSFLQRYSSDPTGALTE DSIDDTFLPVPEYINQSVPKRPAGSVQNPVYHN QPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQP TCVNSTFDSPAHWAQKGSHQISLDNPDYQQDF FPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA	147
EGFR(955-1186;Y974F,d1045-1057)	VIQGDERMHLPSPTDSNFFRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNS TVACIDRNGLQSCPIKEDSFLQRIDDTFLPVPEYI NQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHY QDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHW AQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGS TAENAEYLRVAPQSSEFIGA	148
EGFR(955-1009;Y974F)	VIQGDERMHLPSPTDSNFFRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTP	149
EGFR(1019-1085)	NNSTVACIDRNGLQSCPIKEDSFLQRIDDTFLPV PEYINQSVPKRPAGSVQNPV	150
EGFR(1037-1103;Y1068/1101F,d1045-1057)	KEDSFLQRIDDTFLPVPEFINQSVPKRPAGSVQN PVYHNQPLNPAPSRDPHFQD	151
EGFR(1066-1118;Y1068/1086F)	VPEFINQSVPKRPAGSVQNPVFHNQPLNPAPSR DPHYQDPHSTAVGNPEYLNTV	152
EGFR(1122-1165)	PEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLD NPDYQQDFFPKEAKPNGIFKG	153
EGFR(1133-1186;Y1148F)	WAQKGSHQISLDNPDFQQDFFPKEAKPNGIFKG STAENAEYLRVAPQSSEFIGA	154
IL12Rb2(775-825)	SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	155
IL7R(376-416)	ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLP	156
IL7R(424-459)	GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQ NQ	157
IL7R(376-416,424-459)	ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPQGQPILTSLGSNQEEAYVTMSSFYQ NQ	158
IL7R(424-459;Y456F)	GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFFQ NQ	159
IL7R(376-416,424-459,Y456F)	ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPQGQPILTSLGSNQEEAYVTMSSFFQ NQ	160
IL2Rbsmall(393-433)	DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	161
IL2Rbsmall(518-551)	GQGEFRALNARLPLNTDAYLSLQELQGQDPTHL V	162
IL2Rbsmall(339-379,393-433)	QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA	163

	YCTFPSRDDLLLFSPS	
IL2Rbsmall(339-379,518-551)	QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	164
IL2Rbsmall(393-433,518-551)	DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	165
IL2Rbsmall(339-379,393-433,518-551)	QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	166
IFNAR2small(310-352)	KKKVWDYNYDDESDSDTEAAPRTSGGGYTMHGLTVRPLGQASA	167
IFNAR2small(486-515)	EGLWSEDAPSDQSDTSESDVDLGDGYIMR	168
IFNAR2small(310-352,486-515)	KKKVWDYNYDDESDSDTEAAPRTSGGGYTMHGLTVRPLGQASAEGLWSEDAPSDQSDTSESDVDLGDGYIMR	169
BLNK(53-208)	ASESPADEEEQWSDDFDSDYENPDEHSDSEMYVMPAEENADDSYEPPPVEQETRPVHPALPFARGEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARLTSTLPALTALQKPQVPPKPKGLLEDEADYVVPVEDNDENYIHPTESSSPPPEKAPMVNR	170
BLNK(53-208;Y72F)	ASESPADEEEQWSDDFDSDFENPDEHSDSEMYVMPAEENADDSYEPPPVEQETRPVHPALPFARGEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARLTSTLPALTALQKPQVPPKPKGLLEDEADYVVPVEDNDENYIHPTESSSPPPEKAPMVNR	171
BLNK(53-208;Y72F,Y96F)	ASESPADEEEQWSDDFDSDFENPDEHSDSEMYVMPAEENADDSFEPPPVEQETRPVHPALPFARGEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARLTSTLPALTALQKPQVPPKPKGLLEDEADYVVPVEDNDENYIHPTESSSPPPEKAPMVNR	172
EpoR(339-508)	WGTMQAVEPGTDDEGPLLEPVGSEHAQDTYLVLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGSEASSCSSALASKPSPEGASAASFEYTILDPSSQLLRPWTLCPELPPTPPHLKYLYLVVSDSGISTDYSSGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPPSYVACS	173
IL12Rb2(714-862)	VTPVFRHPPCSNWPQREKGIQGHQASEKDMMHSASSPPPPRALQAESRQLVDLYKVLESRGSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQHISLSVFPSSSLHPLTFSCGDKLTLDQLKMRCDSLML	174
IL12Rb1(622-662)	WDKGERTEPLEKTELPEGAPELALDTELSLEDGDRCKAKM	175
IL10R1(304-578)	VSPELKNLDLHGSTDSGFGSTKPSLQTEEPQFLLPDPHPQADRTLGNREPPVLGDSCSSGSSNSTDSGICLQEPSLSPSTGPTWEQQVGSNSRGQDDSGIDLVQNSEGRAGDTQGGSALGHHSPPEPEVPGEEDPAAVAFQGYLRQTRCAEEKATKTGCLE	176

	EESPLTDGLGPKFGRCLVDEAGLHPPALAKGYL KQDPLEMTLASSGAPTGQWNQPTEEWSLLALS SCSDLGISDWSFAHDLAPLGCVAAPGGLLGSFN SDLVTLPLISSLQSSE	
Other constructs	**Amino acid sequence**	**SEQ ID**
Myristoyl-Myd88-CD40-FKBP(F36V)x2 (GoCART)	MGSSKSKPKDPSQRMAAGGPGAGSAAPVSST SSLPLAALNMRVRRRLSLFLNVRTQVAADWTAL AEEMDFEYLEIRQLETQADPTGRLLDAWQGRP GASVGRLLELLTKLGRDDVLLELGPSIEEDCQKY ILKQQQEEAEKPLQVAAVDSSVPRTAELAGITTL DDPLGHMPERFDAFICYCPSDIKKVAKKPTNKA PHPKQEPQEINFPDDLPGSNTAAPVQETLHGCQ PVTQEDGKESRISVQERQGVQVETISPGDGRTF PKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFK FMLGKQEVIRGWEEGVAQMSVGQRAKLTISPD YAYGATGHPGIIPPHATLVFDVELLKLGVQVETIS PGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSR DRNKPFKFMLGKQEVIRGWEEGVAQMSVGQR AKLTISPDYAYGATGHPGIIPPHATLVFDVELLKL E	177
TagBFP	MSELIKENMHMKLYMEGTVDNHHFKCTSEGEG KPYEGTQTMRIKVVEGGPLPFAFDILATSFLYGS KTFINHTQGIPDFFKQSFPEGFTWERVTTYEDG GVLTATQDTSLQDGCLIYNVKIRGVNFTSNGPV MQKKTLGWEAFTETLYPADGGLEGRNDMALKL VGGSHLIANIKTTYRSKKPAKNLKMPGVYYVDY RLERIKEANNETYVEQHEVAVARYCDLPSKLGH KLN	178

[0264] Exemplary transmembrane and JAK-binding sequences of, or derived from, TPOR/MPLR useful in the inducible chimeric cytokine receptors provided herein are shown in Table 1C.

Table 1C

Tyrosine kinase activating domain comprising a JAK binding domain and transmembrane domain variants of TPOR	**Amino acid sequence**	**SEQ ID**
PD1(156-191)-TPOR/MPLR (514-582)	PSPSPRPAGQFQTLVVGVVGGLLGSLVLLVWVL AVI RWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL	104

TPOR/MPLR(478-582) (wildtype sequence)	SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL	105
TPOR/MPLR(N-1)	SDPTRVETATETWISLVTALHLVLGLSAVLGLLLL RWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL	106
TPOR/MPLR(N-2)	SDPTRVETATETISLVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRDT AALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL	107
TPOR/MPLR(N-2+1)	SDPTRVETATETLISLVTALHLVLGLSAVLGLLLL RWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL	108
TPOR/MPLR(N-3)	SDPTRVETATETSLVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRDT AALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL	109
TPOR/MPLR(N-4)	SDPTRVETATETLVTALHLVLGLSAVLGLLLLRW QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTA ALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	110
TPOR/MPLR(N-4+1)	SDPTRVETATETILVTALHLVLGLSAVLGLLLLRW QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTA ALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	111
TPOR/MPLR(N-5)	SDPTRVETATETVTALHLVLGLSAVLGLLLLRWQ FPAHYRRLRHALWPSLPDLHRVLGQYLRDTAAL SPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	112
TPOR/MPLR(N-6)	SDPTRVETATETTALHLVLGLSAVLGLLLLRWQF PAHYRRLRHALWPSLPDLHRVLGQYLRDTAALS PPKATVSDTCEEVEPSLLEILPKSSERTPLPL	113
TPOR/MPLR(N-7)	SDPTRVETATETALHLVLGLSAVLGLLLLRWQFP AHYRRLRHALWPSLPDLHRVLGQYLRDTAALSP PKATVSDTCEEVEPSLLEILPKSSERTPLPL	114
TPOR/MPLR(N-8)	SDPTRVETATETLHLVLGLSAVLGLLLLRWQFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP KATVSDTCEEVEPSLLEILPKSSERTPLPL	115
TPOR/MPLR(N-9)	SDPTRVETATETHLVLGLSAVLGLLLLRWQFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP KATVSDTCEEVEPSLLEILPKSSERTPLPL	116
TPOR/MPLR(N-10)	SDPTRVETATETLVLGLSAVLGLLLLRWQFPAHY RRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL	117
TPOR/MPLR(N-11)	SDPTRVETATETVLGLSAVLGLLLLRWQFPAHY RRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL	118
TPOR/MPLR(N-12)	SDPTRVETATETLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKAT VSDTCEEVEPSLLEILPKSSERTPLPL	119

TPOR/MPLR(N-13)	SDPTRVETATETGLSAVLGLLLLRWQFPAHYRR LRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPL	120
TPOR/MPLR(N-14)	SDPTRVETATETLSAVLGLLLLRWQFPAHYRRL RHALWPSLPDLHRVLGQYLRDTAALSPPKATVS DTCEEVEPSLLEILPKSSERTPLPL	121
TPOR/MPLR(N-15)	SDPTRVETATETSAVLGLLLLRWQFPAHYRRLR HALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPL	122
TPOR/MPLR(N-16)	SDPTRVETATETAVLGLLLLRWQFPAHYRRLRH ALWPSLPDLHRVLGQYLRDTAALSPPKATVSDT CEEVEPSLLEILPKSSERTPLPL	123
TPOR/MPLR(N-17)	SDPTRVETATETVLGLLLLRWQFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPL	124
TPOR/MPLR(N-18)	SDPTRVETATETLGLLLLRWQFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPPKATVSDTCE EVEPSLLEILPKSSERTPLPL	125
TPOR/MPLR(N+1)	SDPTRVETATETAWLISLVTALHLVLGLSAVLGLL LLRWQFPAHYRRLRHALWPSLPDLHRVLGQYL RDTAALSPPKATVSDTCEEVEPSLLEILPKSSER TPLPL	126
TPOR/MPLR(N+2)	SDPTRVETATETAWVLISLVTALHLVLGLSAVLG LLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQY LRDTAALSPPKATVSDTCEEVEPSLLEILPKSSE RTPLPL	127
TPOR/MPLR(N+3)	SDPTRVETATETAWLVLISLVTALHLVLGLSAVL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKS SERTPLPL	128
TPOR/MPLR(N+4)	SDPTRVETATETAWILVLISLVTALHLVLGLSAVL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKS SERTPLPL	129
TPOR/MPLR(N+5)	SDPTRVETATETAWLILVLISLVTALHLVLGLSAV LGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLG QYLRDTAALSPPKATVSDTCEEVEPSLLEILPKS SERTPLPL	130
TPOR/MPLR(N+6)	SDPTRVETATETAWLLILVLISLVTALHLVLGLSA VLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVL GQYLRDTAALSPPKATVSDTCEEVEPSLLEILPK SSERTPLPL	131
TPOR/MPLR(N+7)	SDPTRVETATETAWVLLILVLISLVTALHLVLGLS AVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRV LGQYLRDTAALSPPKATVSDTCEEVEPSLLEILP KSSERTPLPL	132
TPOR/MPLR(N+8)	SDPTRVETATETAWLVLLILVLISLVTALHLVLGL SAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHR VLGQYLRDTAALSPPKATVSDTCEEVEPSLLEIL PKSSERTPLPL	133

[0265] In another aspect provided herein are isolated immune cells comprising one or more inducible chimeric cytokine receptors disclosed herein. In other embodiments, isolated immune cells provided herein comprise (i) one or more inducible chimeric cytokine receptors disclosed herein and (ii) a chimeric antigen receptor (CAR). Advantageously, the isolated immune cells provided herein exhibit improved persistence upon contact with a ligand that binds to the dimerization domain relative to cells that do not express the inducible chimeric cytokine receptor. In some embodiments, the isolated immune cells provided herein exhibit improved cytotoxicity, increased expansion, and/or increased levels of memory phenotype markers upon contact with a ligand that binds to the dimerization domain relative to cells that do not express the inducible chimeric cytokine receptor. The improvement in persistence, cytotoxicity, expansion, and/or memory phenotype markers exhibited by isolated immune cells comprising inducible chimeric cytokine receptors described herein can be *in vitro* or *in vivo*. In some embodiments, isolated immune cell is selected from the group consisting of: T cell, dendritic cell, killer dendritic cell, mast cell, NK-cell, macrophage, monocyte, and B-cell.

[0266] In some embodiments, isolated immune cell is an isolated T cell. In some embodiments, isolated T cells provided herein comprise one or more inducible chimeric cytokine receptors disclosed herein. In other embodiments, isolated T cells provided herein comprise (i) one or more inducible chimeric cytokine receptors disclosed herein and (ii) a chimeric antigen receptor (CAR). Advantageously, the isolated T cells provided herein exhibit improved *in vivo* persistence upon contact with a ligand that binds to the dimerization domain relative to cells that do not express the inducible chimeric cytokine receptor. In some embodiments, the isolated T cells provided herein exhibit improved cytotoxicity, increased expansion, and/or increased levels of memory phenotype markers upon contact with a ligand that binds to the dimerization domain relative to cells that do not express the inducible chimeric cytokine receptor. The improvement in one or more of these features can be *in vitro* or *in vivo*.

[0267] In some embodiments, the isolated immune cell comprising one or more inducible chimeric cytokine receptors disclosed herein exhibits (i) increased *in vivo* persistence, (ii) increased STAT activation, (iii) increased cytotoxicity, (iv) increased levels of memory phenotype markers, (v) increased expansion (proliferation), or combinations of these functional features, upon contact with a ligand that binds to the dimerization domain, relative to an isolated immune cell that does not express the

inducible chimeric cytokine receptor. In some embodiments, the improvement in the one or more functional features described herein is dose-dependent, i.e., the functional activity of the immune cell comprising the inducible chimeric cytokine receptors increases upon contact with increasing doses of the ligand that binds to the dimerization domain. In some embodiments, STATs activated by the inducible chimeric cytokine receptors include STAT1, STAT2, STAT3, STAT4, STAT5, STAT6, or combinations thereof. Activation of STAT includes recruitment of STAT, phosphoyration of STAT, and/or dimerization of STAT or translocation of STAT. In some embodiments, memory phenotype markers increased or maintained by the immune cell comprising the inducible chimeric cytokine receptor include stem cell memory (Tscm) marker and central memory (Tcm) marker.

[0268] In some embodiments, the improvement in one or more functional features exhibited by an immune cell comprising an inducible chimeric cytokine receptor provided herein is at least about 2 fold, 2.5 fold, 3 fold, 3.5 fold, 4 fold, 4.5 fold, 5 fold, 6 fold, 7 fold, 8 fold, 9 fold, 10 fold, 15 fold, 20 fold, 25 fold, 30 fold, 40 fold, 50 fold, 60 fold, 70 fold, 80 fold, 90 fold, 100 fold, 125 fold, 150 fold, 200 fold, 250 fold, 300 fold, 350 fold, 400 fold, 450 fold, or even about 500 fold, including values and ranges therebetween, compared to an immune cell that does not express the inducible chimeric cytokine receptor.

[0269] In some embodiments, the improvement in one or more functional features exhibited by an immune cell comprising an inducible chimeric cytokine receptor provided herein is at least about 10%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 70%, 75%, 80%, 90%, 100%, 125%, 150%, 200%, 250%, 300%, 350%, 400%, or even about 500%, including values and ranges therebetween, compared to an immune cell that does not express the inducible chimeric cytokine receptor.

[0270] In some embodiments, an isolated immune cell, such as an isolated T cell, of the invention comprises an inducible chimeric cytokine receptor shown in Table 2A.

Table 2A: Exemplary inducible chimeric cytokine receptor sequences

Receptor name	Amino acid sequence	SEQ ID
CD8 SS-Myc-FKBP(F36V)-EpoR(237-508;L241G,L242P)-V5	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV	1

	AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C WGTMQAVEPGTDDEGPLLEPVGSEHAQDTYLV LDKWLLPRNPPSEDLPGPGGSVDIVAMDEGSE ASSCSSALASKPSPEGASAASFEYTILDPSSQLL RPWTLCPELPPTPPHLKYLYLVVSDSGISTDYSS GDSQGAQGGLSDGPYSNPYENSLIPAAEPLPPS YVACS IPNPLLGLDST	
V5-EpoR(273-508)-FKBP(F36V)-FKBP(F36V)	IPNPLLGLDST SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER CWGTMQAVEPGTDDEGPLLEPVGSEHAQDTYL VLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGS EASSCSSALASKPSPEGASAASFEYTILDPSSQL LRPWTLCPELPPTPPHLKYLYLVVSDSGISTDYS SGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPP SYVACS MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLGVQVETISPGDGRTFPKRGQTCVV HYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVI RGWEEGVAQMSVGQRAKLTISPDYAYGATGHP GIIPPHATLVFDVELLKLE	2
V5-EpoR(273-508)-FKBP(E31G,36V,R71G,K105E)-FKBP(E31G,36V,R71G,K105E)	IPNPLLGLDST SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER CWGTMQAVEPGTDDEGPLLEPVGSEHAQDTYL VLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGS EASSCSSALASKPSPEGASAASFEYTILDPSSQL LRPWTLCPELPPTPPHLKYLYLVVSDSGISTDYS SGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPP SYVACS MGVQVETISPGDGRTFPKRGQTCVVHYTGMLG DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQGAKLTISPDYAYGATGHPGIIPPHATL VFDVELLELGVQVETISPGDGRTFPKRGQTCVV	3

	HYTGMLGDGKKVDSSRDRNKPFKFMLGKQEVI RGWEEGVAQMSVGQGAKLTISPDYAYGATGHP GIIPPHATLVFDVELLELE	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-GHR(353-638)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C PDEKTEESDTDRLLSSDHEKSHSNLGVKDGDS GRTSCCEPDILETDFNANDIHEGTSEVAQPQRL KGEADLLCLDQKNQNNSPYHDACPATQQPSVI QAEKNKPQPLPTEGAESTHQAAHIQLSNPSSLS NIDFYAQVSDITPAGSVVLSPGQKNKAGMSQCD MHPEMVSLCQENFLMDNAYFCEADAKKCIPVAP HIKVESHIQPSLNQEDIYITTESLTTAAGRPGTGE HVPGSEMPVPDYTSIHIVQSPQGLILNATALPLP DKEFLSSCGYVSTDQLNKIMP	4
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYF FFHLPDALEIEACQVYFTYDPYSEEDPDEGVAG APTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFS PSLLGGPSPPSTAPGGSGAGEERMPPSLQERV PRDWDPQPLGPPTPGVPDLVDFQPPPELVLRE AGEEVPDAGPREGVSFPWSRPPGQGEFRALNA RLPLNTDAYLSLQELQGQDPTHLV	5
CD8 SS-Myc-	MALPVTALLLPLALLLHAARP	6

FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)	EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC VTPVFRHPPCSNWPQREKGIQGHQASEKDMMHSASSPPPPRALQAESRQLVDLYKVLESRGSDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPSHEAPLADSLEELEPQHISLSVFPSSSLHPLTFSCGDKLTLDQLKMRCDSLML	7
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSER	8

	C SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	9
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C KKKVWDYNYDDESDSDTEAAPRTSGGGYTMH GLTVRPLGQASATSTESQLIDPESEEEPDLPEVD VELPTMPKDSPQQLELLSGPCERRKSPLQDPFP EEDYSSTEGSGGRITFNVDLNSVFLRVLDDEDS DDLEAPLMLSSHLEEMVDPEDPDNVQSNHLLAS GEGTQPTFPSPSSEGLWSEDAPSDQSDTSESD VDLGDGYIMR	10
CD8 SS-Myc-FKBP(F36V)-	MALPVTALLLPLALLLHAARP	11

EpoR(237-338;L241G,L242P)-IFNAR1(300-520)	EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C RGVRPTPRVRAPATQQTRWKKDLAEDEEEEDE EDTEDGVSFQPYIEPPSFLGQEHQAPGHSEAG GVDSGRPRAPLVPSEGSSAWDSSDRSWASTV DSSWDRAGSSGYLAEKGPGQGPGGDGHQESL PPPEFSKDSGFLEELPEDNLSSWATWGTLPPEP NLVPGGPPVSLQTLTFCWESSPEEEEEARESEI EDSDAGSWGAESTQRTEDRGRTLGHYMAR	
CD8 SS-Myc-FKBP(F36V)-muEpoR(236-337;L264G,L265P)-mulL2Rb(337-539)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPASLLTASDLDPLILTLSLILVLISLGPTVLALLS HRRTLQQKIWPGIPSPESEFEGLFTTHKGNFQL WLLQRDGCLWWSPGSSFPEDPPAHLEVLSEPR AVQLLLLQKDSAPLPSPSGHSQASCFTNQGYFF FHLPNALEIESCQVYFTYDPCVEEEVEEDGSRL PEGSPHPPLLPLAGEQDDYCAFPPRDDLLLFSP SLSTPNTAYGGSRAPEERSPLSLHEGLPSLASR DLMGLQRPLERMPEGDGEGLSANSSGEQASVP EGNLHGQDQDRGQGPILTLNTDAYLSLQELQAQ DSVHLI	12
CD8 SS-Myc-FKBP(F36V)-muEpoR(236-337;L264G,L265P)-mulL7R(316-459)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPASLLTASDLDPLILTLSLILVLISLGPTVLALLS	13

	HRRTLQQKIWPGIPSPESEFEGLFTTHKGNFQL WLLQRDGCLWWSPGSSFPEDPPAHLEVLSEPR ARDEVESFLPNDLPAQPEELETQGHRAAVHSAN RSPETSVSPPETVRRESPLRCLARNLSTCNAPP LLSSRSPDYRDGDRNRPPVYQDLLPNSGNTNV PVPVPQPLPFQSGILIPVSQRQPISTSSVLNQEE AYVTMSSFYQNK	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	14
CD8 SS-Myc-FKBP(F36V)-GP130(609-700)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE TTPKFAQGEIEAIVVPVCLAFLLTTLLGVLFCFNK RDLIKKHIWPNVPDPSKSHIAQWSPHTPPRHNF NSKDQMYSDGNFTDVSVVEIEAND ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	15

	SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	
CD8 SS-Myc-FKBP(F36V)-PrlR(221-319)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE ATFIQIPSDFTMNDTTVWISVAVLSAVICLIIVWAV ALKGYSMVTCIFPPVPGPKIKGFDAHLLEKGKSE ELLSALGCQDFPPTSDYEDLLVEYLEVDD ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	16
CD8 SS-Myc-FKBP(F36V)-GHR(251-352)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE LPQMSQFTCEEDFYFPWLLIIIFGIFGLTVMLFVF LFSKQQRIKMLILPPVPVPKIKGIDPDLLKEGKLE EVNTILAIHDSYKPEFHSDDSWVEFIELDIDE ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	17
CD8 SS-Myc-FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-	MALPVTALLLPLALLLHAARP EQKLISEEDL	18

IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE LTLMTLTPEGSELHIILGLFGLLLLLTCLCGTAWL CCSPNRKNPLWPSVPDPAHSSLGSWVPTIMEE DAFQLPGLGTPPITKLTVLEEDEKKPVPWE ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	
CD8 SS-Myc-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	19
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL	20

	SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLP	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(424-459)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQ NQ	21
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPQGQPILTSLGSNQEEAYVTMSSFYQ NQ	22
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(424-459;Y456F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE	23

	SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFFQ NQ	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459;Y456F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPQGQPILTSLGSNQEEAYVTMSSFFQ NQ	24
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(393-433)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPS	25
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(518-551)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE	26

	SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C GQGEFRALNARLPLNTDAYLSLQELQGQDPTHL V	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPS	27
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,518-551)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQ GQGEFRALNARLPLNTDAYLSLQELQGQDPTHL V	28
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(393-433,518-	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE	29

551)	DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433,518-551)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	30
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1186)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VIQGDERMHLPSPTDSNFYRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNS TVACIDRNGLQSCPIKEDSFLQRYSSDPTGALTE DSIDDTFLPVPEYINQSVPKRPAGSVQNPVYHN QPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQP TCVNSTFDSPAHWAQKGSHQISLDNPDYQQDF	31

	FPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1044,1058-1186;Y974F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VIQGDERMHLPSPTDSNFFRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNS TVACIDRNGLQSCPIKEDSFLQRIDDTFLPVPEYI NQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHY QDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHW AQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGS TAENAEYLRVAPQSSEFIGA	32
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1009;Y974F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VIQGDERMHLPSPTDSNFFRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTP	33
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1019-1085)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL	34

	SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C NNSTVACIDRNGLQSCPIKEDSFLQRIDDTFLPV PEYINQSVPKRPAGSVQNPV	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1037-1044,1058-1103;Y1068/1101F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C KEDSFLQRIDDTFLPVPEFINQSVPKRPAGSVQN PVYHNQPLNPAPSRDPHFQD	35
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1066-1118;Y1068/1086F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VPEFINQSVPKRPAGSVQNPVFHNQPLNPAPSR DPHYQDPHSTAVGNPEYLNTV	36
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1122-1165)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL	37

	SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C PEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLD NPDYQQDFFPKEAKPNGIFKG	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1133-1186;Y1148F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C WAQKGSHQISLDNPDFQQDFFPKEAKPNGIFKG STAENAEYLRVAPQSSEFIGA	38
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-BLNK(53-208)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ASESPADEEEQWSDDFDSDYENPDEHSDSEMY VMPAEENADDSYEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	39
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL	40

	VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ASESPADEEEQWSDDFDSDFENPDEHSDSEMY VMPAEENADDSYEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F,Y96F)	MALPVTALLLPLALLLHAARP EQKLISEEDL MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ASESPADEEEQWSDDFDSDFENPDEHSDSEMY VMPAEENADDSFEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	41
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	42

CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rb(333-551)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL VTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYF FFHLPDALEIEACQVYFTYDPYSEEDPDEGVAG APTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFS PSLLGGPSPPSTAPGGSGAGEERMPPSLQERV PRDWDPQPLGPPTPGVPDLVDFQPPPELVLRE AGEEVPDAGPREGVSFPWSRPPGQGEFRALNA RLPLNTDAYLSLQELQGQDPTHLV	43
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	44
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD	45

	AYLSLQELQGQDPTHLV	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	46
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL21R(322-538)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	47
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL21R(322-538)-	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE	48

IL7R(316-459)	DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	
CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)- IL2Rbsmall(393- 433,518-551)- IL21R(322-538)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	49
CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)- IL21R(322-538)- IL2Rbsmall(393-	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV	50

433,518-551)	AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)-IL21R(322-538)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	51
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL21R(322-538)-IL2Rbsmall(339-379,393-433,518-551)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE	52

	SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)-IL7R(316-459)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	53
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL2Rbsmall(393-433,518-551)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT	54

	PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)-IL7R(316-459)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	55
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL2Rbsmall(339-379,393-433,518-551)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA	56

	YVTMSSFYQNQ QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	
CD8 SS-FKBP(F36V)- PD1(156-191)- TPOR/MPLR (514- 582)-IL7R(316-459)- IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE PSPSPRPAGQFQTLVVGVVGGLLGSLVLLVWVL AVI RWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	57
CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)- EGFR(1122-1165)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL PEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLD NPDYQQDFFPKEAKPNGIFKG	58
CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)- IL7R(316-459)- IL12Rb2(775-825) FKBP switch containing wildtype TpoR TM	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLR	187

sequence	WQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAAL SPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-1)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETWISLVTALHLVLGLSAVLGLLLLRW QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSP PKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	188
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-2)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETISLVTALHLVLGLSAVLGLLLLRWQF PAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	189
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-2+1)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLISLVTALHLVLGLSAVLGLLLLRWQ FPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP KATVSDTCEEVEPSLLEILPKSSERTPLPL	190

	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-3)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETSLVTALHLVLGLSAVLGLLLLRWQF PAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	191
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-4)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLVTALHLVLGLSAVLGLLLLRWQFP AHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	192
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-4+1)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETILVTALHLVLGLSAVLGLLLLRWQFP AHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP	193

	SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-5)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETVTALHLVLGLSAVLGLLLLRWQFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKAT VSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	194
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-6)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETTALHLVLGLSAVLGLLLLRWQFPAH YRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	195
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-7)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETALHLVLGLSAVLGLLLLRWQFPAHY RRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVS DTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS	196

	GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-8)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLHLVLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	197
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-9)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETHLVLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	198
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-10)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLVLGLSAVLGLLLLRWQFPAHYRRL RHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ	199

	SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-11)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETVLGLSAVLGLLLLRWQFPAHYRRL RHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	200
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-12)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLGLSAVLGLLLLRWQFPAHYRRLR HALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCE EVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	201
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-13)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETGLSAVLGLLLLRWQFPAHYRRLRH ALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEE VEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	202

CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-14)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLSAVLGLLLLRWQFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEV EPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	203
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-15)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETSAVLGLLLLRWQFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVE PSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	204
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-16)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAVLGLLLLRWQFPAHYRRLRHALW PSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEP SLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	205
CD8 SS-FKBP(F36V)-	MALPVTALLLPLALLLHAARP	206

TPOR/MPLR(478-582;N-17)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETVLGLLLLRWQFPAHYRRLRHALWP SLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPS LLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-18)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLGLLLLRWQFPAHYRRLRHALWPS LPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLL EILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	207
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+1)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWLISLVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAAL SPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	208
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+2)-IL7R(316-459)-	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK	209

IL12Rb2(775-825)	KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWVLISLVTALHLVLGLSAVLGLLLL RWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAA LSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+3)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWLVLISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTA ALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	210
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+4)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWILVLISLVTALHLVLGLSAVLGLL LLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDT AALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	211
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+5)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE	212

	SDPTRVETATETAWLILVLISLVTALHLVLGLSAVLGL LLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+6)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWLLILVLISLVTALHLVLGLSAVLG LLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	213
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWVLLILVLISLVTALHLVLGLSAVL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYL RDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	214
CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)	MALPVTALLLPLALLLHAARP MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE	215

	SDPTRVETATETAWLVLLILVLISLVTALHLVLGLSAVL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYL RDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	

[0271] In some embodiments, an isolated immune cell, such as an isolated T cell, of the invention comprises an inducible chimeric cytokine receptor shown in Table 2B.

Table 2B: Exemplary inducible chimeric cytokine receptor sequences

Receptor name	Amino acid sequence	SEQ ID
FKBP(F36V)-EpoR(237-508;L241G,L242P)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C WGTMQAVEPGTDDEGPLLEPVGSEHAQDTYLV LDKWLLPRNPPSEDLPGPGGSVDIVAMDEGSE ASSCSSALASKPSPEGASAASFEYTILDPSSQLL RPWTLCPELPPTPPHLKYLYLVVSDSGISTDYSS GDSQGAQGGLSDGPYSNPYENSLIPAAEPLPPS YVACS	225
EpoR(273-508)-FKBP(F36V)-FKBP(F36V)	SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER CWGTMQAVEPGTDDEGPLLEPVGSEHAQDTYL VLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGS EASSCSSALASKPSPEGASAASFEYTILDPSSQL LRPWTLCPELPPTPPHLKYLYLVVSDSGISTDYS SGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPP SYVACS MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLGVQVETISPGDGRTFPKRGQTCVV	226

	HYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVI RGWEEGVAQMSVGQRAKLTISPDYAYGATGHP GIIPPHATLVFDVELLKLE	
EpoR(273-508)-FKBP(E31G,36V,R71G,K105E)-FKBP(E31G,36V,R71G,K105E)	SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER CWGTMQAVEPGTDDEGPLLEPVGSEHAQDTYL VLDKWLLPRNPPSEDLPGPGGSVDIVAMDEGS EASSCSSALASKPSPEGASAASFEYTILDPSSQL LRPWTLCPELPPTPPHLKYLYLVVSDSGISTDYS SGDSQGAQGGLSDGPYSNPYENSLIPAAEPLPP SYVACS MGVQVETISPGDGRTFPKRGQTCVVHYTGMLG DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQGAKLTISPDYAYGATGHPGIIPPHATL VFDVELLELGVQVETISPGDGRTFPKRGQTCVV HYTGMLGDGKKVDSSRDRNKPFKFMLGKQEVI RGWEEGVAQMSVGQGAKLTISPDYAYGATGHP GIIPPHATLVFDVELLELE	227
FKBP(F36V)-EpoR(237-338;L241G,L242P)-GHR(353-638)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C PDEKTEESDTDRLLSSDHEKSHSNLGVKDGDS GRTSCCEPDILETDFNANDIHEGTSEVAQPQRL KGEADLLCLDQKNQNNSPYHDACPATQQPSVI QAEKNKPQPLPTEGAESTHQAAHIQLSNPSSLS NIDFYAQVSDITPAGSVVLSPGQKNKAGMSQCD MHPEMVSLCQENFLMDNAYFCEADAKKCIPVAP HIKVESHIQPSLNQEDIYITTESLTTAAGRPGTGE HVPGSEMPVPDYTSIHIVQSPQGLILNATALPLP DKEFLSSCGYVSTDQLNKIMP	228
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C	229

	VTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYF FFHLPDALEIEACQVYFTYDPYSEEDPDEGVAG APTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFS PSLLGGPSPPSTAPGGSGAGEERMPPSLQERV PRDWDPQPLGPPTPGVPDLVDFQPPPELVLRE AGEEVPDAGPREGVSFPWSRPPGQGEFRALNA RLPLNTDAYLSLQELQGQDPTHLV	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	230
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VTPVFRHPPCSNWPQREKGIQGHQASEKDMM HSASSPPPPRALQAESRQLVDLYKVLESRGSDP KPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQHISLSVFPSSSLHPLTFSC GDKLTLDQLKMRCDSLML	231
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD	232

	LPSHEAPLADSLEELEPQ	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC PRSPAKRLQLTELQEPAELVESDGVPKPSFWPTAQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGPCTWPCSCEDDGYPALDLDAGLEPSPGLEDPLLDAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPPLADGEDWAGGLPWGGRSPGGVSESEAGSPLAGLDMDTFDSGFVGSDCSSPVECDFTSPGDEGPPRSYLRQWVVIPPPLSSPGPQAS	233
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC KKKVWDYNYDDESDSDTEAAPRTSGGGYTMHGLTVRPLGQASATSTESQLIDPESEEEPDLPEVDVELPTMPKDSPQQLELLSGPCERRKSPLQDPFPEEDYSSTEGSGGRITFNVDLNSVFLRVLDDEDSDDLEAPLMLSSHLEEMVDPEDPDNVQSNHLLASGEGTQPTFPSPSSEGLWSEDAPSDQSDTSESDVDLGDGYIMR	234
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR1(300-520)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC RGVRPTPRVRAPATQQTRWKKDLAEDEEEEDEEDTEDGVSFQPYIEPPSFLGQEHQAPGHSEAGGVDSGRPRAPLVPSEGSSAWDSSDRSWASTV	235

	DSSWDRAGSSGYLAEKGPGQGPGGDGHQESL PPPEFSKDSGFLEELPEDNLSSWATWGTLPPEP NLVPGGPPVSLQTLTFCWESSPEEEEEARESEI EDSDAGSWGAESTQRTEDRGRTLGHYMAR	
FKBP(F36V)- muEpoR(236- 337;L264G,L265P)- mulL2Rb(337-539)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPASLLTASDLDPLILTLSLILVLISLGPTVLALLS HRRTLQQKIWPGIPSPESEFEGLFTTHKGNFQL WLLQRDGCLWWSPGSSFPEDPPAHLEVLSEPR AVQLLLLQKDSAPLPSPSGHSQASCFTNQGYFF FHLPNALEIESCQVYFTYDPCVEEEVEEDGSRL PEGSPHPPLLPLAGEQDDYCAFPPRDDLLLFSP SLSTPNTAYGGSRAPEERSPLSLHEGLPSLASR DLMGLQRPLERMPEGDGEGLSANSSGEQASVP EGNLHGQDQDRGQGPILTLNTDAYLSLQELQAQ DSVHLI	236
FKBP(F36V)- muEpoR(236- 337;L264G,L265P)- mulL7R(316-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPASLLTASDLDPLILTLSLILVLISLGPTVLALLS HRRTLQQKIWPGIPSPESEFEGLFTTHKGNFQL WLLQRDGCLWWSPGSSFPEDPPAHLEVLSEPR ARDEVESFLPNDLPAQPEELETQGHRAAVHSAN RSPETSVSPPETVRRESPLRCLARNLSTCNAPP LLSSRSPDYRDGDRNRPPVYQDLLPNSGNTNV PVPVPQPLPFQSGILIPVSQRQPISTSSVLNQEE AYVTMSSFYQNK	237
FKBP(F36V)- EpoR(237- 338;L241G,L242P)- IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA	238

	YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	
FKBP(F36V)- GP130(609-700)- IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE TTPKFAQGEIEAIVVPVCLAFLLTTLLGVLFCFNK RDLIKKHIWPNVPDPSKSHIAQWSPHTPPRHNF NSKDQMYSDGNFTDVSVVEIEAND ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	239
FKBP(F36V)-PrlR(221- 319)-IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE ATFIQIPSDFTMNDTTVWISVAVLSAVICLIIVWAV ALKGYSMVTCIFPPVPGPKIKGFDAHLLEKGKSE ELLSALGCQDFPPTSDYEDLLVEYLEVDD ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	240
FKBP(F36V)-GHR(251- 352)-IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE LPQMSQFTCEEDFYFPWLLIIIFGIFGLTVMLFVF LFSKQQRIKMLILPPVPVPKIKGIDPDLLKEGKLE EVNTILAIHDSYKPEFHSDDSWVEFIELDIDE ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP	241

	NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	
FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE LTLMTLTPEGSELHIILGLFGLLLLLTCLCGTAWL CCSPNRKNPLWPSVPDPAHSSLGSWVPTIMEE DAFQLPGLGTPPITKLTVLEEDEKKPVPWE ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	242
FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	243
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL	244

	SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLP	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(424-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQ NQ	245
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPQGQPILTSLGSNQEEAYVTMSSFYQ NQ	246
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(424-459;Y456F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFFQ NQ	247
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416,424-	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE	248

459;Y456F)	SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ACDAPILSSSRSLDCRESGKNGPHVYQDLLLSL GTTNSTLPQGQPILTSLGSNQEEAYVTMSSFFQ NQ	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(393-433)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPS	249
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(518-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C GQGEFRALNARLPLNTDAYLSLQELQGQDPTHL V	250
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPS	251
FKBP(F36V)-	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE	252

EpoR(237-338;L241G,L242P)-IL2Rb(339-379,518-551)	DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQ GQGEFRALNARLPLNTDAYLSLQELQGQDPTHL V	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(393-433,518-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	253
FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433,518-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	254
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1186)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C	255

	VIQGDERMHLPSPTDSNFYRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNS TVACIDRNGLQSCPIKEDSFLQRYSSDPTGALTE DSIDDTFLPVPEYINQSVPKRPAGSVQNPVYHN QPLNPAPSRDPHYQDPHSTAVGNPEYLNTVQP TCVNSTFDSPAHWAQKGSHQISLDNPDYQQDF FPKEAKPNGIFKGSTAENAEYLRVAPQSSEFIGA	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1044,1058-1186;Y974F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VIQGDERMHLPSPTDSNFFRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTPLLSSLSATSNNS TVACIDRNGLQSCPIKEDSFLQRIDDTFLPVPEYI NQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHY QDPHSTAVGNPEYLNTVQPTCVNSTFDSPAHW AQKGSHQISLDNPDYQQDFFPKEAKPNGIFKGS TAENAEYLRVAPQSSEFIGA	256
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1009;Y974F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C VIQGDERMHLPSPTDSNFFRALMDEEDMDDVV DADEYLIPQQGFFSSPSTSRTP	257
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1019-1085)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C NNSTVACIDRNGLQSCPIKEDSFLQRIDDTFLPV	258

	PEYINQSVPKRPAGSVQNPV	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1037-1044,1058-1103;Y1068/1101F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC KEDSFLQRIDDTFLPVPEFINQSVPKRPAGSVQNPVYHNQPLNPAPSRDPHFQD	259
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1066-1118;Y1068/1086F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC VPEFINQSVPKRPAGSVQNPVFHNQPLNPAPSRDPHYQDPHSTAVGNPEYLNTV	260
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1122-1165)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC PEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLDNPDYQQDFFPKEAKPNGIFKG	261
FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1133-1186;Y1148F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALLSHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQLWLYQNDGCLWWSPCTPFTEDPPASLEVLSERC	262

	WAQKGSHQISLDNPDFQQDFFPKEAKPNGIFKG STAENAEYLRVAPQSSEFIGA	
FKBP(F36V)-EpoR(237-338;L241G,L242P)-BLNK(53-208)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ASESPADEEEQWSDDFDSDYENPDEHSDSEMY VMPAEENADDSYEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	263
FKBP(F36V)-EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ASESPADEEEQWSDDFDSDFENPDEHSDSEMY VMPAEENADDSYEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	264
FKBP(F36V)-EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F,Y96F)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SEPVSGPTPSDLDPLILTLSLILVVILVGPTVLALL SHRRALKQKIWPGIPSPESEFEGLFTTHKGNFQ LWLYQNDGCLWWSPCTPFTEDPPASLEVLSER C ASESPADEEEQWSDDFDSDFENPDEHSDSEMY VMPAEENADDSFEPPPVEQETRPVHPALPFAR GEYIDNRSSQRHSPPFSKTLPSKPSWPSEKARL TSTLPALTALQKPQVPPKPKGLLEDEADYVVPV EDNDENYIHPTESSSPPPEKAPMVNR	265

FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCPSEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRSLDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ	266
FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rb(333-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL VTQLLLQQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQVYFTYDPYSEEDPDEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSLLGGPSPPSTAPGGSGAGEERMPPSLQERVPRDWDPQPLGPPTPGVPDLVDFQPPPELVLREAGEEVPDAGPREGVSFPWSRPPGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	267
FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSRDDLLLFSPSGQGEFRALNARLPLNTDAYLSLQELQGQDPTHLV	268
FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(339-	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL	269

379,393-433,518-551)	VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	
FKBP(F36V)- TPOR/MPLR(478-582)- IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	270
FKBP(F36V)- TPOR/MPLR(478-582)- IL7R(316-459)- IL21R(322-538)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA	271

	GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	
FKBP(F36V)-TPOR/MPLR(478-582)-IL21R(322-538)-IL7R(316-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	272
FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)-IL21R(322-538)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	273
FKBP(F36V)-TPOR/MPLR(478-582)-	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV	274

IL21R(322-538)-IL2Rbsmall(393-433,518-551)	AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	
FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)-IL21R(322-538)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS	275
FKBP(F36V)-TPOR/MPLR(478-582)-IL21R(322-538)-IL2Rbsmall(339-379,393-433,518-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT	276

	PLPL PRSPAKRLQLTELQEPAELVESDGVPKPSFWPT AQNSGGSAYSEERDRPYGLVSIDTVTVLDAEGP CTWPCSCEDDGYPALDLDAGLEPSPGLEDPLL DAGTTVLSCGCVSAGSPGLGGPLGSLLDRLKPP LADGEDWAGGLPWGGRSPGGVSESEAGSPLA GLDMDTFDSGFVGSDCSSPVECDFTSPGDEGP PRSYLRQWVVIPPPLSSPGPQAS QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	
FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)-IL7R(316-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	277
FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL2Rbsmall(393-433,518-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	278

	DEGVAGAPTGSSPQPLQPLSGEDDAYCTFPSR DDLLLFSPSGQGEFRALNARLPLNTDAYLSLQEL QGQDPTHLV	
FKBP(F36V)-TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)-IL7R(316-459)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ	279
FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL2Rbsmall(339-379,393-433,518-551)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ QQDKVPEPASLSSNHSLTSCFTNQGYFFFHLPD ALEIEACQDEGVAGAPTGSSPQPLQPLSGEDDA YCTFPSRDDLLLFSPSGQGEFRALNARLPLNTD AYLSLQELQGQDPTHLV	280
FKBP(F36V)-PD1(156-191)-TPOR/MPLR (514-582)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE	281

	PSPSPRPAGQFQTLVVGVVGGLLGSLVLLVWVL AVI RWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSP NCPSEDVVITPESFGRDSSLTCLAGNVSACDAPI LSSSRSLDCRESGKNGPHVYQDLLLSLGTTNST LPPPFSLQSGILTLNPVAQGQPILTSLGSNQEEA YVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDD LPSHEAPLADSLEELEPQ	
FKBP(F36V)-TPOR/MPLR(478-582)-EGFR(1122-1165)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLE DGKKVDSSRDRNKPFKFMLGKQEVIRGWEEGV AQMSVGQRAKLTISPDYAYGATGHPGIIPPHATL VFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLR DTAALSPPKATVSDTCEEVEPSLLEILPKSSERT PLPL PEYLNTVQPTCVNSTFDSPAHWAQKGSHQISLD NPDYQQDFFPKEAKPNGIFKG	282
FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825) FKBP switch containing wildtype TpoR TM sequence	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAAL SPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	283
FKBP(F36V)-TPOR/MPLR(478-582;N-1)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETWISLVTALHLVLGLSAVLGLLLLRW QFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSP PKATVSDTCEEVEPSLLEILPKSSERTPLPL	284

	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
FKBP(F36V)- TPOR/MPLR(478-582;N- 2)-IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETISLVTALHLVLGLSAVLGLLLLRWQF PAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	285
FKBP(F36V)- TPOR/MPLR(478-582;N- 2+1)-IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLISLVTALHLVLGLSAVLGLLLLRWQ FPAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPP KATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	286
FKBP(F36V)- TPOR/MPLR(478-582;N- 3)-IL7R(316-459)- IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETSLVTALHLVLGLSAVLGLLLLRWQF PAHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPK ATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	287

FKBP(F36V)-TPOR/MPLR(478-582;N-4)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLVTALHLVLGLSAVLGLLLLRWQFP AHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	288
FKBP(F36V)-TPOR/MPLR(478-582;N-4+1)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETILVTALHLVLGLSAVLGLLLLRWQFP AHYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKA TVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	289
FKBP(F36V)-TPOR/MPLR(478-582;N-5)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETVTALHLVLGLSAVLGLLLLRWQFPA HYRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKAT VSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	290
FKBP(F36V)-TPOR/MPLR(478-582;N-6)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETTALHLVLGLSAVLGLLLLRWQFPAH YRRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATV SDTCEEVEPSLLEILPKSSERTPLPL	291

	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
FKBP(F36V)-TPOR/MPLR(478-582;N-7)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETALHLVLGLSAVLGLLLLRWQFPAHY RRLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVS DTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	292
FKBP(F36V)-TPOR/MPLR(478-582;N-8)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLHLVLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	293
FKBP(F36V)-TPOR/MPLR(478-582;N-9)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETHLVLGLSAVLGLLLLRWQFPAHYR RLRHALWPSLPDLHRVLGQYLRDTAALSPPKATVSD TCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	294

FKBP(F36V)-TPOR/MPLR(478-582;N-10)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLVLGLSAVLGLLLLRWQFPAHYRRL RHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	295
FKBP(F36V)-TPOR/MPLR(478-582;N-11)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETVLGLSAVLGLLLLRWQFPAHYRRL RHALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTC EEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	296
FKBP(F36V)-TPOR/MPLR(478-582;N-12)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLGLSAVLGLLLLRWQFPAHYRRLR HALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCE EVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	297
FKBP(F36V)-TPOR/MPLR(478-582;N-13)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETGLSAVLGLLLLRWQFPAHYRRLRH ALWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEE VEPSLLEILPKSSERTPLPL	298

	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
FKBP(F36V)-TPOR/MPLR(478-582;N-14)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLSAVLGLLLLRWQFPAHYRRLRHA LWPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEV EPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	299
FKBP(F36V)-TPOR/MPLR(478-582;N-15)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETSAVLGLLLLRWQFPAHYRRLRHAL WPSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVE PSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	300
FKBP(F36V)-TPOR/MPLR(478-582;N-16)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAVLGLLLLRWQFPAHYRRLRHALW PSLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEP SLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	301

FKBP(F36V)-TPOR/MPLR(478-582;N-17)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETVLGLLLLRWQFPAHYRRLRHALWP SLPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPS LLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	302
FKBP(F36V)-TPOR/MPLR(478-582;N-18)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETLGLLLLRWQFPAHYRRLRHALWPS LPDLHRVLGQYLRDTAALSPPKATVSDTCEEVEPSLL EILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	303
FKBP(F36V)-TPOR/MPLR(478-582;N+1)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWLISLVTALHLVLGLSAVLGLLLLR WQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAAL SPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	304
FKBP(F36V)-TPOR/MPLR(478-582;N+2)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWVLISLVTALHLVLGLSAVLGLLLL RWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTAA LSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL	305

	ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	
FKBP(F36V)-TPOR/MPLR(478-582;N+3)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWLVLISLVTALHLVLGLSAVLGLLL LRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDTA ALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	306
FKBP(F36V)-TPOR/MPLR(478-582;N+4)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWILVLISLVTALHLVLGLSAVLGLL LLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRDT AALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	307
FKBP(F36V)-TPOR/MPLR(478-582;N+5)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWLILVLISLVTALHLVLGLSAVLGL LLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	308

FKBP(F36V)-TPOR/MPLR(478-582;N+6)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWLLILVLISLVTALHLVLGLSAVLG LLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYLRD TAALSPPKATVSDTCEEVEPSLLEILPKSSERTPLPL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	309
FKBP(F36V)-TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWVLLILVLISLVTALHLVLGLSAVL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYL RDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	310
FKBP(F36V)-TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)	MGVQVETISPGDGRTFPKRGQTCVVHYTGMLEDGK KVDSSRDRNKPFKFMLGKQEVIRGWEEGVAQMSVG QRAKLTISPDYAYGATGHPGIIPPHATLVFDVELLKLE SDPTRVETATETAWVLLLILVLISLVTALHLVLGLSAVL GLLLLRWQFPAHYRRLRHALWPSLPDLHRVLGQYL RDTAALSPPKATVSDTCEEVEPSLLEILPKSSERTPL PL ARDEVEGFLQDTFPQQLEESEKQRLGGDVQSPNCP SEDVVITPESFGRDSSLTCLAGNVSACDAPILSSSRS LDCRESGKNGPHVYQDLLLSLGTTNSTLPPPFSLQS GILTLNPVAQGQPILTSLGSNQEEAYVTMSSFYQNQ SDPKPENPACPWTVLPAGDLPTHDGYLPSNIDDLPS HEAPLADSLEELEPQ	311

[0272] The invention encompasses modifications to the inducible chimeric cytokine receptors of the invention embodiments shown in Tables 2A and 2B, including functionally equivalent proteins having modifications which do not significantly affect

their properties and variants which have enhanced or decreased activity and/or affinity. Modification of polypeptides is routine practice in the art and need not be described in detail herein. Examples of modified polypeptides include polypeptides with conservative substitutions of amino acid residues, one or more deletions or additions of amino acids which do not significantly deleteriously change the functional activity, or which mature (enhance) the affinity of the polypeptide for its ligand, or use of chemical analogs.

[0273] Amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from one residue to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include an antibody with an N-terminal methionyl residue or the antibody fused to an epitope tag.

[0274] Substitution variants have at least one amino acid residue in the inducible chimeric cytokine receptor removed and a different residue inserted in its place. Conservative substitutions are shown in Table 3 under the heading of "conservative substitutions." If such substitutions result in a change in biological activity, then more substantial changes, denominated "exemplary substitutions" in Table 3, or as further described below in reference to amino acid classes, may be introduced and the products screened.

Table 3: Amino Acid Substitutions

Original Residue (naturally occurring amino acid)	Conservative Substitutions	Exemplary Substitutions
Ala (A)	Val	Val; Leu; Ile
Arg (R)	Lys	Lys; Gln; Asn
Asn (N)	Gln	Gln; His; Asp, Lys; Arg
Asp (D)	Glu	Glu; Asn
Cys (C)	Ser	Ser; Ala
Gln (Q)	Asn	Asn; Glu
Glu (E)	Asp	Asp; Gln
Gly (G)	Ala	Ala
His (H)	Arg	Asn; Gln; Lys; Arg
Ile (I)	Leu	Leu; Val; Met; Ala; Phe; Norleucine
Leu (L)	Ile	Norleucine; Ile; Val; Met; Ala; Phe
Lys (K)	Arg	Arg; Gln; Asn

Original Residue (naturally occurring amino acid)	Conservative Substitutions	Exemplary Substitutions
Met (M)	Leu	Leu; Phe; Ile
Phe (F)	Tyr	Leu; Val; Ile; Ala; Tyr
Pro (P)	Ala	Ala
Ser (S)	Thr	Thr
Thr (T)	Ser	Ser
Trp (W)	Tyr	Tyr; Phe
Tyr (Y)	Phe	Trp; Phe; Thr; Ser
Val (V)	Leu	Ile; Leu; Met; Phe; Ala; Norleucine

[0275] In some embodiments, inducible chimeric cytokine receptors may be synthesized in situ in an isolated immune cell, such as a CAR-T cell, after introduction of polynucleotides encoding the inducible chimeric cytokine receptors into the cell. Alternatively, inducible chimeric cytokine receptors may be produced outside of cells, and then introduced into cells. Methods for introducing a polynucleotide construct into cells are known in the art. In some embodiments, stable transformation methods can be used to integrate the polynucleotide construct into the genome of the cell. In other embodiments, transient transformation methods can be used to transiently express the polynucleotide construct, and the polynucleotide construct not integrated into the genome of the cell. In other embodiments, virus-mediated methods can be used. The polynucleotides may be introduced into a cell by any suitable means such as for example, recombinant viral vectors (e.g. retroviruses, adenoviruses), liposomes, and the like. Transient transformation methods include, for example without limitation, microinjection, electroporation or particle bombardment. Polynucleotides may be included in vectors, such as for example plasmid vectors or viral vectors.

[0276] In some embodiments, an isolated immune cell, such as an isolated T cell, of the invention can comprise at least one inducible chimeric cytokine receptor and at least one CAR. In some embodiments, an isolated immune cell, such as an isolated T cell, can comprise at least a population of different inducible chimeric cytokine receptors and at least one CAR. For example, a population of different inducible chimeric cytokine receptors present in an isolated immune cell may comprise receptors with the same dimerization domain but different tyrosine kinase activating domains and different

tyrosine effector domains, or receptors with the same dimerization domains, same tyrosine kinase activating domains but different tyrosine effector domains, or receptors with all three domains being different from each other, and the like. In some embodiments, an isolated immune cell, such as an isolated T cell, can comprise at least one inducible chimeric cytokine receptor and a population of CARs, each CAR comprising different extracellular ligand-binding domains.

[0277] Introducing a population of different inducible chimeric cytokine receptors into an immune cell can allow manipulation of the cell's functional outcome and/or phenotype. For example, different inducible chimeric cytokine receptors present in the isolated immune cell can activate different intracellular signaling events, each resulting in a particular functional outcome and/or directing the cell to a particular phenotype. By manipulating the population of the inducible chimeric cytokine receptors introduced into the cell, the cell's functional outcome and/or phenotype can be manipulated. For example, the population of inducible chimeric cytokine receptors introduced into the immune cell can be manipulated to comprise a greater number of receptors that activate one STAT transcription factor over the other STATs thereby skewing the cell's functional outcome and/or phenotype to the one governed by that STAT.

[0278] In some embodiments of an isolated immune cell, such as an isolated T cell provided herein, a CAR can comprise an extracellular ligand-binding domain (e.g., a single chain variable fragment (scFv)), a transmembrane domain, and an intracellular signaling domain. In some embodiments, the extracellular ligand-binding domain, transmembrane domain, and intracellular signaling domain are in one polypeptide, i.e., in a single chain. Multichain CARs and polypeptides are also provided herein. In some embodiments, the multichain CARs comprise: a first polypeptide comprising a transmembrane domain and at least one extracellular ligand-binding domain, and a second polypeptide comprising a transmembrane domain and at least one intracellular signaling domain, wherein the polypeptides assemble together to form a multichain CAR.

[0279] The extracellular ligand-binding domain of a CAR specifically binds to a target of interest. The target of interest can be any molecule of interest, including, for example without limitation BCMA, EGFRvIII, Flt-3, WT-1, CD20, CD23, CD30, CD38, CD70, CD33, CD133, LeY, NKG2D, CS1, CD44v6, ROR1, CD19, Claudin-18.2 (Claudin-18A2, or Claudin18 isoform 2), DLL3 (Delta-like protein 3, Drosophila Delta homolog 3, Delta3), Muc17 (Mucin17, Muc3, Muc3), FAP alpha (Fibroblast Activation Protein alpha),

Ly6G6D (Lymphocyte antigen 6 complex locus protein G6d, c6orf23, G6D, MEGT1, NG25), RNF43 (E3 ubiquitin-protein ligase RNF43, RING finger protein 43).

[0280] In some embodiments, the extracellular ligand-binding domain of a CAR comprises an scFv comprising the light chain variable (VL) region and the heavy chain variable (VH) region of a target antigen specific monoclonal antibody joined by a flexible linker. Single chain variable region fragments are made by linking light and/or heavy chain variable regions by using a short linking peptide (Bird et al., Science 242:423-426, 1988). An example of a linking peptide is the GS linker having the amino acid sequence $(GGGGS)_3$ (SEQ ID NO: 224), which bridges approximately 3.5 nm between the carboxy terminus of one variable region and the amino terminus of the other variable region. Linkers of other sequences have been designed and used (Bird et al., 1988, supra). In general, linkers can be short, flexible polypeptides and preferably comprised of about 20 or fewer amino acid residues. Linkers can in turn be modified for additional functions, such as attachment of drugs or attachment to solid supports. The single chain variants can be produced either recombinantly or synthetically. For synthetic production of scFv, an automated synthesizer can be used. For recombinant production of scFv, a suitable plasmid containing polynucleotide that encodes the scFv can be introduced into a suitable host cell, either eukaryotic, such as yeast, plant, insect or mammalian cells, or prokaryotic, such as E. coli. Polynucleotides encoding the scFv of interest can be made by routine manipulations such as ligation of polynucleotides. The resultant scFv can be isolated using standard protein purification techniques known in the art.

[0281] The intracellular signaling domain of a CAR according to the invention is responsible for intracellular signaling following the binding of extracellular ligand-binding domain to the target resulting in the activation of the immune cell and immune response. The intracellular signaling domain has the ability to activate of at least one of the normal effector functions of the immune cell in which the CAR is expressed. For example, the effector function of a T cell can be a cytolytic activity or helper activity including the secretion of cytokines.

[0282] In some embodiments, an intracellular signaling domain for use in a CAR can be the cytoplasmic sequences of, for example without limitation, the T cell receptor and co-receptors that act in concert to initiate signal transduction following antigen receptor engagement, as well as any derivative or variant of these sequences and any synthetic sequence that has the same functional capability. Intracellular signaling domains

comprise two distinct classes of cytoplasmic signaling sequences: those that initiate antigen-dependent primary activation, and those that act in an antigen- independent manner to provide a secondary or co-stimulatory signal. Primary cytoplasmic signaling sequences can comprise signaling motifs which are known as immunoreceptor tyrosine-based activation motifs of ITAMs. ITAMs are well defined signaling motifs found in the intracytoplasmic tail of a variety of receptors that serve as binding sites for syk/zap70 class tyrosine kinases. Examples of ITAM used in the invention can include as non-limiting examples those derived from TCRζ, FcRγ, FcRβ, FcRε, CD3γ, CD3δ, CD3ε, CD5, CD22, CD79a, CD79b and CD66d. In some embodiments, the intracellular signaling domain of the CAR can comprise the CD3ζ signaling domain. In some embodiments the intracellular signaling domain of the CAR of the invention comprises a domain of a co-stimulatory molecule.

[0283] In some embodiments, the intracellular signaling domain of a CAR of the invention comprises a part of co-stimulatory molecule selected from the group consisting of fragment of 41BB (GenBank: AAA53133.) and CD28 (NP_006130.1).

[0284] CARs are expressed on the surface membrane of the cell. Thus, the CAR can comprise a transmembrane domain. Suitable transmembrane domains for a CAR disclosed herein have the ability to (a) be expressed at the surface of a cell, preferably an immune cell such as, for example without limitation, lymphocyte cells or Natural killer (NK) cells, and (b) interact with the ligand-binding domain and intracellular signaling domain for directing cellular response of immune cell against a predefined target cell. The transmembrane domain can be derived either from a natural or from a synthetic source. The transmembrane domain can be derived from any membrane-bound or transmembrane protein. As non-limiting examples, the transmembrane polypeptide can be a subunit of the T cell receptor such as α, β, γ or δ, polypeptide constituting CD3 complex, IL-2 receptor p55 (a chain), p75 (β chain) or γ chain, subunit chain of Fc receptors, in particular Fcγ receptor III or CD proteins. Alternatively, the transmembrane domain can be synthetic and can comprise predominantly hydrophobic residues such as leucine and valine. In some embodiments said transmembrane domain is derived from the human CD8α chain (e.g., NP_001139345.1). The transmembrane domain can further comprise a stalk domain between the extracellular ligand-binding domain and said transmembrane domain. A stalk domain may comprise up to 300 amino acids, preferably 10 to 100 amino acids and most preferably 25 to 50 amino acids. Stalk region may be derived from all or part of naturally occurring molecules, such as from all or part

of the extracellular region of CD8, CD4, or CD28, or from all or part of an antibody constant region. Alternatively the stalk domain may be a synthetic sequence that corresponds to a naturally occurring stalk sequence, or may be an entirely synthetic stalk sequence. In some embodiments said stalk domain is a part of human CD8α chain (e.g., NP_001139345.1). In another particular embodiment, said transmembrane and hinge domains comprise a part of human CD8α chain. In some embodiments, CARs disclosed herein can comprise an extracellular ligand-binding domain that specifically binds BCMA, CD8α human hinge and transmembrane domains, the CD3ζ signaling domain, and 4-1BB signaling domain. In some embodiments, a CAR can be introduced into an immune cell as a transgene via a plasmid vector. In some embodiments, the plasmid vector can also contain, for example, a selection marker which provides for identification and/or selection of cells which received the vector.

[0285] Table 4 provides exemplary sequences of CAR components that can be used in the CARs disclosed herein.

Table 4: Exemplary sequences of CAR Components

Domain	Amino acid sequence	SEQ ID
V5 epitope tag	KPIPNPLLGLDST	179
2173 scFv	EIQLVQSGAEVKKPGESLRISCKGSGFNIEDYYI HWVRQMPGKGLEWMGRIDPENDETKYGPIFQG HVTISADTSINTVYLQWSSLKASDTAMYYCAFR GGVYWGQGTTVTVSSGGGGSGGGGSGGGGS GGGGSDVVMTQSPDSLAVSLGERATINCKSSQ SLLDSDGKTYLNWLQQKPGQPPKRLISLVSKLD SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC WQGTHFPGTFGGGTKVEIK	180
26C8 scFv	QVQLQESGPGLVKPSETLSLTCTVSDNSISNYY WSWIRQPPGKGLEWIAYIYYSGTTNYNPSLKSR VTISLDTSKNQFSLQLSSVTAADAAVYYCARVFH WGFAFDIWGQGTMVTVSSGGGGSGGGGSGG GGSEIVLTQSPGTLSLSPGERATLSCRASQRVS NTYLAWYQQNPGQAPRLLIYGASSRATGIPDRF SGSGSGTDFTLTISRLEPEDFAVYYCQQYGTSP LTFGGGTKVEIK	181
CD8 hinge and transmembrane	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGA VHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC	182
4-1BB intracellular signaling	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFP EEEEGGCEL	183
CD3z intracellular signaling	RVKFSRSADAPAYQQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGERRRGKGHDGLYQGLST ATKDTYDALHMQALPPR	184

BFP	MSELIKENMHMKLYMEGTVDNHHFKCTSEGEG KPYEGTQTMRIKVVEGGPLPFAFDILATSFLYGS KTFINHTQGIPDFFKQSFPEGFTWERVTTYEDG GVLTATQDTSLQDGCLIYNVKIRGVNFTSNGPV MQKKTLGWEAFTETLYPADGGLEGRNDMALKL VGGSHLIANIKTTYRSKKPAKNLKMPGVYYVDY RLERIKEANNETYVEQHEVAVARYCDLPSKLGH KLN	185
P2A	GSGATNFSLLKQAGDVEENPGP	186

[0286] CAR polypeptides may be synthesized in situ in the cell after introduction of polynucleotides encoding the CAR polypeptides into the cell. Alternatively, CAR polypeptides may be produced outside of cells, and then introduced into cells. Methods for introducing a polynucleotide construct into cells are known in the art. In some embodiments, stable transformation methods can be used to integrate the polynucleotide construct into the genome of the cell. In other embodiments, transient transformation methods can be used to transiently express the polynucleotide construct, and the polynucleotide construct not integrated into the genome of the cell. In other embodiments, virus-mediated methods can be used. The polynucleotides may be introduced into a cell by any suitable means such as for example, recombinant viral vectors (e.g. retroviruses, adenoviruses), liposomes, and the like. Transient transformation methods include, for example without limitation, microinjection, electroporation or particle bombardment. Polynucleotides may be included in vectors, such as for example plasmid vectors or viral vectors.

[0287] Also provided herein are isolated immune cells comprising at least one inducible chimeric cytokine receptor described herein. The isolated immune cells may further comprise a chimeric antigenic receptor (CAR). Isolated immune cells modified to express an inducible chimeric cytokine receptor and/or a CAR as referred throughout the specification are also interchangeably referred to as engineered immune cells. These isolated immune cells can be prepared according to any one of the methods described herein. Any immune cell capable of expressing heterologous DNAs can be used for the purpose of expressing the inducible chimeric cytokine receptor and CAR of interest. In some embodiments, the isolated immune cell is a T cell. In some embodiments, an immune cell can be derived from, for example without limitation, a stem cell. The stem cells can be adult stem cells, non-human embryonic stem cells, more particularly non-human stem cells, cord blood stem cells, progenitor cells, bone marrow stem cells, induced pluripotent stem cells, totipotent stem cells or hematopoietic

stem cells. Representative human cells are CD34+ cells. In some embodiments, the isolated immune cell can be a dendritic cell, killer dendritic cell, a mast cell, a NK-cell, a macrophage, a monocyte, a B-cell or a T cell. In some embodiments, the isolated immune cell can be a T cell selected from the group consisting of inflammatory T-lymphocytes, cytotoxic T-lymphocytes, regulatory T-lymphocytes or helper T-lymphocytes. In some embodiments, the cell can be derived from the group consisting of CD4+ T-lymphocytes and CD8+ T-lymphocytes. In some embodiments, the isolated immune cell is an autologous T cell. In some embodiments, the isolated immune cell is an allogeneic T cell.

[0288] In some embodiments, the CAR-immune cell (e.g., CAR-T cell) of the disclosure comprises a polynucleotide encoding a suicide polypeptide, such as for example RQR8. See, e.g., WO2013153391A, which is hereby incorporated by reference in its entirety. In some embodiments, a suicide polypeptide is expressed on the surface of the cell. In some embodiments, a suicide polypeptide is included in the CAR construct. In some embodiments, a suicide polypeptide is not part of the CAR construct.

[0289] In some embodiments, the extracellular domain of any one of CARs disclosed herein may comprise one or more epitopes specific for (specifically recognized by) a monoclonal antibody. These epitopes are also referred to herein as mAb-specific epitopes. Exemplary mAb-specific epitopes are disclosed in International Patent Publication No. WO 2016/120216, which is incorporated herein in its entirety. In these embodiments, the extracellular domain of the CARs comprise antigen binding domains that specifically bind to a target of interest and one or more epitopes that bind to one or more monoclonal antibodies (mAbs). CARs comprising the mAb-specific epitopes can be single-chain or multi-chain.

[0290] The inclusion of epitopes specific for monoclonal antibodies in the extracellular domain of the CARs described herein allows sorting and depletion of engineered immune cells expressing the CARs. In some embodiments, allowing for depletion provides a safety switch in case of deleterious effects, e.g., upon administration to a subject.

[0291] Prior to expansion and genetic modification, a source of cells can be obtained from a subject through a variety of non-limiting methods. Cells can be obtained from a number of non-limiting sources, including peripheral blood mononuclear cells, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection,

ascites, pleural effusion, spleen tissue, and tumors. In some embodiments, any number of immune cell lines, such as T cell lines, available and known to those skilled in the art, may be used. In some embodiments, cells can be derived from a healthy donor, from a subject diagnosed with cancer or from a subject diagnosed with an infection. In some embodiments, cells can be part of a mixed population of cells which present different phenotypic characteristics.

[0292] Also provided herein are cell lines obtained from a transformed immune cell, such as a transformed T cell, according to any of the methods described herein. In some embodiments, an isolated immune cell such as an isolated T cell according to the invention comprises a polynucleotide encoding an inducible chimeric cytokine receptor. In some embodiments, an isolated immune cell according to the invention comprises a polynucleotide encoding an inducible chimeric cytokine receptor and a polynucleotide encoding a CAR. In some embodiments, an isolated immune cell according to the invention comprises a polynucleotide encoding an inducible chimeric cytokine receptor, a polynucleotide encoding a CAR, and a polynucleotide encoding an NK cell antagonist.

[0293] The isolated immune cells, such as isolated T cells, of the invention can be activated and expanded, either prior to or after genetic modification of the T cells, using methods as generally described, for example without limitation, in U.S. Patents 6,352,694; 6,534,055; 6,905,680; 6,692,964; 5,858,358; 6,887,466; 6,905,681; 7,144,575; 7,067,318; 7,172,869; 7,232,566; 7,175,843; 5,883,223; 6,905,874; 6,797,514; 6,867,041; and U.S. Patent Application Publication No. 20060121005. Immune cells can be expanded *in vitro* or *in vivo*. Generally, the T cells of the invention can be expanded, for example, by contact with an agent that stimulates a CD3 TCR complex and a co-stimulatory molecule on the surface of the T cells to create an activation signal for the T cell. For example, chemicals such as calcium ionophore A23187, phorbol 12-myristate 13-acetate (PMA), or mitogenic lectins like phytohemagglutinin (PHA) can be used to create an activation signal for the T cell.

[0294] In some embodiments, immune cell populations may be stimulated *in vitro* by contact with an appropriate antibody or antigen-binding fragment thereof. For example, T cell populations may be stimulated *in vitro* by contact with, for example, an anti-CD3 antibody, or antigen-binding fragment thereof, or an anti-CD28 antibody immobilized on a surface, or by contact with a protein kinase C activator (e.g., bryostatin) in conjunction with a calcium ionophore. For co-stimulation of an accessory molecule on the surface of the T cells, a ligand that binds the accessory molecule is used. For example, a

population of T cells can be contacted with an anti-CD3 antibody and an anti-CD28 antibody, under conditions appropriate for stimulating proliferation of the T cells. Conditions appropriate for T cell culture include an appropriate media (e.g., Minimal Essential Media or RPMI Media 1640 or, X-vivo 5, (Lonza)) that may contain factors necessary for proliferation and viability, including serum (e.g., fetal bovine or human serum), interleukin-2 (IL-2), insulin, IFN-γ, IL-4, IL-7, GM-CSF, IL-10, IL-2, IL-15, TGFp, and TNF, or any other additives for the growth of cells known to the skilled artisan. Other additives for the growth of cells include, but are not limited to, surfactant, plasmanate, and reducing agents such as N-acetyl- cysteine and 2-mercaptoethanoi. Media can include RPMI 1640, A1M-V, DMEM, MEM, a- MEM, F-12, X-Vivo 1, and X-Vivo 20, Optimizer, with added amino acids, sodium pyruvate, and vitamins, either serum-free or supplemented with an appropriate amount of serum (or plasma) or a defined set of hormones, and/or an amount of cytokine(s) sufficient for the growth and expansion of T cells. Antibiotics, e.g., penicillin and streptomycin, are included only in experimental cultures, not in cultures of cells that are to be infused into a subject. The target cells are maintained under conditions necessary to support growth, for example, an appropriate temperature (e.g., 37° C) and atmosphere (e.g., air plus 5% CO_2). T cells that have been exposed to varied stimulation times may exhibit different characteristics

[0295] In some embodiments, the cells of the invention can be expanded by co-culturing with tissue or cells. The cells can also be expanded *in vivo*, for example in the subject's blood after administrating the cell into the subject.

[0296] In another aspect, the invention provides compositions (such as a pharmaceutical compositions) comprising any of the cells of the invention. In some embodiments, the composition comprises an isolated T cell comprising a polynucleotide encoding any of the inducible chimeric cytokine receptors described herein, and a polynucleotide encoding a CAR.

[0297] Expression vectors and administration of polynucleotide compositions are further described herein.

[0298] In another aspect, the invention provides a method of making any of the polynucleotides described herein.

[0299] Polynucleotides complementary to any such sequences are also encompassed by the invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a

DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

[0300] Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes an antibody or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants contain one or more substitutions, additions, deletions and/or insertions such that the immunoreactivity of the encoded polypeptide is not diminished, relative to a native immunoreactive molecule. The effect on the immunoreactivity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably, at least about 80% identity, yet more preferably, at least about 90% identity, and most preferably, at least about 95% identity to a polynucleotide sequence that encodes a native antibody or a portion thereof.

[0301] Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, or 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

[0302] Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O., 1978, A model of evolutionary change in proteins - Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J., 1990, Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M., 1989, CABIOS 5:151-153; Myers, E.W. and Muller W., 1988, CABIOS 4:11-17; Robinson, E.D., 1971, Comb. Theor. 11:105; Santou, N., Nes, M., 1987, Mol. Biol. Evol. 4:406-425; Sneath,

P.H.A. and Sokal, R.R., 1973, Numerical Taxonomy the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J., 1983, Proc. Natl. Acad. Sci. USA 80:726-730.

[0303] Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (i.e., gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

[0304] Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native antibody (or a complementary sequence).

[0305] Suitable “moderately stringent conditions” include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1 % SDS.

[0306] As used herein, "highly stringent conditions" or "high stringency conditions" are those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C. The skilled artisan will

recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

[0307] It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

[0308] The polynucleotides of this invention can be obtained using chemical synthesis, recombinant methods, or PCR. Methods of chemical polynucleotide synthesis are well known in the art and need not be described in detail herein. One of skill in the art can use the sequences provided herein and a commercial DNA synthesizer to produce a desired DNA sequence.

[0309] For preparing polynucleotides using recombinant methods, a polynucleotide comprising a desired sequence can be inserted into a suitable vector, and the vector in turn can be introduced into a suitable host cell for replication and amplification, as further discussed herein. Polynucleotides may be inserted into host cells by any means known in the art. Cells are transformed by introducing an exogenous polynucleotide by direct uptake, endocytosis, transfection, F-mating or electroporation. Once introduced, the exogenous polynucleotide can be maintained within the cell as a non-integrated vector (such as a plasmid) or integrated into the host cell genome. The polynucleotide so amplified can be isolated from the host cell by methods well known within the art. See, e.g., Sambrook et al., 1989.

[0310] Alternatively, PCR allows reproduction of DNA sequences. PCR technology is well known in the art and is described in U.S. Patent Nos. 4,683,195, 4,800,159, 4,754,065 and 4,683,202, as well as PCR: The Polymerase Chain Reaction, Mullis et al. eds., Birkauswer Press, Boston, 1994.

[0311] RNA can be obtained by using the isolated DNA in an appropriate vector and inserting it into a suitable host cell. When the cell replicates and the DNA is transcribed

into RNA, the RNA can then be isolated using methods well known to those of skill in the art, as set forth in Sambrook et al., 1989, supra, for example.

[0312] Suitable cloning vectors may be constructed according to standard techniques, or may be selected from a large number of cloning vectors available in the art. While the cloning vector selected may vary according to the host cell intended to be used, useful cloning vectors will generally have the ability to self-replicate, may possess a single target for a particular restriction endonuclease, and/or may carry genes for a marker that can be used in selecting clones containing the vector. Suitable examples include plasmids and bacterial viruses, e.g., pUC18, pUC19, Bluescript (e.g., pBS SK+) and its derivatives, mp18, mp19, pBR322, pMB9, ColE1, pCR1, RP4, phage DNAs, and shuttle vectors such as pSA3 and pAT28. These and many other cloning vectors are available from commercial vendors such as BioRad, Strategene, and Invitrogen.

[0313] Expression vectors generally are replicable polynucleotide constructs that contain a polynucleotide according to the invention. It is implied that an expression vector must be replicable in the host cells either as episomes or as an integral part of the chromosomal DNA. Suitable expression vectors include but are not limited to plasmids, viral vectors, including adenoviruses, adeno-associated viruses, retroviruses, cosmids, and expression vector(s) disclosed in PCT Publication No. WO 87/04462. Vector components may generally include, but are not limited to, one or more of the following: a signal sequence; an origin of replication; one or more marker genes; suitable transcriptional controlling elements (such as promoters, enhancers and terminator). For expression (i.e., translation), one or more translational controlling elements are also usually required, such as ribosome binding sites, translation initiation sites, and stop codons.

[0314] The vectors containing the polynucleotides of interest can be introduced into the host cell by any of a number of appropriate means, including electroporation, transfection employing calcium chloride, rubidium chloride, calcium phosphate, DEAE-dextran, or other substances; microprojectile bombardment; lipofection; and infection (e.g., where the vector is an infectious agent such as vaccinia virus). The choice of introducing vectors or polynucleotides will often depend on features of the host cell.

[0315] A polynucleotide encoding an inducible chimeric cytokine receptor or a CAR disclosed herein may exist in an expression cassette or expression vector (e.g., a plasmid for introduction into a bacterial host cell, or a viral vector such as a baculovirus vector for transfection of an insect host cell, or a plasmid or viral vector such as a

lentivirus for transfection of a mammalian host cell). In some embodiments, a polynucleotide encoding an inducible chimeric cytokine receptor and/or a CAR is introduced into an isolated immune cell using a non-viral vector. Exemplary non-viral vectors that may be used in the methods of the present disclosure include, but are not limited to, transposon-based vectors such as piggyBac™, *Frog Prince*, *Sleeping Beauty* (e.g., SB100X vector), and the like. In some embodiments, a polynucleotide encoding an inducible chimeric cytokine receptor and/or a CAR is integrated into the cell's genome. In some embodiments, the integration is site-specific. Exemplary methods to provide site-specific integration include methods employing genome-editing nucleases, such as meganucleases, zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and clustered, regularly interspaced, short palindromic repeat-associated nucleases (CRISPR) such as Cas9 endonuclease.

[0316] In some embodiments, a polynucleotide or vector can include a nucleic acid sequence encoding ribosomal skip sequences such as, for example without limitation, a sequence encoding a 2A peptide. 2A peptides, which were identified in the Aphthovirus subgroup of picornaviruses, causes a ribosomal "skip" from one codon to the next without the formation of a peptide bond between the two amino acids encoded by the codons (see (Donnelly and Elliott 2001; Atkins, Wills et al. 2007; Doronina, Wu et al. 2008)). By "codon" is meant three nucleotides on an mRNA (or on the sense strand of a DNA molecule) that are translated by a ribosome into one amino acid residue. Thus, two, three, four, or more polypeptides can be synthesized from a single, contiguous open reading frame within an imRNA when the polypeptides are separated by a 2A oligopeptide sequence that is in frame. Such ribosomal skip mechanisms are well known in the art and are known to be used by several vectors for the expression of several proteins encoded by a single messenger RNA.

[0317] To direct transmembrane polypeptides into the secretory pathway of a host cell, in some embodiments, a secretory signal sequence (also known as a leader sequence, prepro sequence or pre sequence) is provided in a polynucleotide sequence or vector sequence. The secretory signal sequence is operably linked to the transmembrane nucleic acid sequence, i.e., the two sequences are joined in the correct reading frame and positioned to direct the newly synthesized polypeptide into the secretory pathway of the host cell. Secretory signal sequences are commonly positioned 5' to the nucleic acid sequence encoding the polypeptide of interest, although certain secretory signal sequences may be positioned elsewhere in the nucleic acid sequence of interest (see,

e.g., Welch et al., U.S. Patent No. 5,037,743; Holland et al., U.S. Patent No. 5,143,830). In some embodiments the signal peptide comprises the amino acid sequence shown in SEQ ID NO: 318 or 329. Those skilled in the art will recognize that, in view of the degeneracy of the genetic code, considerable sequence variation is possible among these polynucleotide molecules. In some embodiments, nucleic acid sequences of the invention are codon-optimized for expression in mammalian cells, preferably for expression in human cells. Codon-optimization refers to the exchange in a sequence of interest of codons that are generally rare in highly expressed genes of a given species by codons that are generally frequent in highly expressed genes of such species, such codons encoding the amino acids as the codons that are being exchanged.

[0318] Methods of preparing immune cells for use in immunotherapy are provided herein. In some embodiments, the methods comprise introducing an inducible chimeric cytokine receptor and a CAR into immune cells, and expanding the cells. In some embodiments, the invention relates to a method of engineering an immune cell comprising: providing a cell and expressing an inducible chimeric cytokine receptor, and expressing at the surface of the cell at least one CAR. In some embodiments, the method comprises: transfecting the cell with at least one polynucleotide encoding an inducible chimeric cytokine receptor, and at least one polynucleotide encoding a CAR, and expressing the polynucleotides in the cell. In some embodiments, the method comprises: transfecting the cell with at least one polynucleotide encoding an inducible chimeric cytokine receptor, at least one polynucleotide encoding a CAR, and expressing the polynucleotides in the cell.

[0319] In some embodiments, the polynucleotides encoding the inducible chimeric cytokine receptor and CAR are present in one or more expression vectors for stable expression in the cells. In some embodiments, the polynucleotides are present in viral vectors for stable expression in the cells. In some embodiments, the viral vectors may be for example, lentiviral vectors or adenoviral vectors.

[0320] In some embodiments, polynucleotides encoding polypeptides according to the present invention can be mRNA which is introduced directly into the cells, for example by electroporation. In some embodiments, cytoPulse technology, such as PulseAgile, can be used to transiently permeabilize living cells for delivery of material into the cells (e.g. http://cytopulse.com; US 6,078,490; PCT/US2011/000827; and PCT/US2004/005237). Parameters can be modified in order to determine conditions for high transfection efficiency with minimal mortality.

[0321] Also provided herein are methods of transfecting an immune cell, such as a T cell. In some embodiments, the method comprises: contacting an immune cell with RNA and applying to an immune cell an agile pulse sequence consisting of: (a) an electrical pulse with a voltage range from about 2250 to 3000 V per centimeter; (b) a pulse width of 0.1 ms; (c) a pulse interval of about 0.2 to 10 ms between the electrical pulses of step (a) and (b); (d) an electrical pulse with a voltage range from about 2250 to 3000 V with a pulse width of about 100 ms and a pulse interval of about 100 ms between the electrical pulse of step (b) and the first electrical pulse of step (c); and (e) four electrical pulses with a voltage of about 325 V with a pulse width of about 0.2 ms and a pulse interval of 2 ms between each of 4 electrical pulses. In some embodiments, a method of transfecting an immune cell comprises contacting said immune cell with RNA and applying to immune cell an agile pulse sequence comprising: (a) an electrical pulse with a voltage of about 2250, 2300, 2350, 2400, 2450, 2500, 2550, 2400, 2450, 2500, 2600, 2700, 2800, 2900 or 3000V per centimeter; (b) a pulse width of 0.1 ms; (c) and a pulse interval of about 0.2, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 ms between the electrical pulses of step (a) and (b); (d) one electrical pulse with a voltage range from about 2250, of 2250, 2300, 2350, 2400, 2450, 2500, 2550, 2400, 2450, 2500, 2600, 2700, 2800, 2900 or 3000V with a pulse width of 100 ms and a pulse interval of 100 ms between the electrical pulse of step (b) and the first electrical pulse of step (c); and (e) 4 electrical pulses with a voltage of about 325 V with a pulse width of about 0.2 ms and a pulse interval of about 2 ms between each of 4 electrical pulses. Any values included in the value range described above are disclosed in the present application. Electroporation medium can be any suitable medium known in the art. In some embodiments, the electroporation medium has conductivity in a range spanning about 0.01 to about 1.0 milliSiemens.

[0322] In some embodiments, the method can further comprise a step of genetically modifying a cell by inactivating at least one gene expressing, for example without limitation, a component of the TCR, a target for an immunosuppressive agent, an HLA gene, and/or an immune checkpoint protein such as, for example, PDCD1 or CTLA-4. By inactivating a gene it is intended that the gene of interest is not expressed in a functional protein form. In some embodiments, the gene to be inactivated is selected from the group consisting of, for example without limitation, TCRα, TCRβ, CD52, GR, deoxycytidine kinase (DCK), PD-1, and CTLA-4. In some embodiments the method comprises inactivating one or more genes by introducing into the cells a rare-cutting

endonuclease able to selectively inactivate a gene by selective DNA cleavage. In some embodiments the rare-cutting endonuclease can be, for example, a transcription activator-like effector nuclease (TALE-nuclease) or Cas9 endonuclease.

[0323] In another aspect, a step of genetically modifying cells can comprise: modifying the immune cells by inactivating at least one gene expressing a target for an immunosuppressive agent, and; expanding the cells, optionally in presence of the immunosuppressive agent. An immunosuppressive agent is an agent that suppresses immune function by one of several mechanisms of action. An immunosuppressive agent can diminish the extent and/or voracity of an immune response. Non-limiting examples of immunosuppressive agents iinclude calcineurin inhibitors, targets of rapamycin, interleukin-2 α-chain blockers, inhibitors of inosine monophosphate dehydrogenase, inhibitors of dihydrofolic acid reductase, corticosteroids, and immunosuppressive antimetabolites. Some cytotoxic immunosuppressants act by inhibiting DNA synthesis. Others may act through activation of T cells or by inhibiting the activation of helper cells. The methods according to the invention allow conferring immunosuppressive resistance to T cells for immunotherapy by inactivating the target of the immunosuppressive agent in T cells. As non-limiting examples, targets for immunosuppressive agent can be a receptor for an immunosuppressive agent such as for example without limitation CD52, glucocorticoid receptor (GR), FKBP family gene members, and cyclophilin family gene members.

Therapeutic Methods

[0324] Isolated immune cells obtained by the methods described above, or cell lines derived from such isolated immune cells, can be administered to a subject in need thereof and used as a medicament. In some embodiments, the isolated immune cell is a T cell. In some embodiments, such a medicament can be used for treating a disorder such as for example a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease. In some embodiments, the cancer can be selected from the group consisting of gastric cancer, sarcoma, lymphoma, leukemia, head and neck cancer, thymic cancer, epithelial cancer, salivary cancer, liver cancer, stomach cancer, thyroid cancer, lung cancer, ovarian cancer, breast cancer, prostate cancer, esophageal cancer, pancreatic cancer, glioma, leukemia, multiple myeloma, renal cell carcinoma, bladder cancer, cervical cancer, choriocarcinoma, colon cancer, oral cancer, skin cancer, and melanoma. In some

embodiments, the subject is a previously treated adult subject with locally advanced or metastatic melanoma, squamous cell head and neck cancer (SCHNC), ovarian carcinoma, sarcoma, or relapsed or refractory classic Hodgkin's Lymphoma (cHL).

[0325] In some embodiments, isolated immune cells, such as isolated T cells, according to the invention, or cell line derived from the isolated immune cells, can be used in the manufacture of a medicament for treatment of a disorder in a subject in need thereof. In some embodiments, the disorder can be, for example, a cancer, an autoimmune disorder, or an infection.

[0326] Also provided herein are methods for treating subjects. In some embodiments, the method comprises providing an isolated immune cell comprising an inducible chimeric cytokine receptor of the invention to a subject in need thereof. In some embodiments, the method comprises a step of administering isolated immune cells of the invention to a subject in need thereof. In an exemplary embodiment, the method comprises providing an isolated T cell comprising an inducible chimeric cytokine receptor of the invention to a subject in need thereof. In some embodiments, the method comprises a step of administering isolated T cells of the invention to a subject in need thereof.

[0327] In some embodiments, isolated immune cells of the invention can undergo robust *in vivo* cell expansion and can persist for an extended amount of time.

[0328] The methods can further comprise administering one or more therapeutic agents to a subject prior to administering the engineered immune cells bearing a CAR and an inducible chimeric cytokine receptor provided herein. In certain embodiments, the agent is a lymphodepleting (preconditioning) regimen. For example, methods of lymphodepleting a subject in need of such therapy comprise administering to the subject specified beneficial doses of cyclophosphamide (between 200 mg/m^2/day and 2000 mg/m^2/day, about 100 mg/m^2/day and about 2000 mg/m^2/day; *e.g.*, about 100 mg/m^2/day, about 200 mg/m^2/day, about 300 mg/m^2/day, about 400 mg/m^2/day, about 500 mg/m^2/day, about 600 mg/m^2/day, about 700 mg/m^2/day, about 800 mg/m^2/day, about 900 mg/m^2/day, about 1000 mg/m^2/day, about 1500 mg/m^2/day or about 2000 mg/m^2/day) and specified doses of fludarabine (between 20 mg/m^2/day and 900 mg/m^2/day, between about 10 mg/m^2/day and about 900 mg/m^2/day; *e.g.*, about 10 mg/m^2/day, about 20 mg/m^2/day, about 30 mg/m^2/day, about 40 mg/m^2/day, about 40 mg/m^2/day, about 50 mg/m^2/day, about 60 mg/m^2/day, about 70 mg/m^2/day, about 80 mg/m^2/day, about 90 mg/m^2/day, about 100 mg/m^2/day, about 500 mg/m^2/day or about

900 mg/m^2/day). An exemplary dosing regimen involves treating a subject comprising administering daily to the patient about 300 mg/m^2/day of cyclophosphamide in combination or before or after administering about 30 mg/m^2/day of fludarabine for three days prior to administration of a therapeutically effective amount of engineered immune cells to the patien.

[0329] In some embodiments, notably in the case when the engineered cells provided herein have been gene edited to eliminate or minimize surface expression of CD52, lymphodepletion further comprises administration of an anti-CD52 antibody, such as alemtuzumab. In some embodiments, the CD52 antibody is administered at a dose of about 1-20 mg/day IV, e.g., about 13 mg/day IV for 1, 2, 3 or more days. The antibody can be administered in combination with, before, or after administration of other elements of a lymphodepletion regime (e.g., cyclophosphamide and/or fludarabine).

[0330] In certain embodiments, compositions comprising CAR-expressing immune effector cells disclosed herein may be administered in conjunction with any number of chemotherapeutic agents.

[0331] Methods of treatment of the invention can be ameliorating, curative or prophylactic. The method of the invention may be either part of an autologous immunotherapy or part of an allogenic immunotherapy treatment. The invention is particularly suitable for allogeneic immunotherapy. In an exemplary embodiment, T cells from donors can be transformed into non-alloreactive cells using standard protocols and reproduced as needed, thereby producing CAR-T cells which may be administered to one or several subjects. Such CAR-T cell therapy can be made available as an "off the shelf" therapeutic product.

[0332] In another aspect, the invention provides a method of inhibiting tumor growth or progression in a subject who has a tumor, comprising administering to the subject an effective amount of isolated immune cells as described herein. In another aspect, the invention provides a method of inhibiting or preventing metastasis of cancer cells in a subject, comprising administering to the subject in need thereof an effective amount of isolated immune cells as described herein. In another aspect, the invention provides a method of inducing tumor regression in a subject who has a tumor, comprising administering to the subject an effective amount of isolated immune cells as described herein. In an exemplary embodiment, the isolated immune cell is a T cell.

[0333] In some embodiments, the isolated immune cells can be administered parenterally in a subject. In some embodiments, the subject is a human.

[0334] Also provided is the use of any of the isolated immune cells provided herein in the manufacture of a medicament for the treatment of cancer or for inhibiting tumor growth or progression in a subject in need thereof. In an exemplary embodiment, the isolated immune cell is a T cell.

[0335] In some embodiments, treatment can be administrated into subjects undergoing an immunosuppressive treatment. Indeed, the invention preferably relies on cells or population of cells, which have been made resistant to at least one immunosuppressive agent due to the inactivation of a gene encoding a receptor for such immunosuppressive agent. In this aspect, the immunosuppressive treatment should help the selection and expansion of the immune cells according to the invention within the subject. The administration of the cells or population of cells according to the invention may be carried out in any convenient manner, including by aerosol inhalation, injection, ingestion, transfusion, implantation or transplantation. The compositions described herein may be administered to a subject subcutaneously, intradermaliy, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous or intralymphatic injection, or intraperitoneally. In some embodiments, the cell compositions of the invention are preferably administered by intravenous injection.

[0336] In some embodiments the administration of the cells or population of cells can comprise administration of, for example, about 10^4 to about 10^9 cells per kg body weight including all integer values of cell numbers within those ranges. In some embodiments the administration of the cells or population of cells can comprise administration of about 10^5 to 10^6 cells per kg body weight including all integer values of cell numbers within those ranges. The cells or population of cells can be administrated in one or more doses. In some embodiments, said effective amount of cells can be administrated as a single dose. In some embodiments, said effective amount of cells can be administrated as more than one dose over a period time. Timing of administration is within the judgment of managing physician and depends on the clinical condition of the subject. The cells or population of cells may be obtained from any source, such as a blood bank or a donor. While individual needs vary, determination of optimal ranges of effective amounts of a given cell type for a particular disease or conditions within the skill of the art. An effective amount means an amount which provides a therapeutic or prophylactic benefit. The dosage administrated will be dependent upon the age, health and weight of the recipient, kind of concurrent treatment, if any, frequency of treatment and the nature of the effect desired. In some embodiments, an effective amount of cells or composition

comprising those cells are administrated parenterally. In some embodiments, administration can be an intravenous administration. In some embodiments, administration can be directly done by injection within a tumor.

Kits

[0337] The invention also provides kits for use in the instant methods. Kits of the invention include one or more containers comprising an isolated immune cell comprising one or more polynucleotide(s) encoding an inducible chimeric cytokine receptor and a CAR as described herein, and instructions for use in accordance with any of the methods of the invention described herein. Generally, these instructions comprise a description of administration of the isolated immune cell for the above described therapeutic treatments. In an exemplary embodiment, kits may comprise an isolated T cell.

[0338] The instructions relating to the use of the isolated immune cells as described herein generally include information as to dosage, dosing schedule, and route of administration for the intended treatment. The containers may be unit doses, bulk packages (e.g., multi-dose packages) or sub-unit doses. Instructions supplied in the kits of the invention are typically written instructions on a label or package insert (e.g., a paper sheet included in the kit), but machine-readable instructions (e.g., instructions carried on a magnetic or optical storage disk) are also acceptable.

[0339] The kits of this invention are in suitable packaging. Suitable packaging includes, but is not limited to, vials, bottles, jars, flexible packaging (e.g., sealed Mylar or plastic bags), and the like. Also contemplated are packages for use in combination with a specific device, such as an inhaler, nasal administration device (e.g., an atomizer) or an infusion device such as a minipump. A kit may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). The container may also have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). At least one active agent in the composition is an isolated immune cell comprising an inducible chimeric cytokine receptor and a CAR. The container may further comprise a second pharmaceutically active agent.

[0340] Kits may optionally provide additional components such as buffers and interpretive information. Normally, the kit comprises a container and a label or package insert(s) on or associated with the container.

[0341] The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the invention in any way. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

NUMBERED EMBODIMENTS

[0342] The inventions disclosed herein may be defined by reference to the following numbered illustrative embodiments.

[0343] Embodiment 1. An inducible chimeric cytokine receptor comprising:

a dimerization domain;

a tyrosine kinase activating domain; and

a tyrosine effector domain.

[0344] Embodiment 2. The inducible chimeric cytokine receptor of embodiment 1, wherein the dimerization domain binds a small molecule.

[0345] Embodiment 3. The inducible chimeric cytokine receptor of embodiment 1 or 2, wherein the dimerization domain binds to the dimeric ligand AP1903, AP20187, dimeric FK506, or a dimeric FK506-like analog.

[0346] Embodiment 4. The inducible chimeric cytokine receptor of any one of embodiments 1 to 3, wherein the dimerization domain comprises an FKBP12 polypeptide.

[0347] Embodiment 5. The inducible chimeric cytokine receptor of embodiment 4, wherein the FKBP12 polypeptide contains the amino acid substitution F36V.

[0348] Embodiment 6. The inducible chimeric cytokine receptor of embodiment 1, wherein the dimerization domain binds a protein.

[0349] Embodiment 7. The inducible chimeric cytokine receptor of embodiment 1, wherein the dimerization domain comprises a polypeptide of a protein selected from the group consisting of: FKBP, cyclophilin, steroid binding protein, estrogen binding protein, glucocorticoid binding protein, vitamin D binding protein, tetracycline binding protein, extracellular domain of a cytokine receptor, receptor tyrosine kinase, TNFR-family receptor, and immune co-receptor.

[0350] Embodiment 8. The inducible chimeric cytokine receptor of embodiment 7, wherein the immune co-receptor is selected from the group consisting of: erythropoietin receptor, prolactin receptor, growth hormone receptor, thrombopoietin receptor,

granulocyte colony-stimulating factor receptor, GP130, common gamma chain receptor, common beta chain receptor, IFN alpha receptor, IFN gamma receptor, IFN lambda receptor, IL2/IL15 receptor, IL3 receptor, IL4 receptor, IL5 receptor, IL7 receptor, IL9 receptor, IL10 receptor, IL12 receptor, IL13 receptor, IL20 receptor, IL21 receptor, IL22 receptor, IL23 receptor, IL27 receptor, TSLP Receptor, G-CSF receptor, GM-CSF receptor, CNTF receptor, OSM receptor, LIF receptor, CT-1 receptor, TGFBR1/ALKL5, TGFBR2, EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, RTK106, TNFR1, Fas, TRAILR1, TRAILR2, NGFR, DR3, DR6, EDAR, TNFR2, LTbR, OX40, CD40, CD27, CD30, 4-1BB, RANK, Fn14, TACI, BAFFR, HVEM, BCMA, GITR, TROY, RELT, XEDAR, TRAILR3, TRAILR4, OPG, DcR3, PD-1, CD80, CD86, ICOS-L, ICOS, CTLA-4, BTLA, CD160, LAG3, and TIM3.

[0351] Embodiment 9. The inducible chimeric cytokine receptor of any one of embodiments 1 to 8, wherein the tyrosine kinase activating domain is derived from, or comprises a polypeptide of, a protein selected from the group consisting of: common gamma chain receptor, common beta chain receptor, IFN alpha receptor, IFN gamma receptor, IFN lambda receptor, IL2/IL15 receptor, IL3 receptor, IL4 receptor, IL5 receptor, IL7 receptor, IL9 receptor, IL10 receptor, IL12 receptor, IL13 receptor, IL20 receptor, IL21 receptor, IL22 receptor, IL23 receptor, IL27 receptor, TSLP Receptor, G-CSF receptor, GM-CSF receptor, CNTF receptor, OSM receptor, LIF receptor, CT-1 receptor, EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, and RTK106 receptor.

[0352] Embodiment 10. The inducible chimeric cytokine receptor of any one of embodiments 1 to 9, wherein the tyrosine effector domain is derived from, or comprises a polypeptide of, a protein selected from the group consisting of: common gamma chain

receptor, common beta chain receptor, IFN alpha receptor, IFN gamma receptor, IFN lambda receptor, IL2/IL15 receptor, IL3 receptor, IL4 receptor, IL5 receptor, IL7 receptor, IL9 receptor, IL10 receptor, IL12 receptor, IL13 receptor, IL20 receptor, IL21 receptor, IL22 receptor, IL23 receptor, IL27 receptor, TSLP Receptor, G-CSF receptor, GM-CSF receptor, CNTF receptor, OSM receptor, LIF receptor, CT-1 receptor, EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, RTK106, ALX, BLNK, Grb7, Nsp, SLP-76, SOCS, TSAd, APS, Bam32, Crk, Gads, Grb2, Nck, SLAP, Shc, FRS2, Dab, Dok, IRS, eps8, AFAP110, Gab, ADAP, Carma1, Cas, CIN85, Cortactin, E3B1, Vinexin, SKAP-55, BANK, BCAP, Dof, Paxillin, LAT, LAX, LIME, NTAL, PAG, SIT, and TRIM.

[0353] Embodiment 11. The inducible chimeric cytokine receptor of any one of embodiments 1 to 10, wherein the dimerization domain is located at the N-terminus of the inducible chimeric cytokine receptor.

[0354] Embodiment 12. The inducible chimeric cytokine receptor of any one of embodiments 1 to 10, wherein the dimerization domain is located at the C-terminus of the inducible chimeric cytokine receptor.

[0355] Embodiment 13. The inducible chimeric cytokine receptor of any one of embodiments 1 to 12, wherein the inducible chimeric cytokine receptor comprises a transmembrane domain.

[0356] Embodiment 14. The inducible chimeric cytokine receptor of any one of embodiments 1 to 13, wherein the inducible chimeric cytokine receptor comprises a membrane-targeting motif.

[0357] Embodiment 15. The inducible chimeric cytokine receptor of embodiment 14, wherein the membrane-targeting motif comprises a CD8 signal sequence or myristoyl.

[0358] Embodiment 16. The inducible chimeric cytokine receptor of any one of embodiments 1 to 15, wherein the receptor is myristoylated.

[0359] Embodiment 17. The inducible chimeric cytokine receptor of embodiment 1, wherein the dimerization domain comprises an FKBP polypeptide, the tyrosine kinase

activating domain comprises an EpoR or TpoR polypeptide, and the tyrosine effector domain comprises an IL7 receptor (IL7R) polypeptide.

[0360] Embodiment 18. The inducible chimeric cytokine receptor of embodiment 17, wherein the tyrosine effector domain further comprises an EGFR polypeptide.

[0361] Embodiment 19. The inducible chimeric cytokine receptor of embodiment 17, wherein the tyrosine effector domain comprises IL7R(316-459), IL12Rb2(775-825), and/or EGFR(1122-1165).

[0362] Embodiment 20. A polynucleotide comprising a nucleic acid sequence encoding the inducible chimeric cytokine receptor of any one of embodiments 1 to 19.

[0363] Embodiment 21. An expression vector comprising the polynucleotide of embodiment 20.

[0364] Embodiment 22. An engineered immune cell comprising the inducible chimeric cytokine receptor of any one of embodiments 1 to 19 or the polynucleotide of embodiment 20.

[0365] Embodiment 23. The engineered immune cell of embodiment 22, wherein the cell further comprises a chimeric antigen receptor (CAR) or a polynucleotide encoding a CAR.

[0366] Embodiment 24. The engineered immune cell of embodiment 22 or 23, wherein the immune cell is a T cell.

[0367] Embodiment 25. A method of modulating an engineered immune cell in a subject, the method comprising administering a dimeric ligand to a subject that has previously been administered an engineered immune cell of any one of embodiments 22 to 24, wherein the dimeric ligand binds to the dimerization domain of the inducible chimeric cytokine receptor.

[0368] Embodiment 26. The method of embodiment 25, wherein the ligand is AP1903.

[0369] Embodiment 27. A method of preparing an engineered immune cell, the method comprising introducing a polynucleotide of embodiment 20 or an expression vector of embodiment 21 into the immune cell.

[0370] Embodiment 28. An isolated T cell comprising

(i) an inducible chimeric cytokine receptor comprising a dimerization domain, a tyrosine kinase activating domain, and a tyrosine effector domain of a cytokine receptor; and

(ii) a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain.

[0371] Embodiment 29. The isolated T cell of embodiment 28, wherein the inducible chimeric cytokine receptor is the inducible chimeric cytokine receptor of any one of embodiments 1 to 19.

[0372] Embodiment 30. The isolated T cell of embodiment 28 or 29, wherein the isolated T cell exhibits improved in vivo persistence relative to in vivo persistence of a second isolated T cell, wherein the second isolated T cell comprises all components of the isolated T cell except it does not comprise the inducible chimeric cytokine receptor.

[0373] Embodiment 31. A method of generating an isolated T cell, wherein the method comprises the steps of:

(a) providing a T cell;

(b) modifying the T cell to express a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain; and

(c) modifying the T cell to express an inducible chimeric cytokine receptor.

[0374] Embodiment 32. The method of embodiment 31 wherein step c) comprises stably introducing the inducible chimeric cytokine receptor into the cell.

[0375] Embodiment 33. The method of embodiment 31 or 32, wherein step c) comprises introducing a polynucleotide that encodes inducible chimeric cytokine receptor to the cell by a transposon/transposase system, a viral-based gene transfer system, or electroporation.

[0376] Embodiment 34. The method of any one of embodiments 31 to 33, wherein step b) comprises introducing a polynucleotide that encodes the chimeric antigen receptor to the cell by a transposon/transposase system or a viral-based gene transfer system.

[0377] Embodiment 35. The method of embodiment 34, wherein the viral-based gene transfer system comprises recombinant retrovirus or lentivirus.

[0378] Embodiment 36. The method of any one of embodiments 31 to 35, wherein step (b) occurs prior to step (c).

[0379] Embodiment 37. The method of any one of embodiments 31 to 35, wherein step (c) occurs prior to step (b).

[0380] Embodiment 38. A pharmaceutical composition comprising the isolated T cell of any one of embodiments 28 to 30 for use in treating a disorder.

[0381] Embodiment 39. The pharmaceutical composition of embodiment 38, wherein the disorder is cancer, autoimmune disease, or infection.

[0382] Embodiment 40. The pharmaceutical composition of embodiment 38 or 39, wherein the cells are to be provided more than once.

[0383] Embodiment 41. The pharmaceutical composition of embodiment 40, wherein the cells are to be provided to the individual at least about 1, 2, 3, 4, 5, 6, 7, or more days apart.

[0384] Embodiment 42. The pharmaceutical composition of embodiment 41, wherein the disorder is a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease.

[0385] Embodiment 43. A method for treating a disorder in a subject, wherein the method comprises administering the isolated T cell of any one of embodiments 28 to 30 to the subject.

[0386] Embodiment 44. The method of 43, wherein the cells are provided to the subject more than once.

[0387] Embodiment 45. The method of embodiment 43 or 44, wherein the subject has been previously treated with a therapeutic agent prior to administration of the isolated T cell.

[0388] Embodiment 46. The method of embodiment 45, wherein the therapeutic agent is an antibody or chemotherapeutic agent.

[0389] Embodiment 47. The method of any one of embodiments 43 to 46, wherein the disorder is a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease.

[0390] Embodiment 48. The method according to embodiment 47, wherein the cancer is a hematological malignancy or a solid cancer.

[0391] Embodiment 49. The method according to embodiment 48, wherein the hematological malignancy is selected from acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), chronic eosinophilic leukemia (CEL), myelodysplasia syndrome (MDS), non-Hodgkin's lymphoma (NHL), or multiple myeloma (MM).

[0392] Embodiment 50. The method according to embodiment 49, wherein the solid cancer is selected from biliary cancer, bladder cancer, bone and soft tissue carcinoma, brain tumor, breast cancer, cervical cancer, colon cancer, colorectal adenocarcinoma, colorectal cancer, desmoid tumor, embryonal cancer, endometrial cancer, esophageal

cancer, gastric cancer, gastric adenocarcinoma, glioblastoma multiforme, gynecological tumor, head and neck squamous cell carcinoma, hepatic cancer, lung cancer, malignant melanoma, osteosarcoma, ovarian cancer, pancreatic cancer, pancreatic ductal adenocarcinoma, primary astrocytic tumor, primary thyroid cancer, prostate cancer, renal cancer, renal cell carcinoma, rhabdomyosarcoma, skin cancer, soft tissue sarcoma, testicular germ- cell tumor, urothelial cancer, uterine sarcoma, or uterine cancer.

EXAMPLES

Example 1A: Inducible chimeric cytokine receptors

[0393] Cytokines known to enhance T cell persistence and function, such as IL-2, IL-7 and IL-15, signal through natural heterodimeric cytokine receptors that in turn activate JAK1 and JAK3 kinases (exemplary activation of JAK kinases is shown in FIG. 1). Inducible chimeric cytokine receptors (FIG. 1) were designed and demonstrated to be efficacious in regulating cytokine signaling in CAR-T cells (Examples *infra*). The AP1903-inducible chimeric cytokine receptor is an AP1903-responsive $FKBP^{F36V}$ fusion protein. Endogenous FKBP binds rapamycin to inhibit mTOR (FIG. 2A). $FKBP^{F36V}$ binds to rapamycin-like compounds (Rapalogs) (FIG. 2B). AP1903 is a clinically-safe rapalog dimer that dimerizes $FKBP^{F36V}$ (FIG. 2C).

[0394] Of more than forty known cytokine receptors, there are five homodimers. These five homodimers couple to JAK2. JAK2 activates as a homodimer. One exemplary embodiment of an inducible chimeric cytokine receptor provided herein is shown in FIG. 3.

[0395] To utilize AP1903 with a variety of different receptors, heterodimeric cytokine receptors are converted into homodimers.

[0396] In some embodiments, FKBP is located at the N-terminus of an inducible chimeric cytokine receptor. In other embodiments, FKBP is located at the C-terminus of an inducible chimeric cytokine receptor. In some embodiments, an inducible chimeric cytokine receptor provided herein has a transmembrane domain. In other embodiments, an inducible chimeric cytokine receptor provided herein lacks a transmembrane domain. In some embodiments, an inducible chimeric cytokine receptor provided herein is myristoylated. In other embodiments, an inducible chimeric cytokine receptor provided herein is not myristoylated.

Example 2: Comparison of small-molecule inducible Epo receptors

[0397] This example illustrates efficacy of various inducible chimeric cytokine receptors provided herein.

[0398] In this study, the following inducible chimeric cytokine receptors tested for activity:

a. CD8 SS-Myc-FKBP(F36V)-EpoR(237-508;L241G,L242P)-V5 (SEQ ID NO: 1)
b. V5-EpoR(273-508)
c. V5-EpoR(273-508)-FKBP(F36V)
d. V5-EpoR(273-508)-FKBP(E31G,F36V,R71G,K105E)
e. Myristoyl-V5-EpoR(273-508)-FKBP(F36V)
f. Myristoyl-V5-EpoR(273-508)-FKBP(E31G,F36V,R71G,K105E)
g. V5-EpoR(273-508)-FKBP(F36V)-FKBP(F36V) (SEQ ID NO 2)
h. V5-EpoR(273-508)-FKBP(E31G,F36V,R71G,K105E)-FKBP(E31G,F36V,R71G,K105E) (SEQ ID NO: 3)
i. CD8 SS-Myc-FKBP(F36V)-CD8(138-206)-EpoR(273-508)-V5
j. FKBP(F36V,L106P)-FKBP(F36V,L106P)-EpoR(273-508)-V5
k. FKBP(F36V,L106P)-EpoR(273-508)-V5
l. FKBP(F36V)-EpoR(273-508)-V5
m. FKBP(F36V)-FKBP(F36V)-EpoR(273-508)-V5

[0399] According to the construct name, receptors contain a membrane-targeting motif (CD8 signal sequence (CD8 SS) or myristoyl), a dimerization domain (FKBP(F36V) or mutants thereof), a portion of the EpoR that contains a transmembrane (EpoR(237-272)), a JAK2 binding motif (EpoR(273-338)), and/or a tyrosine effector domain (EpoR(339-508)). Constructs may also include epitope tags (Myc or V5) for western blot or flow analyses.

[0400] Vectors encoding the inducible chimeric cytokine receptors were transfected into HEK293T cells along with a luciferase reporter for the STAT5 transcription factor (Promega E4651). The reporter vector consists of a firefly luficerase expressed under the control of a STAT5 responsive DNA element. Upon addition of erythropoietin (Epo), the erythropoietin receptor (EpoR) activates the JAK2 kinase which then phosphorylates tyrosines on the EpoR cytotail to generate binding sites for STAT5. Bound STAT5 is then phosphorylated, activating STAT5 to engage DNA motifs and promote transcription. Epo was added to samples with cells transfected with EpoR, and AP1903 was added to the samples with cells transfected with fusions of the EpoR to FKBP. No

Epo or AP1903 was added to samples to assess baseline signaling. Results of the STAT5 assay are summarized in FIG. 4. In FIG. 4, "ligand" is either Epo or AP1903.

[0401] Signaling of CD8 SS-Myc-FKBP(F36V)-EpoR(237-508;L241G,L242P)-V5, was the closest to the EpoR(1-508) positive control (FIG. 4).

[0402] These results demonstrate that certain AP1903-inducible chimeric cytokine receptors can effectively signal upon dimerization by AP1903 to activate a reporter. AP1903-inducible chimeric cytokine receptor construct CD8 SS-Myc-FKBP(F36V)-EpoR(237-508;L241G,L242P)-V5 demonstrated robust activity.

Example 3A: Chimeric small-molecule inducible Epo receptors to generate IL2, IL7, IL12, IL21, and IFNa/b signals

[0403] By changing the tyrosine effector domain (cytotail) of the chimeric cytokine receptor (e.g. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-Cytotail XYZ), the receptor can be redirected to signaling of choice. The inducible chimeric cytokine receptors tested utilized the CD8 SS membrane-targeting motif, the FKBP(F36V) dimerization domain, the EpoR(237-338;L241G,L242P) tyrosine kinase activating domain, and tyrosine effector domains from either the EpoR, GHR, IL2Rb, IL7R, IL12Rb2, IL21R, IFNAR2, or IFNLR1 receptors. A negative control lacking the JAK2 binding motifs and tyrosine effector tail is included CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P). The following inducible chimeric cytokine receptors were tested in this study:

a. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EpoR(339-508)-V5 (SEQ ID NO 1)
b. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-GHR(353-638) (SEQ ID NO 4)
c. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551) (SEQ ID NO 5)
d. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459) (SEQ ID NO 6)
e. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862) (SEQ ID NO 7)
f. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(775-825) (SEQ ID NO 8)

g. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538) (SEQ ID NO 9)
h. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515) (SEQ ID NO 410)
i. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520) (SEQ ID NO 11)

[0404] HEK293 cells were transiently transfected with constructs encoding the above inducible chimeric cytokine receptors above, and a luciferase reporter for the indicated pathway. Cells were treated with ligand for 24h. Results are summarized in FIG. 5A. In this study, the "control dimerizer" is a tail-less construct.

[0405] In FIG. 5A, the black boxes induction >5 fold. All STAT4 experiments were done with co-transfection of STAT4.

Example 3B: An intact JAK-binding domain and phosphorylatable tyrosines in the cytotail domain are necessary for signaling

[0406] To identify components essential for the inducible chimeric cytokine receptor to signal, we generated FKBP switches that lacked either the JAK-binding domains or tyrosine residues in the cytotail domain. Specifically, either one or both JAK-binding motifs from TpoR(478-582) were replaced with glycine linkers, or all or a single (i.e. Y449) tyrosine residue(s) in the IL7R(316-459) cytotail was mutated to phenylalanine. The term "switch" as used in the Example section refers to the inducible chimeric cytokine receptor. For example, an "FKBP switch" as used herein is an inducible chimeric cytokine receptor comprising FKBP as the dimerization domain.

[0407] A HEK293T cell reporter assay was used to test how each of these domains affected cytokine signaling. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. A chimeric cytokine receptor (2.5 ng), a Stat response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated, or

treated with the indicated concentrations of AP1903 (Apex Bio) diluted in serum-free media, and Stat reporter activity was determined 5 hours post-treatment using the Dual-Glo Luciferase Assay System (Promega). The FKBP switch bearing two intact JAK-binding motifs from TpoR(478-582) and the unmutated IL7R(316-459) was used as a positive control. As a negative control (i.e. Mock transfected), cells were transfected with all components with the exception of the chimeric cytokine receptor. Fold induction of Stat reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the inducible cytokine receptor and that were left untreated. Triplicate wells were set up for each condition.

[0408] Figure 5B shows Stat5 reporter activity of the FKBP switch lacking the indicated domains following AP1903 treatment. Compared to the positive control, the removal of one (i.e. No JAK 2; IL7) or both (i.e. No JAK 1,2; IL7) JAK-binding motifs abrogated AP1903-induced Stat5 reporter activity. Similarly, the mutation of all 3 tyrosine residues in the IL7R(317-459) cytotail to phenylalanine abrogated AP1903-induced Stat5 reporter activity. In this example, Y499 in the IL7R(317-459) cytotail was identified as the key tyrosine residue that mediated Stat5 activation.

Example 4: Murine receptors for syngeneic studies

[0409] Murine versions of the engineered inducible receptors were generated. As FKBP is highly conserved, the FKBP(F36V) sequence was not changed. However, the transmembrane and JAK2 binding portions of mouse EpoR, and the tyrosine effector domains of mouse IL2Rb and IL7R receptors were used. The following inducible chimeric cytokine receptors were tested in this study:

a. CD8 SS-Myc-FKBP(F36V)-muEpoR(236-337;L264G,L265P)-mulL2Rb(337-539) (SEQ ID NO 12)
b. CD8 SS-Myc-FKBP(F36V)-muEpoR(236-337;L264G,L265P)-mulL7R(316-459) (SEQ ID NO 13)

[0410] Vectors encoding the inducible chimeric cytokine receptors were transfected into HEK293T cells along with a luciferase reporter for STAT5, and dimerizer for the indicated pathway was added. Results are summarized in FIG. 6.

[0411] The murine constructs were able to signal (6 h of ligands on transiently transfected HEK293 cells) (FIG. 6).

Example 5A: Inducible chimeric cytokine receptors with improved signaling

[0412] In another study, the EpoR portion of the previous design (FKBP-EpoRm TM-EpoR JAK box-cytotail) was replaced with comparable domains of other homodimeric cytokine receptors. To identify transmembrane domains that exhibit stronger and/or faster signaling, an early time point where the EpoR dimerizer signals poorly (6-8 h, right image) was selected.

[0413] For this study, several tyrosine kinase activating domains were compared using a otherwise identical inducible cytokine receptor design. The tyrosine effector domain consists of a STAT5-activating sequence from IL7R fused to a STAT4-activating sequence from IL12Rb2. Each construct contains a membrane-targeting motif (CD8 SS), a dimerization domain (FKBP(F36V)), a tyrosine kinase activating domain derived from either the EpoR, GP130, PrlR, GHR, GCSFR, or TPOR/MPLR receptors, and a tyrosine effector domain consisting of the IL7R(316-459) cytotail fused to the IL12Rb2(775-825) peptide. Chimeric cytokine receptors also include an epitope tag for detection (Myc). The following inducible chimeric cytokine receptors were tested in this study:

a. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 14)
b. CD8 SS-Myc-FKBP(F36V)-GP130(609-700)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 15)
c. CD8 SS-Myc-FKBP(F36V)-PrlR(221-319)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 16)
d. CD8 SS-Myc-FKBP(F36V)-GHR(251-352)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 17)
e. CD8 SS-Myc-FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 18)
f. CD8 SS-Myc-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 19)

[0414] HEK293 cells were transfected with constructs encoding the above inducible chimeric cytokine receptors, and a luciferase reporter for either STAT4 or STAT5. The luciferase reporters (Promega) encoded a luciferase under the control of either a STAT4 or STAT5 responsive element. As HEK293 cells lack STAT4, in wells transfected with the STAT4 reporter, a plasmid encoding constiutively-expressed STAT4 was transfected

as well added. Transfected EpoR, GHR, and IL12Rb1+IL12Rb2 (the IL12 receptor) were used as positive controls. Results are summarized in FIGS. 7, 8, 9, and 10A. The ligand added to inducible chimeric cytokine receptors was AP1903. Epo was added to EpoR transfected cells, Growth Hormone to GHR transfected cells, and IL-12 to IL12 receptor transfected cells

[0415] The tyrosine kinase activating domain with EpoR components was the weakest signaling construct (FIG. 7). The greatest fold induction of both STAT5 and STAT4 was achieved by a TPOR/MPLR-based dimerizer: CD8 SS-Myc-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 19) (FIG. 7).

[0416] The EpoR-based cytokine receptor (CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 14)) demonstrated the lowest basal signaling (essentially equivalent to reporter alone). The GCSFR construct (CD8 SS-Myc-FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825) (SEQ ID NO 18)) had the strongest signaling for STAT4 (FIG. 9) but had basal signaling.

Example 5B: Optimizing potency of signaling output by modulating ectodomain affinity

[0417] To determine if the responsiveness/sensitivity of the inducible chimeric cytokine receptor may be tuned by modulating the affinity of the ectodomain to its ligand, we generated FKBP switches that signaled through the same JAK-binding domains and cytotails, but with FKBP ectodomain variants that had reduced affinities to AP1903.

[0418] A HEK293T cell reporter assay was used to test how ectodomain affinity affected the responsiveness of cytokine signaling. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. An chimeric cytokine receptor (2.5 ng), a Stat response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated, or treated with the indicated concentrations of AP1903 (Apex Bio) diluted in serum-free media, and Stat reporter activity was determined 5 hours post-treatment using the Dual-Glo Luciferase Assay System (Promega). Fold induction of Stat reporter activity was

normalized to that of HEK293T cells transfected with all vectors except for the inducible cytokine receptor and that were left untreated. Triplicate wells were set up for each condition.

[0419] Figure 10B shows Stat5 reporter activity of FKBP switch ectodomain variants in response to AP1903. Compared to the high-affinity FKBP(F36V) mutants, other FKBP variants that weakened the affinity of FKBP for AP1903 also increased the EC50 for Stat5 induction.

Example 5C: An alternative approach for engineering chimeric cytokine receptors with improved signaling capabilities

[0420] Traditional approaches of designing chimeric cytokine receptors involve fusing the extracellular ligand-binding domain of one receptor to the transmembrane and intracellular signaling domains of a second receptor (Mol Ther. 2014 Jun;22(6):1211-1220; Mol Ther. 2017 Jan 4; 25(1): 249–258; Nat Commun. 2018 May 23;9(1):2034.). We devised an alternative approach, in which we leverage the transmembrane and JAK-binding domains derived from certain cytokine receptors that (i) signal as homodimers in their natural form and (ii) retain the ability to signal well as a chimera when coupled to a different ectodomain (i.e. those described in Figure 7). In our approach, the transmembrane and intracellular JAK-binding domain of one receptor is fused to the "cytotail" (i.e. the region after the JAK-binding domain) of a second receptor.

[0421] In Figure 7, the TpoR TM and JAK binding domain generated the strongest signal-to-noise output. Therefore, we generated TpoR-based cytokine receptor chimeras using the traditional approach by fusing the extracellular domain of TpoR (TpoR/MPLR(1-478)) to the transmembrane and intracellular domain of a different cytokine receptor. We also generated analogous chimeras using our approach by fusing the region including the TpoR transmembrane and JAK2-binding domains (i.e. TpoR(478-582)), before fusion with the cytotails of a different cytokine receptor. As a positive control, we used a vector that encodes the full-length (FL) TpoR.

[0422] A HEK293T cell reporter assay was used to test the inducibility and magnitude of cytokine signaling. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. An chimeric cytokine receptor (2.5 ng), a Stat response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were

mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated, treated with 100 ng/ml TPO, or with 10 ug/mL AP1903 (Apex Bio) diluted in serum-free media. Fold induction of Stat reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the inducible cytokine receptor and that were left untreated. Triplicate wells were set up for each condition.

[0423] Figures 10C and 10D show a schematic comparing and contrasting the traditional approach of chimeric cytokine receptor engineering against ours. While the traditional approach (FIG. 10C) fuses only the ectodomain of Receptor A to the transmembrane domain, JAK-binding domain and cytotail of Receptor B, our approach (FIG. 10D) fuses the ectodomain, transmembrane domain and JAK-binding domain of Receptor A to the cytotail of Receptor B.

[0424] Figure 10E shows a schematic of the chimeric receptors tested in Figure 10F.

[0425] Figure 10F shows a heatmap summarizing results from the Stat reporter assay. Each row represents the respective fusion partner; each column represents the respective Stat-responsive Firefly Luciferase reporter. Each box depicts a fold induction, each column is normalized to the highest fold induction of the respective Stat reporter: 2.75 fold for STAT1, 13.5 fold for STAT1/2, 354 fold for STAT3, 38 fold for STAT4, 173 fold for STAT5, and 10.5 fold for STAT6. Compared to chimeric cytokine receptors based on the traditional design, those engineered using our approach showed a greater magnitude of downstream signaling in response to the inducer AP1903.

Example 6: Inducible chimeric cytokine receptors

[0426] This example illustrates inducible chimeric cytokine receptors with improved and specialized functions.

[0427] In some embodiments, cytokine tails can be linked in tandem to stimulate multiple pathways (e.g., the IL7R(316-459)-IL12Rb2(775-825) fragment fusion for pro-persistence STAT5 and pro-inflammatory STAT4). That is, in this embodiment, cytokine tails from at least two receptors were used. In some other embodiments, a cytokine tail from a single receptor was used.

Minimal Tyrosine Effector Domains with STAT5 or AP-1 outputs

[0428] For each cytotail, small tyrosine peptides are responsible for a signaling pathway. Relevant motifs were identified to develop substantially smaller constructs with improved signaling. For example, a IL12Rb2(775-825)peptide containing Y800 was determined to be sufficient to provide STAT4 signaling when used as a tyrosine effector domain (see Examples 3 and 5).

[0429] In this study, IL2Rb, IL7R, and EGFR cytotails were analyzed to identify tyrosines sufficient for key aspects of signaling. For instance, a segment of IL2Rb containing the STAT5-interacting tyrosines Y418 and Y436 might retain STAT5 signaling, but may lose PI3K signaling as this requires Y364 of the IL2Rb cytotail. Inducible chimeric cytokine receptors comprising the IL7R, IL2Rb, and IFNAR2 tails may include one or more tyrosine motifs within the cytotails. Elimination of one or more portions of the tail (e.g., the IL12Rb2 tail) in some cases results in removal of negative regulatory motifs and stronger signaling.

[0430] In this study, signaling by a variety of IL7Ra and IL2Rb derived fragments using the EpoR-based tyrosine kinase activating domain were tested. The following inducible chimeric cytokine receptors were tested in this study:

a. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459) (SEQ ID NO 6)
b. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416) (SEQ ID NO 20)
c. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(424-459) (SEQ ID NO 21)
d. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459) (SEQ ID NO 22)
e. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(424-459;Y456F) (SEQ ID NO 23)
f. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459;Y456F) (SEQ ID NO 24)
g. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551) (SEQ ID NO 5)
h. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(393-433) (SEQ ID NO 25)

i. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(518-551) (SEQ ID NO 26)
j. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433) (SEQ ID NO 27)
k. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,518-551) (SEQ ID NO 28)
l. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(393-433,518-551) (SEQ ID NO 29)
m. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433,518-551) (SEQ ID NO 30)

[0431] IFNAR2 constructs were tested but did not initiate substantial signals with short (8 h) AP1903 treatment using the CD8 SS membrane-targeting motif, the FKBP(F36V) dimerization domain and the EpoR(237-339;L241G,L242P) tyrosine kinase activating domain. Constructs that are plotted include tyrosine effector domains derived from the IL7R and IL2Rb cytotails.

[0432] IL7 signaling through STAT5 was fully recreated by two fragments containing Y401 and Y449 but without the negative regulatory Y456 (IL7R(376-416,424-459;Y456F); SEQ ID NO: 24; FIG. 11). IL2 STAT5 signaling was recreated by two fragments containing Y364, Y418, and Y436, but far greater signaling was observed with a smaller construct lacking Y364 (IL2Rb(393-433,518-551); SEQ ID NO: 29; FIG. 11). Y364 is reported to activate PI3K, which promotes T cell differentiation and proliferation and re-organizes the actin skeleton to promote receptor internalization. Thus Y364 is both a negative regulatory motif for STAT5 signaling, and the key positive regulatory motif for PI3K/AKT/TORC axis. Depending on the desired functional output, Y364 can be included or excluded.

Non-cytokine receptors

[0433] Upon TCR activation, Ca+ mobilization leads to activation of NFAT and upregulation of pro-inflammatory targets (IL2, GzmB, etc.). Many of these promoters are activated not by NFAT alone but rather a heterotrimer of NFAT with AP-1 (coiled-coil of Fos and Jun) (FIG. 12). Exhaustion occurs with excessive antigen stimulation, and is thought to occur when the amount of activated NFAT supercedes the amount of AP-1 resulting in NFAT homo-dimers and activation of different promoters. One way to

prevent exhaustion would be to increase the amount of AP-1 (Fos/Jun) (FIG. 13). Cytokine receptors such as IL2R and IL7R activate JNK (Jun Kinases) that phosphorylate and activate c-Jun. However, this alone is insufficient to upregulate AP-1 as Fos must also be upregulated and phosphorylated. The parallel MEK/ERK pathway leads to upregulation of Fos through Myc/Max, as well as direct phosphorylation of Fos.

[0434] AP-1 is induced by coordinated JNK and ERK signaling. In some embodiments, inducible chimeric cytokine receptors capable of activating JNK and/or MEK/ERK are provided herein. In some embodiments, an inducible chimeric cytokine receptor can potently induce AP-1 to prevent exhaustion.

[0435] Constructs encoding the following inducible chimeric cytokine receptors were tested for activity. Each construct contains of a membrane-targeting motif (CD8 SS), a dimerization domain (FKBP(F36V)), a tyrosine kinase activating domain (EpoR(237-338;L241G,L242P)), and a tyrosine effector domain derived from the cytotail of the RTK EGFR or a cytokine receptor. Chimeric cytokine receptors also include an epitope tag for detection (Myc):

a. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1186) (SEQ ID NO 31)
b. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1044,1058-1186;Y974F) (SEQ ID NO 32)
c. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1009;Y974F) (SEQ ID NO 33)
d.
e. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1019-1085) (SEQ ID NO 34)
f. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1037-1044,1058-1103;Y1068/1101F) (SEQ ID NO 35)
g. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1066-1118;Y1068/1086F) (SEQ ID NO 36)
h. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1122-1165) (SEQ ID NO 37)
i. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1133-1186;Y1148F) (SEQ ID NO 38)
j. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551) (SEQ ID NO 5)

k. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459) (SEQ ID NO 6)
l. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862) (SEQ ID NO 7)
m. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538) (SEQ ID NO 9)
n. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515) (SEQ ID NO 410)

[0436] HEK293 cells were transiently transfected with the above constructs a luciferase reporter for the indicated pathway. STAT5 signaling was measured. Results are summarized in FIG. 14. The ligand for all chimeric antigen receptors is AP1903. The darkest boxes represent induction >10 fold. FLT ligand was added to transfected Flt3 receptor tyrosine kinase. Transfected Flt3 receptor was used as a control instead of EGFR as HEK293 cells express endogenous EGFR receptor.

Receptors that activate PLC->NFkB

[0437] One drawback of allogeneic CAR-T cells is that the TCR knockout or knockdown (to prevent GvHD) results in a loss of basal TCR signaling. Basal TCR signaling increases TCR persistence. Although cytokines can increase persistence through STAT5, this does not replicate TCR exactly. The TCR mobilizes Ca^{2+} to activate PLC leading to NFAT and NFkB.

[0438] The small molecule inducible chimeric cytokine receptors provided herein have been engineered to mobilize calcium and activate NFAT and NFkB.

[0439] The B cell receptor activates Bruton's Tyrosine Kinase (BTK) that then activates PLCy2->PKC->NFAT and NFkB. In this context, BTK recognizes targets through tyrosines on the tyrosine kinase adaptor protein BLNK (FIG. 15).

[0440] Inducible chimeric cytokine receptors comprising a BLNK fusion with the tyrosine kinase activating domain substituting for the endogenous BLNK-phosphorylating kinase BTK (e.g. "CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-XYZ Cytotail") were generated (SEQ ID NOS: 39, 40, and 41). In some embodiments, the inducible chimeric cytokine receptor comprises tandem tyrosine effector domains such as a cytokine receptor cytotail and a tyrosine kinase adaptor protein.

Example 7: Effect of dimerization of inducible chimeric cytokine receptors on CAR-T cell persistence as compared to GoCART

[0441] In this study, lentiviral (pLVX) constructs were generated comprising an SFFV promoter followed by a kozak sequence, the inducible chimeric cytokine receptor, a T2A sequence, and a chimeric antigen receptor. The chimeric antigen receptor was directed towards cells expressing EGFRvIII. For comparison, lentiviral constructs with either TagBFP or GoCART instead of the inducible chimeric cytokine receptor were used. GoCART consists of a myristoylation sequence followed by a portion of MyD88 and CD40 fused to two repeats of FKBP(F36V).

[0442] CD3+ T cells were isolated from human peripheral blood mononuclear cells and cultured with IL-2. The T cells were transduced with lentivirus 2 days after isolation, and 3 days later were FACS sorted by binding APC-labeled EGFRvIII. The sorted EGFRvIII+ cells were cultured until 14 days post isolation.

[0443] At day 14, the 0.5e6 cells were resuspended in a 24-well plate, and grown with either IL2, AP1903, or no treatment for 8 days post production. Live cell count results are summarized in FIG. 16 and FIG. 17.

[0444] Several constructs comprising AP1903 inducible receptors promoted slight growth (e.g. CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551) (SEQ ID NO 5), and GoCART (a previously reported multimerizer, Myristoyl- Myd88-CD40-FKBP(F36V)x2, but only the CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-469) (SEQ NO 6) promoted robust growth (FIG. 16). The IL7R(316-469) cytotail containing receptor and GoCART tails maintain a higher viability with AP1903 comparable to IL2 treatment (FIG. 17).

[0445] At day 8 post production growth with AP1903 or IL2, cells were phenotyped. Results are summarized in FIG. 18 and FIG. 19. Inducible IL7R(316-469) containing receptor demonstrate more stem cell memory whereas the GoCART demonstrated less stem cell memory and more effector memory. Viability of all cells appeared comparable when grown further with IL2; however, the GoCART appeared somewhat more differentiated. The results demonstrate that the small molecule inducible IL7R(316-469) receptor promotes proliferation while preserving a less differentiated state.

[0446] Cytokines were measured on day 2 and day 8. AP1903 data is shown FIG. 20 and FIG. 21. All values were normalized to untreated TagBFP-expressing CAR-T Cells. As GoCART activates the NFkB pathway, this results in robust cytokine release whereas the others do not. The IFN-related tails do incur some cytokine release.

[0447] Without signaling, all constructs provide comparable growth (~ a doubling over a week), with some less growth of cells comprising an inducible chimeric cytokine receptors with the IFNAR2 tail (FIG. 22).

[0448] Induction of cytokines at day 2 and 8 post production without any treatment was measured. Results are summarized in FIG. 23 and FIG. 24. CAR-T cells expressing a small molecule inducible IFNAR2(310-515) construct constitutively release small amounts of IL5 while the CAR-T cells expressing a small molecule inducible IL2Rb(333-551) construct release IL13 and some TNFa (day 2, FIG. 23) that diminishes by day 8 (day 8, FIG. 24). GoCART expressing cells GM-CSF, IL5, IL13, IL22, and MIP1a at day 2 and more so at day 8 time points. The results demonstrate the IFNAR2(310-515) and IL2Rb(333-551) tails are mildly autoactivating while GoCART is strongly so. No cytokine release was observed from the IL7R(316-459) tail construct, and minimal cytokine release was observed for all inducible chimeric cytokine receptor constructs in the absence of small molecule activation.

[0449] FIG. 25 shows a graph summarizing CAR-T cell counts on post-production day 5 and day 8 for CAR T cells transduced with inducible chimeric cytokine receptors having different tails, GoCART, a inducible cytokine receptor with no JAK2 binding motif or tyrosine effector domain (CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P), or TagBFP. The least growth was observed for the IFNAR2 tail; from Day 8 cytokine measurements, it was observed these CAR T cells did not consume as much IL-2.

[0450] The AP1903 inducible cytokine receptor provided herein is a robust platform for instigating IFN, IL2, IL7, IL12, IL21, EGFR, and other tyrosine kinase-based signaling in CAR-T cells. EpoR recruits a kinase that is activated upon homodimerization (JAK2) and phosphorylates signaling effectors entirely dependent on the attached cytotail. Depending on the desired function in a CAR-T cell, engineered cytotails (e.g., IL7 cytotail fused with IL12Rb2(775-825) or EGFR cytotail portions) can be utilized to achieve the desired effect. The signal strength of the system can also be tuned using different tyrosine kinase activating domains. For example, the signal strength can be tuned using tyrosine kinase activating domains comprising different transmembrane variants as described herein.

[0451] The IL7(316-450) tyrosine effector domain provides STAT5 signaling with minimal PI3K that is sufficient to promote growth without driving differentiation or cytokine release. In addition, the IL7 tail is also less internalized and degraded.

Example 8: Engineering inducible cytokine receptors with multiple outputs

[0452] A HEK293T cell reporter assay was used to test the inducibility and magnitude of cytokine signaling. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. An inducible cytokine receptor (2.5 ng), a Stat response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated, or treated with 1 ug/mL AP1903 (Apex Bio) diluted in serum-free media. Fold induction of Stat5 reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the inducible cytokine receptor and that were left untreated.

[0453] Figure 26 shows a schematic example of inducible cytokine receptors with dual IL-7R and IL-21R outputs. As cytokines often have synergistic effects on enhancing T cell responses (e.g. IL-7 with IL-21; IL-2 with IL-21), the ability to mimic multiple cytokine signaling outputs may be beneficial. To generate multiple cytokine signaling outputs, two cytotails were joined in tandem at the intracellular C-terminus of the chimeric receptor.

[0454] When generating multiple outputs, the proximity of individual cytotails to the cell membrane can influence the strength of their respective signaling outputs. Table 5 below shows examples of inducible cytokine receptors with the dual outputs, where each output was placed either proximal or distal to the cell membrane.

[0455] Figure 27 shows a luciferase assay readout for Stat reporter activity in HEK293T cells. The membrane-distal placement of IL-21R cytotail resulted in greater Stat5 (Figure 27a) and Stat3 (Figure 27b) reporter activity. Therefore, maximal signaling strengths of different cytotails can additionally be tuned by their relative placements to the cell membrane.

[0456] To evaluate these dual output inducible cytokine receptors in the context of primary human CAR T cells, inducible cytokine receptors were cloned into a lentiviral vector encoding the EGFRvIII-specific CAR (2173 scFv; described in Sci Transl Med. 2015 Feb 18; 7(275): 275ra22.) to allow stoichiometric co-expression. To facilitate the detection of transduced cells, a v5 epitope tag (KPIPNPLLGLDST) was inserted between the scFv and CD8 hinge domain. To make lentivirus encoding FKBP switch

CARs, HEK293T cells were plated at 0.45 million cells per mL in 2mL of DMEM (Gibco) supplemented with 10% FBS (Hyclone) per well of a 6-well plate on Day -1. On Day 0, the lentivirus was prepared by mixing together lentiviral packaging vectors 1.5 ug psPAX2, 0.5 ug pMD2G, and 0.5 ug of the appropriate transfer CAR vector in 250 uL Opti-MEM (Gibco) per well of the 6-well plate ("DNA mix"). 10 uL Lipofectamine 2000 (Invitrogen) in 250 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 500 uL was slowly added to the sides of the wells containing HEK293T. On Day 0, purified T cells were activated in X-Vivo-15 medium (Lonza) supplemented with 100 IU/mL human IL-2 (Miltenyi Biotec), 10% FBS (Hyclone), and human T TransAct (Miltenyi Biotec, Cat# 130-111-160, 1:100 dilution) in a Grex-24 plate (Wilson Wolf, cat# 80192M). On Day 1, the media from each well of HEK293T cells in the 6-well plate was replaced with 2mL per well of T cell transduction media, i.e., X-Vivo-15 supplemented with 10% FBS. On Day 2, T cells were resuspended at 0.5 million cells per mL in 1 mL of T cell transduction media per well of a Grex-24 plate. The lentiviral supernatants from HEK293T cells were harvested and passed through a 0.45 micron filter (EMD Millipore) to remove cell debris, and then added to the T cells along with 100 IU/mL human IL-2. On Day 5, 4.5 mL of T cell expansion media, i.e., X-Vivo-15 supplemented with 5% human AB serum (Gemini Bio) and 100 IU/mL human IL-2 was added to each well of a Grex-24 plate. Cells were expanded into larger G-Rex vessels (Wilson Wolf) as needed using T cell expansion media. On Day 13 or 14, transduction efficiency was determined by detecting the percentage of T cells that bound a FITC-conjugated v5 tag monoclonal antibody (Thermo Fisher) using flow cytometry. On Day 14 or 15, the CAR-T cell products were cryopreserved and thawed as needed for further assays.

[0457] To determine the percentage of T cells that were successfully transduced, T cells were first incubated with FITC-conjugated v5 tag monoclonal antibody (Thermo Fisher) in PBS+1%BSA for 20 minutes at 4C. Then cells were washed with PBS+1%BSA, and analyzed using flow cytometry.

[0458] Figure 28A shows a schematic for the FKBP switch CAR vector containing the cytotails indicated in Figures 28B and 28C.

[0459] Figure 28B shows transduction efficiencies of FKBP switch CAR T cells as determined by v5 tag staining.

[0460] To determine the inducibility and magnitude of cytokine signaling in FKBP switch CAR T cells, the thawed CAR T cell product was serum starved in 100 uL serum-free RPMI (Corning) for 4 hours in humidified incubator at 37°C with 5% CO2, then treated with 1 ug/ml AP1903 for 1 hour. 40 minutes into AP1903 treatment, an antibody cocktail comprising BUV395-conjugated anti-human CD3 (Biolegend) and FITC-conjugated v5 tag monoclonal antibody (Thermo Fisher) were added to the cells and allowed to incubate for the final 20 minutes. After 1 hour of AP1903 treatment, cells were fixed by the addition of 35 uL of 16% paraformaldehyde was added to each 100 uL sample and allowed to incubate for 15 minutes at 37°C. Cells were then washed three times with PBS, and permeabilized in 100% cold methanol for 1 or 2 nights at -20°C. On the day of FACS analysis, cells were washed three times with PBS, Fc-blocked, and stained with AlexaFluor647-conjugated anti-mouse/human Stat5 (pY694) (BD Biosciences) diluted in PBS+1%BSA. After a 1 hour incubation at room temperature in the dark, cells were washed three times before FACS analysis.

[0461] Figure 28C, bottom-left shows AP1903-induced pStat5 staining by FACS analysis. Consistent with the HEK293T reporter assay, results in primary human CAR T cells revealed that membrane-distal IL-21R cytotail resulted in greater pStat5 induction.

Table 5: Examples of inducible cytokine receptors with dual outputs

Dual output cytotails	Membrane proximal	Membrane distal
IL2Rbsmall(393-433,518-551)/ IL21R(322-538)	IL2Rbsmall(393-433,518-551)	IL21R(322-538)
IL21R(322-538)/ IL2Rbsmall(393-433,518-551)	IL21R(322-538)	IL2Rbsmall(393-433,518-551)
IL2Rbsmall(339-379,393-433,518-551)/IL21R(322-538)	IL2Rbsmall(339-379,393-433,518-551)	IL21R(322-538)
IL21R(322-538)/ IL2Rbsmall(339-379,393-433,518-551)	IL21R(322-538)	IL2Rbsmall(339-379,393-433,518-551)
IL7R (316-459)/IL21R(322-538)	IL7R (316-459)	IL21R(322-538)
IL21R(322-538)/IL7R (316-459)	IL21R(322-538)	IL7R (316-459)

Example 9: The FKBP switch permits tunable cytokine signaling in CAR T cells

[0462] To determine the tunability of cytokine signaling in FKBP switch CAR T cells in response to AP1903, FKBP switch CAR T cells bearing an IL-7R(316-459) cytotail was serum starved in 100 uL serum-free RPMI (Corning) for 4 hours in humidified incubator at 37°C with 5% CO2, then treated with the indicated working concentrations of AP1903 for 1 hour. 40 minutes into AP1903 treatment, an antibody cocktail comprising BUV395-conjugated anti-human CD3 (Biolegend) and FITC-conjugated v5 tag monoclonal antibody (Thermo Fisher) were added to the cells and allowed to incubate for the final 20 minutes. After 1 hour of AP1903 treatment, cells were fixed by the addition of 35 uL of 16% paraformaldehyde was added to each 100 uL sample and allowed to incubate for 15 minutes at 37°C. Cells were then washed three times with PBS, and permeabilized in 100% cold methanol for 1 or 2 nights at -20°C. On the day of FACS analysis, cells were washed three times with PBS, Fc-blocked, and stained with AlexaFluor647-conjugated anti-mouse/human Stat5 (pY694) (BD Biosciences) diluted in PBS+1%BSA. After a 1 hour incubation at room temperature in the dark, cells were washed three times before FACS analysis.

[0463] Figure 29 shows Stat5 activation in FKBP switch CAR+ T cells increases with AP1903 in a dose-dependent fashion. In addition, cytokine signaling was FKBP switch CAR+ T cell-specific, as pStat5 was induced specifically in FKBP switch CAR+ T cells – but not CAR- T cells in the same culture. This suggests that the FKBP switch delivers cytokine signals specifically to therapeutic CAR+ T cells, while (i) preventing bystander immune activation that would accelerate allogeneic CAR T cell rejection and (ii) avoiding the toxicities associated with systemic cytokine administration.

Example 10: AP1903-induced activation of the FKBP switch enhances the anti-tumor activity of CAR T cells

[0464] WM266.4 and DMS 273 cells are DLL3+ target cell lines that were purchased from Sigma. To facilitate target cell imaging via the IncuCyte Live Cell Analysis Imaging System, WM266.4 and DMS 273 cells were stably labelled with nuclear GFP by lentiviral transduction with IncuCyte NucLight Green Lentivirus Reagent (Sartorius) to generate WM266.4-nucGFP and DMS 273-nucGFP, respectively. The FKBP switch was cloned into a DLL3 CAR (26C8 scFv) to allow for stoichiometric co-expression.

[0465] To test whether FKBP switch CAR T cells showed enhanced target cell lysis and potency following repeated exposure to target cells in the presence of AP1903, we

utilized an in vitro serial killing assay in which a low number of CAR-T cells were co-cultured with an excess of targets. These harsh conditions necessitated that single CAR-T cells lysed multiple target cells serially; in turn, CAR-T cells would undergo proliferation and eventually, differentiation and exhaustion. 5,000 WM266.4-nucGFP target cells were seeded and allowed to attach in 96-well plates with black walls and flat clear bottom in 50 uL RPMI containing 10% FBS (Hyclone), non-essential amino acids, sodium pyruvate and 20-25 mM HEPES. DLL3 CAR T cells bearing an FKBP switch, or control CAR T cells were thawed and added to plated target cells at an Effector:Target (E:T) ratio of 1:9.

[0466] Figure 30A shows the schematic of the a DLL3 CAR bearing an FKBP switch with dual outputs (IL7Ra(316-459)/IL12Rb2(775-825) cytotails) that was used.

[0467] Figure 30B and Figure 30C show in vitro cytotoxicity of DLL3 CAR T cells against DLL3+ target cells. While control CAR T cells lacking the FKBP switch failed to effectively lyse target cells at this low, sub-optimal E:T ratio (Figure 30B), AP1903-induced activation of the FKBP switch dramatically enhanced CAR T cell cytotoxicity (Figure 30C). Therefore, AP1903 enhances the potency of FKBP switch CAR T cells.

[0468] A challenge in CAR T cell therapy is the low expression levels of tumor targets, which results in sub-optimal CAR activation and cytotoxicity. To test whether FKBP switch activation enhanced CAR T cells' sensitivity to low target-expressing cells, we utilized the DMS 273-nucGFP target cell line that has a low DLL3 surface expression (400 DLL3/cell). 5,000 DMS 273-nucGFP target cells were seeded and allowed to attach in 96-well plates with black walls and flat clear bottom in 50 uL RPMI containing 10% FBS (Hyclone), non-essential amino acids, sodium pyruvate and 20-25 mM HEPES. DLL3 CAR T cells bearing an FKBP switch, or control CAR T cells were thawed and added to plated target cells at an Effector:Target (E:T) ratio of 1:1.

[0469] Figure 30D and Figure 30E show in vitro cytotoxicity of DLL3 CAR T cells against target cells expressing low levels of DLL3. Figure 30D show that control CAR T cells were ineffective even at a higher E:T ratio of 1:1. In contrast, Figure 30E shows that FKBP switch activation enhanced the cytotoxicity of CAR T cells and increased their sensitivity towards low target-expressing cells.

[0470] We next interrogated the activity of FKBP switch CAR T cells in vivo using a human tumor xenograft model. LN229-EGFRvIII was derived from the human glioblastoma cell line, LN229 (ATCC), by stable transduction with full-length human EGFRvIII. 3 million LN229-EGFRvIII cells in 200 uL serum-free RPMI were implanted

subcutaneously into NSG mice. Tumor growth was monitored by caliper measurements using a digital caliper starting from Day 21 post-implantation. Tumor size was calculated using the formula Tumor volume = (width^2 x length/2). Mice were randomized into groups of 8 based on tumor volume on Day 24 post-implantation, and the average tumor volume per group was 200 mm3. On Day 25 post-implantation, Non-transduced T cells (NTD), control CAR T cells and FKBP switch CAR-T cells bearing IL7Ra(316-459)/IL12Rb2(775-825) cytotails were thawed and counted according to standard procedure. Cells were resuspended in serum-free RPMI and 3 million CAR+ cells/mouse were injected intravenously in a volume of 100 uL/mouse. The day after T cell infusion, and weekly thereafter, each group also received intraperitoneal infusions of either 5 mg/kg AP1903 or vehicle control (n=8 per group). Tumors were then monitored every 3-4 days until the end of the study.

[0471] Figures 31A-31H show the tumor progression and overall survival in each group of treated mice. As compared to control CAR T cells and to FKBP switch CAR T cells coadministered with vehicle control, the activation of the FKBP switch by AP1903 resulted in significantly enhanced tumor control (Figure 31A), allowed for a more durable and complete anti-tumor response (Figures 31B-31G) and prolonged overall survival (Figure 31H).

Example 11: AP1903-induced activation of the FKBP switch enhances the expansion and engraftment of CAR T cells

[0472] Clinical trials revealed that patient response to CD19 CAR T cell therapy correlates with high serum levels of homeostatic cytokines (e.g. IL-15) that were critical for driving an initial burst of CAR T cell expansion and engraftment (J Clin Oncol. 2017 Jun 1;35(16):1803-1813.). Moreover, unlike in hematological malignancies where target cells in the circulation are readily accessible to CAR T cells, the treatment of solid tumors would likely require CAR T cells to spend a longer time in circulation before extravasating and infiltrating the solid tumor; therefore, target-independent, cytokine-supported CAR T cell expansion and survival would be especially crucial. We thus investigated whether AP1903 alone was sufficient to drive target-independent CAR T cell expansion and persistence.

[0473] Control CAR T cells or FKBP switch CAR T cells bearing IL7R(316-459)/IL12Rb2(775-825) cytotails were cultured with the indicated concentrations of AP1903, and in the absence of exogenous cytokines (unless specified in the case of

positive controls) or target cells for 2 weeks. As a positive control, CAR T cells were alternatively supplemented with exogenous recombinant IL-7 (10 ng/mL; Miltenyi) and IL-12p70 (10 ng/mL; Biolegend) to mimic the dual IL-7R/IL12Rb2 outputs transmitted by FKBP switch activation. At the end of the 2-week culture, the number and quality of surviving CAR T cells were determined. Briefly, duplicate samples from each culture condition cells were harvested and stained using the Zombie NIR Fixable Viability Kit (Biolegend). Samples were washed with PBS, Fc blocked, then stained with the following antibody cocktail diluted in PBS+1%BSA: BUV395-conjugated anti-human CD3, BV510-conjugated anti-human CD8, BV605-conjugated human CD4 and FITC-conjugated v5 tag (for CAR detection), PE/Cy7-conjugated anti-human CD62L (Biolegend) and BV785-conjugated anti-human CD45RO (Biolegend). Finally, samples were washed in PBS and cell pellets were resuspended in 130 uL PBS+1%BSA containing 123count eBeads counting beads (Thermo Fisher) (10 uL counting beads in 120 uL PBS+1%BSA) prior to FACS analysis.

[0474] Figure 32A shows AP1903-driven expansion of CAR T cells; the dotted line indicates fold expansion of CAR T cells supplemented with exogenous IL7 and IL12p70. In contrast to control CAR T cells lacking the FKBP switch that declined, FKBP switch CAR T cells treated with AP1903 efficiently expanded. Notably, as low as 1 ng/ml AP1903 was sufficient to reach the level of expansion achieved by exogenous cytokine supplementation.

[0475] Figure 32B shows the absolute number and memory T cell phenotypes of the surviving CAR T cells at the end of the 2-week culture. In addition to increasing the quantity of CAR T cells, FKBP switch activation also improved the quality of CAR T cells, as evident by the maintenance and expansion of the stem cell memory (Tscm) and central memory (Tcm) CAR+ T cells, which are the long-lived, self-renewing populations that mediate long-lasting anti-tumor protection.

Example 12: Engineering inducible cytokine receptors with reduced basal signaling

[0476] In the presence of ligand, homodimeric cytokine/growth factor receptors (e.g. EpoR and TpoR) in their natural forms rely on two requirements for JAK2 activation: (i) receptor homodimerization and (ii) receptor rotation mediated by the transmembrane region that brings the two JAK2's in close enough proximity for trans-phosphorylation and activation. It has been shown that abrogating receptor rotation by mutating key amino acid residues in the transmembrane region abrogates receptor signaling, even in

the presence of ligand. A truly inducible receptor necessitates a clean OFF (no basal activity) in the absence of inducer, and a wide dynamic range of ligand-induced ON for maximal tunability. The tyrosine activation domains from homodimeric cytokine/growth factor receptors demonstrated varying degrees of basal signaling (Figure 9). EpoR and TpoR have been shown to exist in an equilibrium between monomeric and homodimeric forms in the absence of ligand, and this spontaneous homodimerization was found to be mediated by their transmembrane domains; therefore, we hypothesized that the leakiness observed in our untreated chimeric cytokine receptors was due to their spontaneous ligand-independent homodimerization mediated by their transmembrane domains.

[0477] To reduce basal signaling in our chimeric cytokine receptors, we replaced the transmembrane region of EpoR/TpoR with that of PD-1, which exists naturally as a monomer. A HEK293T cell reporter assay was used to evaluate basal signaling in the absence of AP1903, as well as inducibility and magnitude of cytokine signaling in the presence of AP1903. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. An inducible cytokine receptor (2.5 ng), a Stat response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated to assess AP1903-independent basal signaling, or treated with the indicated concentrations of AP1903 (Apex Bio) diluted in serum-free media. Fold induction of Stat5 reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the inducible cytokine receptor and that were left untreated.

[0478] Figure 33A and Figure 33B show basal signaling in the absence of AP1903 by each chimeric receptor, as determined by Stat5 and Stat4 reporter activity, respectively. Compared to the chimeric receptors bearing the TpoR transmembrane region that showed significant basal Stat activity in the absence of AP1903, substitution with the PD-1 transmembrane region abrogated basal Stat activity to levels comparable to a construct containing only the FKBP ectodomain and lacking any JAK-activating domains and cytotails. In some embodiments, basal signaling of an inducible chimeric cytokine

receptor can be further optimized using insertion and/or deletion mutations of transmembrane domains as exemplified in FIG. 38C.

[0479] Figure 33C and Figure 33D shows the response of each chimeric receptor to the indicated concentrations of AP1903, as determined by Stat5 and Stat4 reporter activity, respectively. Compared to their counterparts with the TpoR transmembrane domain, the FKBP switch variant bearing the PD1 transmembrane region responded comparably in magnitude to AP1903 treatment. Although the transmembrane domain is also believed to be critical for rotational activation of the receptor, substituting the TpoR transmembrane region for that of PD-1 preserved AP1903-induced Stat activation. Taken together, we demonstrate that the PD-1 transmembrane region can be used in combination with tyrosine activation domains from homodimeric cytokine/growth factor receptors to reduce basal signaling while preserving ligand-induced receptor activation.

[0480] To test whether substitution with the PD1 transmembrane region preserved the cytotoxic activity of the chimeric receptor, we compared the cytotoxic activity and AP1903-driven expansion of CAR T cells coexpressing either receptor variant. For the in vitro cytotoxicity assay, 5,000 U87KO-EGFRvIII-nucGFP target cells were seeded and allowed to attach in 96-well plates with black walls and flat clear bottom in 50 uL RPMI containing 10% FBS (Hyclone), non-essential amino acids, sodium pyruvate and 20-25 mM HEPES. U87KO-EGFRvIII is a kind gift from Cellectis SA (Paris, France). U87KO-EGFRvIII was derived from the parental cell line, U87MG (ATCC), by first knocking out endogenous wildtype EGFR using Transcription Activator-Like Effector Nucleases (TALEN), and then stably overexpressing full-length human EGFRvIII via lentiviral transduction. To facilitate target cell imaging via the IncuCyte Live Cell Analysis Imaging System, U87KO-EGFRvIII-nucGFP target cells were derived from U87KO-EGFRvIII by a second lentiviral transduction with IncuCyte NucLight Green Lentivirus Reagent (Sartorius). EGFRvIII CAR (2173 scFv) T cells bearing an FKBP switch with either the TpoR or PD1 TM were thawed and added to plated target cells at an Effector:Target (E:T) ratio of 1:4. AP1903 at the indicated concentrations was added to each well. Duplicate wells were set up for each condition

[0481] Figure 34A shows the schematic of FKBP switch CARs bearing IL7R(316-459)/IL12Rb2(775-825) cytotails with either the TpoR TM domain or the PD1 TM domain; CAR T cells coexpressing the FKBP ectodomain (FKBP only control CAR) and without any JAK-activating domain and cytotails were used as a control.

[0482] Figures 34B-34D show that while control CAR T cells were not enhanced by AP1903 treatment, FKBP switches bearing either the TpoR TM domain or the PD1 TM domain were comparably enhanced in the presence of AP1903. Therefore, substitution with the PD1 TM domain can reduce basal FKBP switch activity, while preserving AP1903-inducible switch receptor activation and signaling.

[0483] We next tested whether substitution with the PD1 transmembrane region preserved AP1903-driven expansion of the chimeric receptor. Control CAR T cells or FKBP switch CAR T cells bearing either transmembrane variants were cultured with the indicated concentrations of AP1903, and in the absence of exogenous cytokines (unless specified in the case of positive controls) or target cells for 2 weeks. As a positive control, CAR T cells were alternatively supplemented with exogenous recombinant IL-7 (10 ng/mL; Miltenyi) and IL-12p70 (10 ng/mL; Biolegend) to mimic the dual IL-7R/IL12Rb2 outputs transmitted by FKBP switch activation. At the end of the 2-week culture, the number and quality of surviving CAR T cells were determined. Briefly, duplicate samples from each culture condition cells were harvested and stained using the Zombie NIR Fixable Viability Kit (Biolegend). Samples were washed with PBS, Fc blocked, then stained with the following antibody cocktail diluted in PBS+1%BSA: BUV395-conjugated anti-human CD3, BV510-conjugated anti-human CD8, BV605-conjugated human CD4 and FITC-conjugated v5 tag (for CAR detection), PE/Cy7-conjugated anti-human CD62L (Biolegend) and BV785-conjugated anti-human CD45RO (Biolegend). Finally, samples were washed in PBS and cell pellets were resuspended in 130 uL PBS+1%BSA containing 123count eBeads counting beads (Thermo Fisher) (10 uL counting beads in 120 uL PBS+1%BSA) prior to FACS analysis.

[0484] Figure 34E shows the number of live CAR+ T cells after 2 weeks of culture in the indicated concentrations of AP1903, or in exogenously supplemented IL-7 and IL-12p70. As expected, AP1903 did not support the expansion and survival control CAR T cells, and exogeneous IL7 and IL12p70 supported the expansion and survival of control and FKBP switch CAR T cells. In the presence of AP1903, FKBP switch CAR T cells with the PD1 transmembrane domain expanded equally or better than their counterparts bearing the TpoR transmembrane region.

[0485] Figure 34F shows the number of CAR+ T cells in each memory compartment. Compared to their counterparts bearing the TpoR transmembrane region, FKBP switch CAR T cells with the PD1 transmembrane domain equal or better at maintaining Tscm and Tcm CAR+ cells in response to AP1903. These findings demonstrate that the PD1

transmembrane variant that has reduced basal signaling preserves switch receptor inducibility and functionality in the context of primary human CAR T cells.

Example 13: Improving CAR T cell manufacturing by AP1903-driven CAR T cell expansion

[0486] While lentiviruses have the ability to deliver relatively large cargos, increasing the payload – such as by co-expressing the FKBP switch – inevitably reduces viral titer and subsequent transduction efficiency. Conventional methods of CAR T cell manufacturing entails expanding transduced T cells in the presence of high doses of supplemented cytokines (e.g. IL-2, IL-7 and/or IL-15), which would expand both transduced (CAR+) and untransduced (CAR-) T cells in the same culture. As the activation of the FKBP switch can transmit a cytokine signal capable of driving CAR T cell expansion and enrichment, we leveraged this and hypothesized that substituting AP1903 for supplemented cytokines can overcome low transduction efficiencies during FKBP switch CAR T cell manufacturing.

[0487] On Day 0, Purified T cells were activated in X-Vivo-15 medium (Lonza) supplemented with 100 IU/mL human IL-2 (Miltenyi Biotec), 10% FBS (Hyclone), and human T TransAct (Miltenyi Biotec, Cat# 130-111-160, 1:100 dilution) in a Grex-24 plate (Wilson Wolf, cat# 80192M). On Day 2, T cells were resuspended at 0.5 million cells per mL in 1 mL of T cell transduction media per well of a Grex-24 plate (Wilson Wolf, cat# 80192M). Lentiviral supernatants were made as described above and transduction was performed on Day 2. On Day 5 when transduction was complete, cells were washed to remove residual human IL-2, resuspended in fresh T cell expansion media, i.e., X-Vivo-15 supplemented with 5% human AB serum (Gemini Bio), and expanded in either 20 ng/ml human IL-2, or the indicated concentrations of AP1903, in Grex-24 well plates. Cells were expanded into larger G-Rex vessels (Wilson Wolf) as needed using T cell expansion media. On Days 5, 9 and 15, the enrichment of CAR+ T cells was determined by detecting the percentage of T cells that bound a FITC-conjugated v5 tag monoclonal antibody (Thermo Fisher) using flow cytometry.

[0488] Figure 35A shows a schematic of the control BFP CAR and FKBP switch CARs with various cytotails used. Figures 35B-E show the percentage of CAR+ T cells that were expanded in either IL-2 or AP1903, as determined by FACS analysis on the indicated days. As expected, expansion in 20 ng/ml human IL-2 maintained a stable percentage of CAR+ T cells, due to equivalent expansion of both CAR+ and CAR- T cell

populations within the culture. On the other hand, while AP1903 did not enrich BFP CAR T cells (Figure 35B), the use of AP1903 in place of IL-2 progressively enriched for FKBP switch CAR T cells in a dose-dependent fashion between Days 5 and 14 (Figures 35C-E); Furthermore, effective CAR T cell enrichment could be attained with FKBP switches transmitting various signaling outputs via IL7Ra(316-459)/IL12Rb2(775-825) (Figure 35C), IL2Rb(393-433,518-551)/ IL21R(322-538) (Figure 35D) and IL7Ra(316-459)/IL21R(322-538) (Figure 35E).

Example 14: Inducing cytokine signaling in response to antibodies and other multimerized ligands/inducers

[0489] As dimerization can activate the inducible chimeric cytokine receptor, it is reasonable that with the proper ectodomain, antibodies (or antibody derived molecules), and multimerized ligands/inducers would activate signaling as well.

[0490] To evaluate activation by an antibody, we generated a chimeric cytokine receptor bearing the human OX40(1-214) ectodomain and tested its ability to signal in response to a clinical anti-OX40 antibody (GSK109) in a HEK293T cell-based Stat reporter assay. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. The OX40 ectodomain cytokine receptor (2.5 ng), a Stat response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated, or treated with the anti-OX40 antibody, GSK109, diluted in serum-free media, and Stat reporter activity was determined 5 hours post-treatment using the Dual-Glo Luciferase Assay System (Promega). Fold induction of Stat reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the OX40 ectodomain cytokine receptor and that were left untreated. 4 wells were set up for each condition.

[0491] Figure 36A shows a schematic of a chimeric cytokine receptor bearing an OX40 ectodomain. Figures 36B-36C show the activation of cytokine signaling in response to an antibody. Figure 36B-36C show Stat5 (36B) and Stat4 (36C) reporter activity in the absence and presence of the anti-OX40 antibody, GSK109. Antibody-mediated

dimerization of the OX40 ectodomain induced downstream cytokine signaling, as reflected by an increase in Stat5 and Stat4 reporter activity.

[0492] To test if the panel of ligand inducers and ectodomains can be further extended beyond the AP1903-FKBP(F36V) pairing, we tested signaling in response to other multimeric ligand inducers. As the Tumor Necrosis Family (TNF) superfamily of ligands are trimers, they engage their respective receptors in a multimeric fashion. Therefore, we fused ectodomains derived from the TNFR2 superfamily receptors, such as BCMA(1-54), TACI(1-165) and BAFFR(1-78), to the transmembrane and signaling domains of our chimeric cytokine receptors, and tested signaling in response to soluble trimeric ligand. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. The chimeric cytokine receptor (2.5 ng), a Stat response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated, or treated with soluble BAFF or APRIL trimers diluted in serum-free media, and Stat reporter activity was determined 5 hours post-treatment using the Dual-Glo Luciferase Assay System (Promega). Fold induction of Stat reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the OX40 ectodomain cytokine receptor and that were left untreated. 4 wells were set up for each condition.

[0493] Figure 37A shows a schematic of the various ectodomains derived from the TNFR2 superfamily tested. Figure 37B is a schematic of the interactions between the receptors BCMA, TACI and BAFFR with their ligands BAFF and APRIL (Drug Des Devel Ther. 2015 Jan 7;9:333-47.). Figures 37C-37D show the activation of cytokine signaling in response to multimeric ligand inducers. Figure 37C-37D show Stat5 (37C) and Stat4 (37D) reporter activity in response to soluble BAFF and APRIL trimers. Multimerization of the respective chimeric cytokine receptors by soluble BAFF trimers induced Stat5 and Stat4 activation, and multimerization of the BCMA ectodomain cytokine receptor by soluble APRIL trimers induced downstream Stat activation.

Example 15: Optimizing the signaling strength and sensitivity of the FKBP switch by modifying the TPOR TM helix

[0494] It is well established that the helical transmembrane (TM) region of TpoR is crucial for ligand-induced receptor signaling by controlling JAK2 activation. We hypothesized that in a chimeric cytokine switch where a different ectodomain (e.g. FKBP) is fused with the TpoR TM/JAK2-activating domain, the optimal structural conformation for receptor activation may be perturbed. Leveraging on the importance of the TM region in TpoR activity, we sought to increase the responsiveness of the FKBP switch by modifying the TpoR TM region. To this end, we generated FKBP switch variants with either deletions or insertions in the TpoR TM region and tested them in the HEK293T cell reporter assay.

[0495] Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. An FKBP switch (2.5 ng), a Stat5 response element that drives Firefly Luciferase (100 ng; Promega) and Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM (Gibco) ("DNA mix"). The FKBP switch bearing the wildtype TpoR transmembrane domain was used as the comparator. 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. 24 hours after transfection, cells were either left untreated, or treated with the indicated concentrations of AP1903 (APEX Bio) diluted in serum-free media. 24 hours after treatment, Stat5 reporter activity was evaluated using the Dual-Glo Luciferase Assay System (Promega). Fold induction of Stat5 reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the switch receptor and that were left untreated.

[0496] Figures 38A-38C show the effect of TpoR transmembrane domain modifications on the strength and sensitivity of signaling by the FKBP switch.

[0497] Figures 38A-38B shows the amino acid sequences for the wildtype TpoR and the various TM deletion (Figure 38A) or insertion (Figure 38B) variants.

[0498] Figure 38C shows the response of FKBP switch variants bearing TpoR TM deletions (Figure 38A) and insertions (Figure 38B) in the absence or presence of AP1903. Highlighted with a rectangular box is the FKBP switch bearing the wildtype TpoR TM domain from which TM variants were derived. Compared to the FKBP switch

bearing the wildtype TpoR TM domain (i.e. FKBP switch), TpoR TM deletion variants such as TpoR(478-582;N-3), TpoR(478-582;N-5), TpoR(478-582;N-6) and TpoR(478-582;N-7) increased the strength of AP1903-induced Stat5 activity. Furthermore, several TpoR TM variants also increased the sensitivity in response to very low concentrations of AP1903 (i.e. 1 ng/ml or 0.1 ng/ml), with TpoR(478-582;N-7) and TpoR(478-582;N-9) being the most sensitive. These demonstrate that modulating the TpoR TM region enhanced the responsiveness and sensitivity of the FKBP switch to AP1903.

Example 16: Controlling CAR T cell differentiation via distinct and combinatorial cytotail signal outputs

A. Combining cytotails to activate additive signaling pathways

[0499] Upon TCR activation, Ca+ mobilization leads to activation of NFAT and upregulation of pro-inflammatory targets (IL2, GzmB, etc.). Many of these promoters are activated not by NFAT alone but rather a heterotrimer of NFAT with AP-1 (coiled-coil of Fos and Jun). Exhaustion occurs with excessive antigen stimulation, and is thought to occur when the amount of activated NFAT superceeds the amount of AP-1 resulting in NFAT homo-dimers and activation of different promoters. One way to prevent exhaustion would be to increase the amount of AP-1 (Fos/Jun). Cytokine receptors such as IL2R and IL7R activate JNK (Jun Kinases) that phosphorylate and activate c-Jun. However, this alone is insufficient to upregulate AP-1 as Fos must also be upregulated and phosphorylated. The parallel MEK/ERK pathway leads to upregulation of Fos through Myc/Max, as well as direct phosphorylation of Fos. Thus a hypothetical receptor that activated both JNK and MEK/ERK would lead to gangbuster amounts of AP-1. The EGF receptor (EGFR) is one of the receptor tyrosine kinases well-known to activate the MEK/ERK signaling pathway. By using the EGFR cytotail, we demonstrate the ability to robustly activate Myc/Max, and consequently Fos. By combining the EGFR and IL7R cytotail, we demonstrate the successful induction of both AP-1 and Myc/Max signaling pathways, which prevent the terminal differentiation and exhaustion of CAR T cells.

[0500] To test the signaling pathways activated by different cytotails, we utilized a HEK293T cell reporter assay. Briefly, 20,000 HEK293T cells were plated into each well of a poly-L-lysine-coated 96-well flat-bottom plate and allowed to adhere overnight. An inducible cytokine receptor (2.5 ng), the respective transcription factor response element that drives Firefly Luciferase (100 ng; Promega) and a Renilla Luciferase control reporter vector (1 ng; Promega) were mixed in a final volume of 5 uL in Opti-MEM

(Gibco) ("DNA mix"). 0.3 uL Lipofectamine 2000 (Invitrogen) in 5 uL Opti-MEM was incubated at room temperature for 5 minutes and then added to the DNA mix. The mixture was incubated at room temperature for 20 minutes and the total volume of 10 uL was added to each well containing HEK-293T. As a negative control, the FKBP ectodomain was coupled to the transmembrane and short intracellular region of TpoR(478-528) that lacked the JAK-binding domain and cytotail (i.e. TpoR CTRL). As a comparison, the FKBP ectodomain was coupled to the MyD88/CD40 signaling domains (henceforth referred to as "FKBP-MyD88-CD40"). 24 hours after transfection, cells were either left untreated, or treated with 1 ug/mL AP1903 (Apex Bio) diluted in serum-free media. 6 hours after AP1903 treatment, reporter activity was determined using the Dual-Glo Luciferase Assay System (Promega). Fold induction of Stat5 reporter activity was normalized to that of HEK293T cells transfected with all vectors except for the inducible cytokine receptor and that were left untreated.

[0501] Figure 39A shows a schematic of the chimeric receptors tested.

[0502] Figure 39B shows results of the luciferase assay readout for reporter activity in HEK293T cells using single and combinations of cytotails. Each row represents the respective transcription factor-responsive Firefly Luciferase reporter; each column represents the chimeric receptor bearing the respective cytotail/signaling domains. Each box depicts a fold induction, each row is normalized to the highest fold induction of the respective Firefly Luciferase reporter. As expected, single cytotail outputs activated the desired signaling pathways, with IL7R(316-459) activating Stat5, IL12Rb2small(775-825) activating Stat4, and EGFR(1122-1165) activating the AP-1 and Myc/Max pathways. When individual cytotails that on their own activated distinct signaling pathways were combined, an additive effect ensued – in the presence of AP1903, the IL7R(316-459)/IL12Rb2small(775-825) cytotails induced Stat5 and Stat4 activation, while the IL7R(316-459)/EGFR(1122-1165) cytotails induced Stat5 (albeit to a lower extent), AP-1 and Myc/Max activation. Compared to the inducible nature of FKBP-cytotail receptors, the FKBP-MyD88-CD40 receptor showed high basal signaling in the absence of AP1903.

B. Skewing T cell cytotoxic effector activity and memory differentiation via distinct cytotail outputs

[0503] IL-12 signaling is well-known for promoting T cell cytotoxicity and effector differentiation; on the other hand, Figure Fb suggests that EGFR signaling may prevent

T cell exhaustion and promote memory T cell generation. To test if distinct signaling pathways activated by different cytotails could control CAR T cell effector function and memory differentiation, we co-expressed FKBP switches bearing the same transmembrane and JAK2-binding domain with different cytotails, either singly or doubly in tandem.

[0504] To test whether different cytotail outputs influenced the effector function of CAR T cells, we performed a 4-day in vitro cytotoxicity assay. Briefly, 30,000 U87KO-EGFRvIII-nucRFP target cells were seeded and allowed to attach in 96-well plates with black walls and flat clear bottom in 50 uL RPMI containing 10% FBS (Hyclone), non-essential amino acids, sodium pyruvate and 20-25 mM HEPES. U87KO-EGFRvIII is a kind gift from Cellectis SA (Paris, France). U87KO-EGFRvIII was derived from the parental cell line, U87MG (ATCC), by first knocking out endogenous wildtype EGFR using Transcription Activator-Like Effector Nucleases (TALEN), and then stably overexpressing full-length human EGFRvIII via lentiviral transduction. To facilitate target cell imaging via the IncuCyte Live Cell Analysis Imaging System, U87KO-EGFRvIII-nucRFP target cells were derived from U87KO-EGFRvIII by a second lentiviral transduction with IncuCyte NucLight Red Lentivirus Reagent (Sartorius). EGFRvIII CAR (2173 scFv) T cells bearing an FKBP switch with the respective cytotails were thawed and added to plated target cells at an Effector:Target (E:T) ratio of 1:8. As a comparison, CAR T cells coexpressing FKBP-MyD88-CD40 were included. Wells were either left untreated or treated with 500 ng/ml AP1903 (ApexBio). The number of live target cells at each timepoint was determined by enumerating the number of live nuclearRFP+ cells using the Incucyte Live Cell Analysis Imaging System. Duplicate wells were set up for each condition.

[0505] At the end of the 4-day cytotoxicity assay, plates were spun down and supernatents were collected for the analysis of cytokine release using the MSD assay (Meso Scale Discovery).

[0506] Figures 40A-40F show the results from the in vitro cytotoxicity assay of FKBP switches bearing different cytotails singly or doubly in tandem, in the absence or presence of AP1903.

[0507] Figures 40A-40C show the cytotoxic activity of the stem cell/central memory (Tscm/Tcm) T cell-promoting cytotails tested, i.e. IL7R(316-459) and EGFR(1122-1165). Within the relatively short timeframe of 4 days, the IL7R(316-459) and EGFR(1122-1165) – either singly or combined – did not enhance CAR T cell cytotoxicity in the

presence of AP1903. This may be expected because although T cells of the Tscm/Tcm memory phenotype do self-renew long-term and survive longer, but also exhibit a delay in executing cytotoxic effector functions.

[0508] Figures 40D-40E show the cytotoxic activity of the IL12Rb2small(775-825) cytotail, which mimics IL-12 signaling to promote effector memory/effector (Tem/Temra) T cell differentiation. The IL12Rb2small(775-825) cytotail – either alone or when combined with IL7R(316-459) – enhances CAR T cell cytotoxic potency in the presence of AP1903.

[0509] Figure 40F shows the cytotoxic activity of CAR T cells bearing FKBP-MyD88-CD40. Unlike the cytotails in Figures 40A-40E, CAR T cells bearing FKBP-MyD88-CD40 showed enhanced killing activity in the absence of AP1903. Moreover, the addition of AP1903 did not further enhance cytotoxicity, suggesting that FKBP-MyD88-CD40 receptor is one with a high basal activity and that lacks inducibility.

[0510] Figures 41A-41B show the levels of cytokines in the culture supernatents at the end of the 4-day cytotoxicity assay, in the absence and presence of AP1903. Each row shows the respective cytotail in the absence or presence of AP1903, each column shows the respective cytokine assayed. Each column is normalized to the highest concentration of the respective cytokine assayed, which was set as 100%.

[0511] Figure 41A shows cytokine release of all cytotails, but not including the FKBP-MyD88-CD40 receptor. In the presence of AP1903, FKBP switches containing the effector-promoting IL12Rbsmall(775-825) cytotail released elevated amounts of pro-inflammatory cytokines, including IL-17A/F, IL-21, TNFa and IFNg. Interestingly, the IL12Rbsmall(775-825) cytotail also led to increased IL-10 secretion, which likely arose from a negative-feedback mechanism in response to strong inflammatory signals.

[0512] Figure 41B shows cytokine release of all cytotails, as well as the FKBP-MyD88-CD40 receptor. Compared to FKBP switches bearing cytotails, the FKBP-MyD88-CD40 receptor secreted elevated levels of cytokines even in the absence of AP1903, a result consistent with its high basal activity.

[0513] To test whether different cytotail outputs influenced the memory differentiation and long-term survival of CAR T cells, we performed an AP1903-driven growth assay. CAR T cells bearing the indicated chimeric receptors were thawed and the percentages of CAR+ cells were normalized to the sample with the lowest transduction efficiency (i.e. 20% CAR+) by adding non-transduced T cells. Cells were either left untreated, or treated with 500 ng/ml of AP1903, and in the absence of exogenous cytokines (unless

specified in the case of positive controls) or target cells for 2 weeks. As positive controls, CAR T cells were alternatively supplemented with either exogenous recombinant IL-7 or IL-2 (10 ng/mL each; Miltenyi). On Day 5 of the AP1903-driven growth assay, supernantents were sampled for the analysis of cytokine release using the MSD assay (Meso Scale Discovery). At the end of the 2-week culture, the memory and exhaustion phenotypes of surviving CAR T cells were determined. Briefly, duplicate samples from each culture condition cells were harvested and stained using the Zombie NIR Fixable Viability Kit (Biolegend). Samples were washed with PBS, Fc blocked, then stained with the following antibody cocktail diluted in PBS+1%BSA: BUV395-conjugated anti-human CD3, BV510-conjugated anti-human CD8, BV605-conjugated human CD4 and FITC-conjugated v5 tag (for CAR detection), PE/Cy7-conjugated anti-human CD62L (Biolegend), BV785-conjugated anti-human CD45RO (Biolegend), APC-conjugated anti-human PD-1 (Biolegend), BV711-conjugated anti-human Tim-3 (Biolegend) and PerCP/eFluor710-conjugated anti-human Lag-3 (eBioscience). Finally, samples were washed in PBS and cell pellets were resuspended in PBS+1%BSA for FACS analysis.

[0514] Figures 42A-42B show the levels of cytokines in the culture supernatants on Day 5 of AP1903-driven growth, in presence of AP1903. Each row shows the respective signaling domain in presence of AP1903, each column shows the respective cytokine assayed. Each column is normalized to the highest concentration of the respective cytokine assayed, which was set as 100%.

[0515] Figure 42A shows cytokine release of all cytotails, but not including the FKBP-MyD88-CD40 receptor. Cytotails containing IL12Rbsmall(775-825) secrete elevated amounts of pro-inflammatory cytokines, including IL-17A/F, IL-21, TNFa and especially IFNg.

[0516] Figure 42B shows cytokine release of all cytotails, as well as the FKBP-MyD88-CD40 receptor. As compared to the FKBP-MyD88-CD40 receptor, cytokine release by FKBP-cytotail chimeric receptors during AP1903-driven growth were lower overall.

[0517] Figure 43 shows the AP1903-driven enrichment of cytotail-bearing CAR T cells. The dotted line indicates the percentage of CAR+ cells seeded at the beginning of the assay (i.e. 20%). As expected, treatment with exogenous recombinant IL-7 or IL-2 promoted the expansion and survival of both CAR+ and CAR- T cells within the same culture, leading to the stable maintenance of CAR+ cells at ~20%. In contrast, treatment with AP1903 selected and enriched for CAR T cells expressing the FKBP-cytotail receptors, suggesting that the growth and survival advantage is CAR+ T cell-specific.

[0518] Figures 44A-44G show the memory subset distribution of CAR T cells on Day 14 of AP1903-driven expansion. Compared to the IL7R(424-459;Y456F) cytotail that abrogates Stat5 activity (Figure 5B), the Stat5-competent IL7R(316-459) cytotail promoted the enrichment of Tscm CAR+ T cells to an extent equal or better than exogenous recombinant IL-7. Furthermore, compared to treatment with exogenous recombinant IL-7 or IL-2, AP1903-induced activation of the EGFR(1122-1165) cytotail – either alone or in combination with IL7R(316-459) – resulted in an enrichment of the Tcm CAR+ T cell population, suggesting that EGFR(1122-1165) cytotail signaling promotes Tcm differentiation.

[0519] Figures 45A-45G show the exhaustion phenotype of CAR+ T cells on Day 14 of AP1903-driven expansion. Compared to the IL7R(424-459;Y456F) cytotail that abrogates Stat5 activity (Figure 5B), the Stat5-competent IL7R(316-459) cytotail effectively suppressed the expression of PD-1, Tim-3 and Lag-3 to an extent equal or better than exogenous recombinant IL-7. Furthermore, compared to treatment with exogenous recombinant IL-7 or IL-2, AP1903-induced activation of the EGFR(1122-1165) cytotail – either alone or in combination with IL7R(316-459) – suppressed the expression of Tim-3 and Lag-3.

[0520] Taken together, the enrichment of long-lived CAR T cells may be achieved by incorporating memory-promoting and exhaustion-preventing cytotails, such as IL7R(316-459) and/or EGFR(1122-1165); whereas CAR T cells with potent and immediate cytotoxic functions may be favored by incorporating effector-promoting cytotails, such as Il12Rb2small(775-825).

[0521] Although the disclosed teachings have been described with reference to various applications, methods, kits, and compositions, it will be appreciated that various changes and modifications can be made without departing from the teachings herein and the claimed invention below. The foregoing examples are provided to better illustrate the disclosed teachings and are not intended to limit the scope of the teachings presented herein. While the present teachings have been described in terms of these exemplary embodiments, the skilled artisan will readily understand that numerous variations and modifications of these exemplary embodiments are possible without undue experimentation. All such variations and modifications are within the scope of the current teachings.

[0522] All references cited herein, including patents, patent applications, papers, text books, and the like, and the references cited therein, to the extent that they are not already, are hereby incorporated by reference in their entirety. In the event that one or more of the incorporated literature and similar materials differs from or contradicts this application, including but not limited to defined terms, term usage, described techniques, or the like, this application controls.

[0523] The foregoing description and Examples detail certain specific embodiments of the invention and describes the best mode contemplated by the inventors. It will be appreciated, however, that no matter how detailed the foregoing may appear in text, the invention may be practiced in many ways and the invention should be construed in accordance with the appended claims and any equivalents thereof.

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The claims defining the invention are as follows

1. An inducible chimeric cytokine receptor comprising:

a dimerization domain;

a tyrosine kinase activating domain that is a TPOR/MPLR, an EpoR, a GP130, a PRLR, a GCSFR, or a GHR tyrosine kinase activating domain and which comprises a transmembrane domain and a Janus Kinase (JAK)-binding domain; and

a tyrosine effector domain.

2. The inducible chimeric cytokine receptor of claim 1,

a) wherein the tyrosine effector domain comprises at least two STAT-activation domains;
b) which comprises at least two identical polypeptide monomers, each comprising the dimerization domain, the tyrosine kinase activating domain, and the tyrosine effector domain; or
c) wherein the at least two identical polypeptide monomers each comprise an N-terminal to C-terminal orientation of the dimerization domain, the tyrosine kinase activating domain, and the tyrosine effector domain.

3. The inducible chimeric cytokine receptor of claim 2, wherein the at least two STAT-activation domains are in tandem.

4. The inducible chimeric cytokine receptor of any one of claims 1-3, wherein the tyrosine kinase activating domain is a TPOR/MPLR tyrosine kinase activating domain.

5. The inducible chimeric cytokine receptor of any one of claims 1-3, wherein the tyrosine kinase activating domain is an EpoR tyrosine kinase activating domain.

6. The inducible chimeric cytokine receptor of any one of claims 1-5, wherein the dimerization domain

a) binds to a ligand AP1903, AP20187, dimeric FK506, or a dimeric FK506-like analog; or
b) comprises an FKBP polypeptide.

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7. The inducible chimeric cytokine receptor of claim 6, wherein the FKBP polypeptide

a) is an FKBP12 polypeptide; or

b) contains the amino acid substitution F36V (SEQ ID NO: 218).

8. The inducible chimeric cytokine receptor of any one of claims 1-7, wherein

a) the dimerization domain comprises an amino acid sequence selected from the group consisting of: (i) a FKBP polypeptide containing one or more amino acid substitutions, (ii) two or three tandem repeats of an unmodified FKBP polypeptide, and (iii) two or three tandem repeats of a FKBP polypeptide containing one or more amino acid substitutions;

b) the dimerization domain comprises a dimerization domain sequence selected from SEQ ID NOs: 69-87;

c) the dimerization domain comprises an FKBP dimerization domain sequence selected from SEQ ID NOs. 69-73; or

d) the dimerization domain comprises an amino acid sequence of, or derived from, a polypeptide selected from the group consisting of: FKBP12, FKBP12(F36V), an extracellular domain of OX-40, and an extracellular domain of a TNFR2 superfamily receptors.

9. The inducible chimeric cytokine receptor of claim 8, wherein the TNFR2 superfamily receptor is BCMA, TACI, or BAFFR.

10. The inducible chimeric cytokine receptor of any one of claims 1-9, wherein the

a) dimerization domain binds a small molecule or a protein; or

b) dimerization domain comprises an amino acid sequence of, or derived from, a protein selected from the group consisting of: FKBP, cyclophilin, steroid binding protein, estrogen binding protein, glucocorticoid binding protein, vitamin D binding protein, tetracycline binding protein, extracellular domain of a cytokine receptor, a receptor tyrosine kinase, a TNFR-family receptor, and an immune co-receptor.

11. The inducible chimeric cytokine receptor of claim 10, wherein the immune co-receptor is selected from the group consisting of: erythropoietin receptor, prolactin receptor, growth hormone receptor, thrombopoietin receptor, granulocyte colony-

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stimulating factor receptor, GP130, common gamma chain receptor, common beta chain receptor, IFN alpha receptor, IFN gamma receptor, IFN lambda receptor, IL2/IL15 receptor, IL3 receptor, IL4 receptor, IL5 receptor, IL7 receptor, IL9 receptor, IL10 receptor, IL12 receptor, IL13 receptor, IL20 receptor, IL21 receptor, IL22 receptor, IL23 receptor, IL27 receptor, TSLP Receptor, G-CSF receptor, GM-CSF receptor, CNTF receptor, OSM receptor, LIF receptor, CT-1 receptor, TGFBR1/ALKL5, TGFBR2, EGFR/HER1, ERBB2/HER2, ERBB3/HER3, ERRB4/HER4, INSR, IGF-1R, IRR, PDGFRA, PDGFRB, CSF-1R, KIT/SCFR, FLK2/FLT3, VEGFR1, VEGFR2, VEGFR3, FGFR-1, FGFR-2, FGFR-3, FGFR-4, CCK4, TRKA, TRKB, TRKC, MET, RON, EPHA1, EPHA2, EPHA3, EPHA4, EPHA5, EPHA6, EPHA7, EPHA8, EPHB1, EPHB2, EPHB3, EPHB4, EPHB5, EPHB6, AXL, MER, TYRO3, TIE, TEK, RYK, DDR1, DDR2, RET, ROS, LTK, ALK, ROR1, ROR2, MUSK, AATYK, AATYK2, AATYK3, RTK106, TNFR1, Fas, TRAILR1, TRAILR2, NGFR, DR3, DR6, EDAR, TNFR2, LTbR, OX40, CD40, CD27, CD30, 4-1BB, RANK, Fn14, TACI, BAFFR, HVEM, BCMA, GITR, TROY, RELT, XEDAR, TRAILR3, TRAILR4, OPG, DcR3, PD-1, CD80, CD86, ICOS-L, ICOS, CTLA-4, BTLA, CD160, LAG3, and TIM3.

12. The inducible chimeric cytokine receptor of any one of claims 1-11, wherein

a) the tyrosine kinase activating domain comprises a tyrosine kinase activating domain sequence selected from SEQ ID NOs: 89-97, 104, and 106-133;
b) the transmembrane domain comprises a transmembrane domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, PD-1, and TPOR/MPLR;
c) the transmembrane domain comprises a transmembrane domain derived from TPOR/MPLR;
d) is derived from amino acids 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID No.: 64; or
e) the transmembrane domain comprises a deletion variant or an insertion variant of the amino acid region 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID No.: 64.

13. The inducible chimeric cytokine receptor of claim 12, wherein

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a) the deletion variant comprises a deletion of 1 to 18 amino acids from the region 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID No.: 64;

b) the deletion variant comprises a deletion of 1 to 18 amino acids from the region 489-510 of the naturally occurring TPOR/MPLR sequence of SEQ ID No.: 64;

c) the insertion variant comprises an insertion of 1 to 8 amino acids in the region 478-582 of the naturally occurring TPOR/MPLR sequence of SEQ ID No.: 64; or

d) the insertion variant comprises an insertion of 1 to 8 amino acids in the region 489-510 of the naturally occurring TPOR/MPLR sequence of SEQ ID No.: 64.

14. The inducible chimeric cytokine receptor of claim 13, , wherein the amino acids inserted in the insertion variant are selected from the group consisting of: leucine, valine, and isoleucine.

15. The inducible chimeric cytokine receptor of any one of claims 1-14, wherein the tyrosine kinase activating domain comprises a sequence selected from SEQ ID NOs: 104 and 106-133.

16. The inducible chimeric cytokine receptor of claim 1, wherein

the dimerization domain comprises an FKBP polypeptide;

the transmembrane domain comprises a transmembrane domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, PD-1, and TPOR;

the JAK-binding domain comprises a JAK-binding domain of, or derived from, a protein selected from the group consisting of: EPOR, GP130, PRLR, GHR, GCSFR, and TPOR; and

the STAT-activation domain comprises at least one STAT-activation domain of, or derived from, a receptor selected from the group consisting of: BLNK, IL2RG, EGFR, EpoR, GHR, IFNAR1, IFNAR2, IFNAR1/2, IFNLR1, IL10R1, IL12Rb1, IL12Rb2, IL21R, IL2Rb, IL2small, IL7R, IL7Ra, IL9R, IL15R, and IL21R.

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17. The inducible chimeric cytokine receptor of any one of claims 1-16, wherein

a) the tyrosine effector domain comprises a tyrosine effector domain sequence selected from SEQ ID NOs: 134-176;
b) the tyrosine effector domain comprises at least two STAT-activation domains that comprise an IL7R(316-459) amino acid sequence shown as SEQ ID NO: 134 and an IL12Rb2(775-825) amino acid sequence shown as SEQ ID NO: 155;
c) the dimerization domain is located at the N-terminus or the C-terminus of the inducible chimeric cytokine receptor;
d) the inducible chimeric cytokine receptor comprises a membrane-targeting motif; or
e) the inducible chimeric cytokine receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 1-58, 187-215, and 225-311.

18. The inducible chimeric cytokine receptor of claim 17, wherein the membrane-targeting motif comprises a myristoylation motif or wherein the receptor is myristoylated.

19. A polynucleotide comprising a nucleic acid sequence encoding the inducible chimeric cytokine receptor of any one of claims 1-18.

20. An expression vector comprising the polynucleotide of claim 19.

21. An engineered immune cell comprising at least one inducible chimeric cytokine receptor of any one of claims 1-18 or at least one polynucleotide of claim 19.

22. The engineered immune cell of claim 21, wherein

a) the cell comprises at least two inducible chimeric cytokine receptors of any one of claims 1-18 or at least two polynucleotides of claim 19;
b) the cell comprises at least three or four inducible chimeric cytokine receptors of any one of claims 1-18 or at least three or four polynucleotides of claim 19;
c) when more than one inducible chimeric cytokine receptor is present, the dimerization domain, the tyrosine kinase activating domain, and the tyrosine

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effector domain of each receptor can be the same or different;

d) the cell further comprises a chimeric antigen receptor (CAR) or a polynucleotide encoding a CAR; or

e) the immune cell is selected from the group consisting of: T cell, dendritic cell, killer dendritic cell, mast cell, NK-cell, macrophage, monocyte, B-cell and an immune cell derived from a stem cell.

23. The engineered immune cell of claim 21 or 22 wherein

a) the immune cell is a T cell;

b) the immune cell is an autologous T cell; or

c) the immune cell is an allogeneic T cell.

24. A method of modulating an engineered immune cell in a subject, the method comprising administering a ligand to a subject that has previously been administered an engineered immune cell of any one of claims 21-23, wherein the dimeric ligand binds to the dimerization domain of the inducible chimeric cytokine receptor.

25. The method of claim 24, wherein the ligand is AP1903.

26. A method of preparing an engineered immune cell, the method comprising introducing a polynucleotide of claim 19 or an expression vector of claim 20 into an immune cell.

27. The method of claim 26, wherein the immune cell is selected from the group consisting of: T cell, dendritic cell, killer dendritic cell, mast cell, NK-cell, macrophage, monocyte, B-cell and an immune cell derived from a stem cell.

28. The method of claim 26 or 27, wherein the immune cell is a T cell.

29. An isolated immune cell comprising:

(i) at least one inducible chimeric cytokine receptor comprising a dimerization domain, a tyrosine kinase activating domain, and a tyrosine effector domain, wherein the tyrosine kinase activating domain is a TPOR/MPLR, an EpoR, a GP130, a PRLR, a GCSFR, or a GHR tyrosine kinase activating domain and comprises a transmembrane domain and a Janus Kinase (JAK)-binding domain; and

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(ii) a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain.

30. The isolated immune cell of claim 29,

a) wherein the inducible chimeric cytokine receptor is the inducible chimeric cytokine receptor of any one of claims 1-18;
b) which comprises at least two, three, or four inducible chimeric cytokine receptors; or
c) wherein the extracellular ligand binding domain of the CAR specifically binds BCMA, EGFRvIII, Flt-3, WT-1, CD20, CD23, CD30, CD38, CD70, CD33, CD133, LeY, NKG2D, CS1, CD44v6, ROR1, CD19, Claudin-18.2 (Claudin-18A2, or Claudin18 isoform 2), DLL3 (Delta-like protein 3, Drosophila Delta homolog 3, Delta3), Muc17 (Mucin17, Muc3, Muc3), FAP alpha (Fibroblast Activation Protein alpha), Ly6G6D (Lymphocyte antigen 6 complex locus protein G6d, c6orf23, G6D, MEGT1, NG25), RNF43 (E3 ubiquitin-protein ligase RNF43, or RING finger protein 43).

31. The isolated immune cell of any one of claims 29-30, wherein

a) the immune cell is selected from the group consisting of: T cell, dendritic cell, killer dendritic cell, mast cell, NK-cell, macrophage, monocyte, B-cell and an immune cell derived from a stem cell;
b) the immune cell exhibits improved persistence upon contact with a ligand that binds to the dimerization domain relative to persistence of an isolated immune cell that does not express the inducible chimeric cytokine receptor; or

c) the immune cell exhibits increased activation of STAT upon contact with a ligand that binds to the dimerization domain relative to activation of STAT exhibited by an isolated immune cell that does not express the inducible chimeric cytokine receptor.

32. The isolated immune cell of any one of claims 29-30, wherein the immune cell is a T cell.

33. The isolated immune cell of claim 31, wherein

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a) the STAT is STAT1, STAT2, STAT3, STAT4, STAT5, STAT6, or combinations thereof;

b) the activation of STAT by the isolated immune cell, upon contact with a ligand that binds to the dimerization domain, increases with the dose of the ligand compared to activation of STAT shown by the isolated immune cell that does not express the inducible chimeric cytokine receptor;

c) the isolated immune cell exhibits increased cytotoxicity upon contact with a ligand that binds to the dimerization domain compared to cytotoxicity exhibited by an isolated immune cell that does not express the inducible chimeric cytokine receptor;

d) the isolated immune cell expands upon contact with a ligand that binds to the dimerization domain compared to an isolated immune cell that does not express the inducible chimeric cytokine receptor;

e) the level of cell markers for stem cell memory (Tscm) and/or central memory (Tcm) on the isolated immune cell are increased or maintained upon contact with a ligand that binds to the dimerization domain compared to the level of these markers on an isolated immune cell that does not express the inducible chimeric cytokine receptor;

f) the isolated immune cell is a T cell;

g) the isolated immune cell is an autologous T cell; or

h) the isolated immune cell is an allogeneic T cell.

34. A method of generating an isolated immune cell comprising an inducible chimeric cytokine receptor of any one of claims 1-18, wherein the method comprises the steps of:

a) providing an immune cell;

b) introducing into the immune cell a polynucleotide that encodes a chimeric antigen receptor (CAR) comprising an extracellular ligand-binding domain, a transmembrane domain, and an intracellular signaling domain; and

c) introducing into the immune cell a polynucleotide that encodes the inducible chimeric cytokine receptor.

35. The method of claim 34, wherein

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a) step c) comprises stably expressing the inducible chimeric cytokine receptor into the cell;

b) in step c), the polynucleotide that encodes the inducible chimeric cytokine receptor is introduced into the cell by a transposon/transposase system, a viral-based gene transfer system, or electroporation;

c) in step b), the polynucleotide that encodes the chimeric antigen receptor is introduced into the cell by a transposon/transposase system or a viral-based gene transfer system;

d) either step (b) occurs prior to step (c) or step (c) occurs prior to step (b);

e) the immune cell is selected from the group consisting of: T cell, dendritic cell, killer dendritic cell, mast cell, NK-cell, macrophage, monocyte, B-cell and an immune cell derived from a stem cell.

36. The method of claim 35, wherein the viral-based gene transfer system comprises recombinant retrovirus or lentivirus.

37. The method of any one of claims 34-36, wherein the immune cell is a T cell.

38. A pharmaceutical composition comprising the isolated immune cell of any one of claims 29-33 and a pharmaceutically acceptable carrier.

39. A method for treating a disorder in a subject, wherein the method comprises administering the isolated immune cell of any one of claims 29-33 to the subject or administering the pharmaceutical composition of claim 38 to the subject, wherein the disorder is a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease.

40. The method of 39, wherein

a) the cells or the pharmaceutical composition are provided to the subject more than once;

b) the cells or the pharmaceutical composition are provided to the subject at least about 1, 2, 3, 4, 5, 6, 7, or more days apart; or

c) the subject has been previously treated with a therapeutic agent prior to administration of the isolated immune cell or the pharmaceutical composition.

41. The method of claim 40, wherein

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a) the therapeutic agent is an antibody or chemotherapeutic agent; or
b) the cancer is a hematological malignancy or a solid cancer.

42. The method according to claim 41, wherein

a) the hematological malignancy is selected from acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), chronic eosinophilic leukemia (CEL), myelodysplasia syndrome (MDS), non-Hodgkin's lymphoma (NHL), or multiple myeloma (MM); or
b) the solid cancer is selected from biliary cancer, bladder cancer, bone and soft tissue carcinoma, brain tumor, breast cancer, cervical cancer, colon cancer, colorectal adenocarcinoma, colorectal cancer, desmoid tumor, embryonal cancer, endometrial cancer, esophageal cancer, gastric cancer, gastric adenocarcinoma, glioblastoma multiforme, gynecological tumor, head and neck squamous cell carcinoma, hepatic cancer, lung cancer, malignant melanoma, osteosarcoma, ovarian cancer, pancreatic cancer, pancreatic ductal adenocarcinoma, primary astrocytic tumor, primary thyroid cancer, prostate cancer, renal cancer, renal cell carcinoma, rhabdomyosarcoma, skin cancer, soft tissue sarcoma, testicular germ- cell tumor, urothelial cancer, uterine sarcoma, or uterine cancer.

43. Use of the isolated immune cell of any one of claims 29-33 or the pharmaceutical composition of claim 38 in the manufacture of a medicament for treating a disorder, wherein the disorder is a viral disease, a bacterial disease, a cancer, an inflammatory disease, an immune disease, or an aging- associated disease.

44. The use of claim 43, wherein

a) the cells or the pharmaceutical composition are provided to the subject more than once;
b) the cells or the pharmaceutical composition are provided to the subject at least 1, 2, 3, 4, 5, 6, 7, or more days apart;
c) the subject has been previously treated with a therapeutic agent prior to administration of the isolated immune cell or the pharmaceutical composition;

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or

d) the cancer is a hematological malignancy or a solid cancer.

45. The use of claim 44, wherein the therapeutic agent is an antibody or chemotherapeutic agent.

46. The use according to claim 44, wherein

a) the hematological malignancy is selected from acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), chronic eosinophilic leukemia (CEL), myelodysplasia syndrome (MDS), non-Hodgkin's lymphoma (NHL), or multiple myeloma (MM);

or

b) the solid cancer is selected from biliary cancer, bladder cancer, bone and soft tissue carcinoma, brain tumor, breast cancer, cervical cancer, colon cancer, colorectal adenocarcinoma, colorectal cancer, desmoid tumor, embryonal cancer, endometrial cancer, esophageal cancer, gastric cancer, gastric adenocarcinoma, glioblastoma multiforme, gynecological tumor, head and neck squamous cell carcinoma, hepatic cancer, lung cancer, malignant melanoma, osteosarcoma, ovarian cancer, pancreatic cancer, pancreatic ductal adenocarcinoma, primary astrocytic tumor, primary thyroid cancer, prostate cancer, renal cancer, renal cell carcinoma, rhabdomyosarcoma, skin cancer, soft tissue sarcoma, testicular germ- cell tumor, urothelial cancer, uterine sarcoma, or uterine cancer.

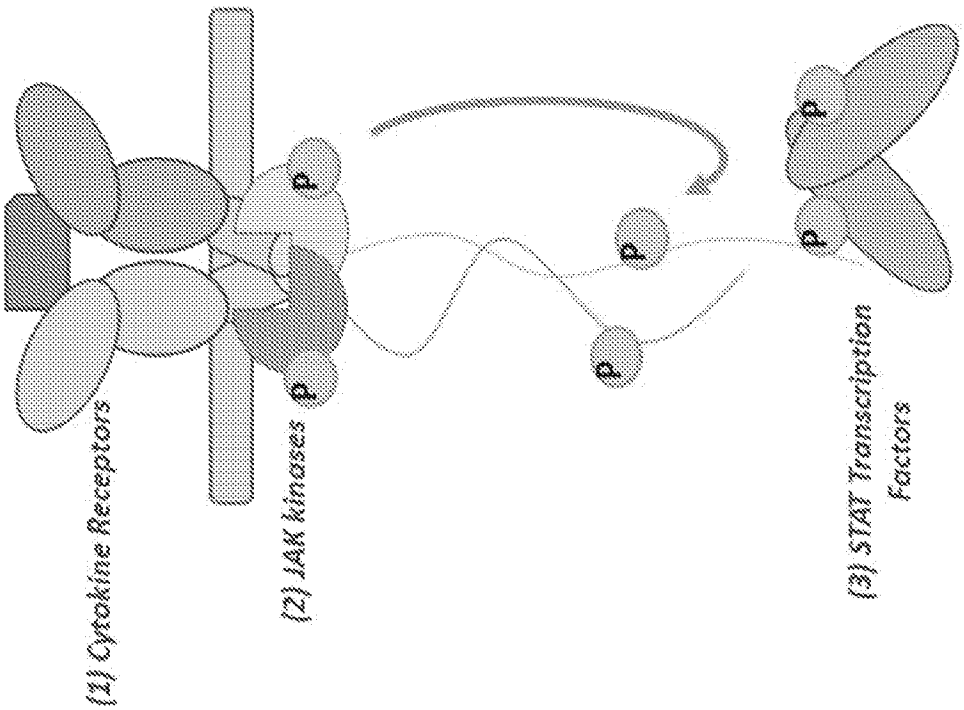

(1) Cytokine Receptors
(2) JAK kinases
(3) STAT Transcription Factors
P

FIG. 1

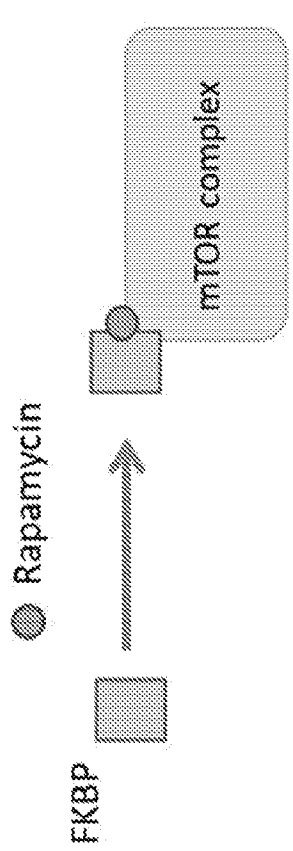


FIG. 2A

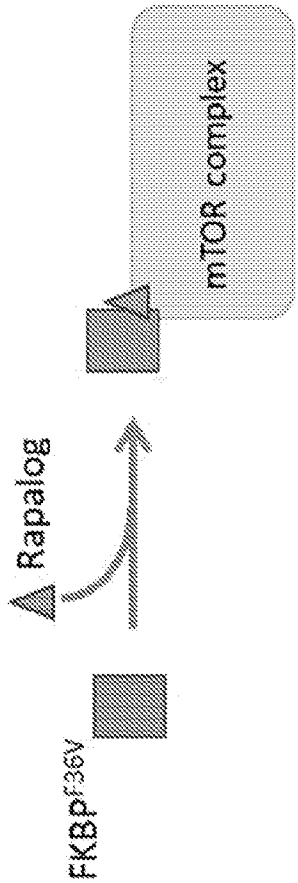


FIG. 2B

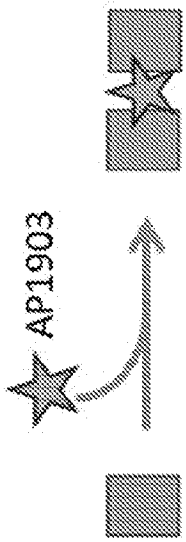


FIG. 2C

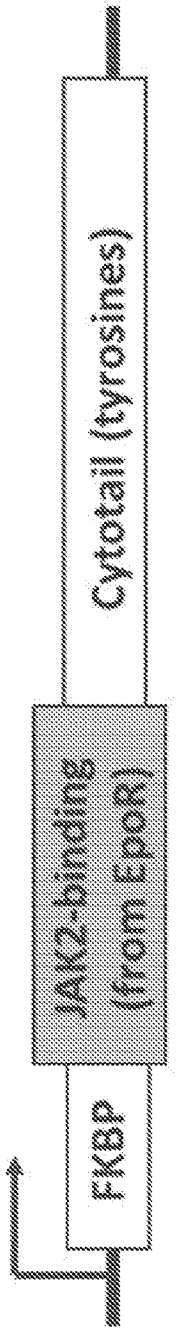


FIG. 3

FIG. 4

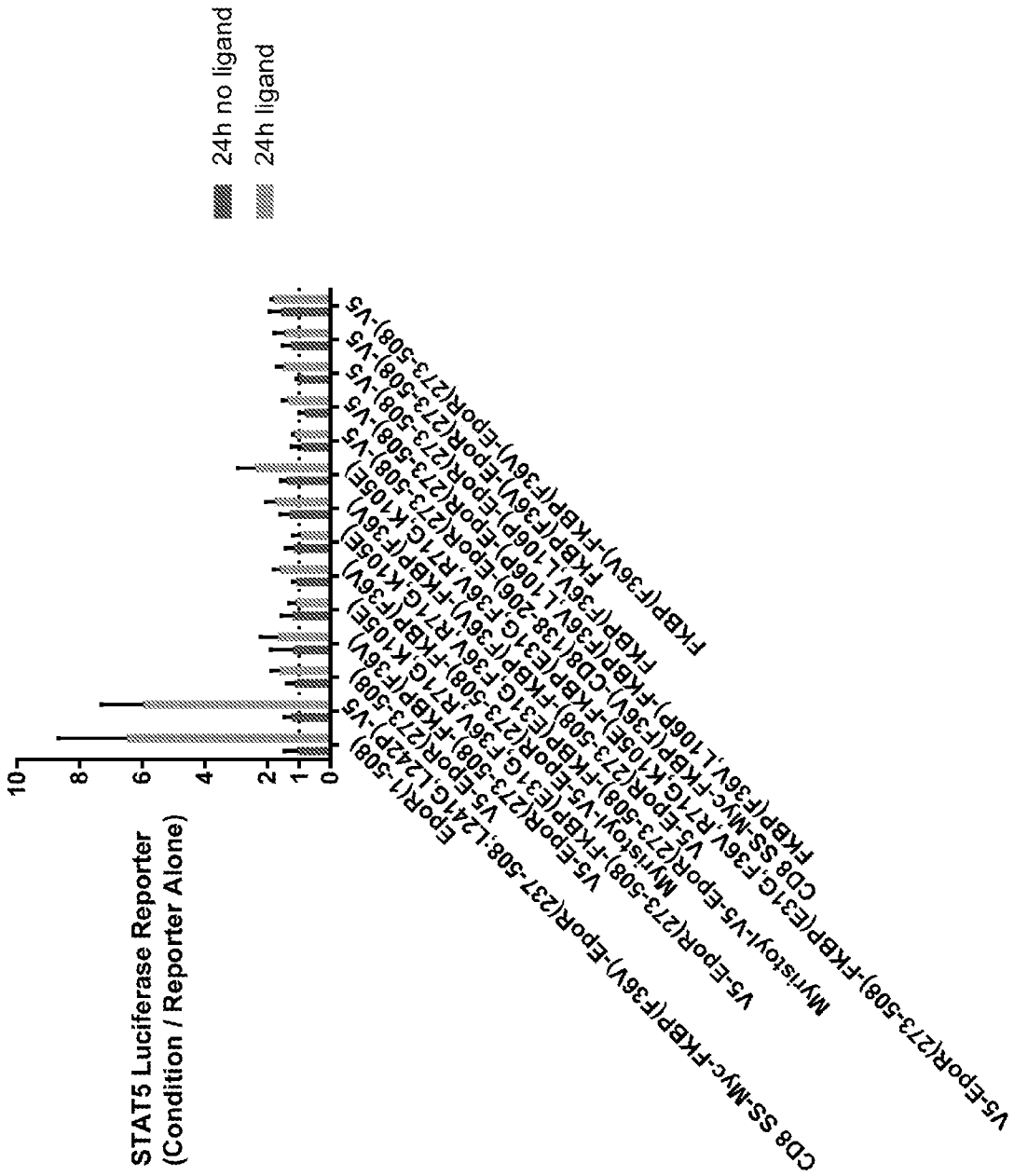
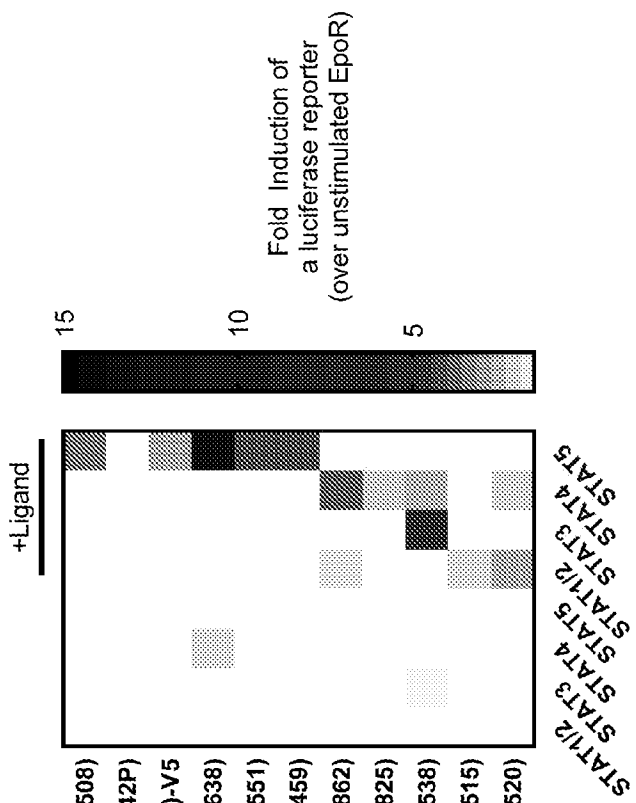

JAK2 dimerizers, fold over reporter alone, 24h
STAT5 Luciferase Reporter (Condition / Reporter Alone)
24h no ligand
24h ligand
0
1
2
4
6
8
10
EpoR(1-508)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-508,L242G,L243R)
V5-EpoR(273-508)-FKBP(F36V)
Myristoyl-V5-EpoR(273-508)-FKBP(E31G,F36V,R71G,K105E)
V5-EpoR(273-508)-FKBP(E31G,F36V,R71G,K105E)
Myristoyl-V5-EpoR(273-508)-FKBP(E31G,F36V,R71G,K105E)-V5
CD8 SS-Myc-FKBP(F36V,L106P)-EpoR(273-508)-V5
FKBP(F36V,L106P)-EpoR(273-508)-V5
FKBP(F36V,L106P)-FKBP(F36V)-EpoR(273-508)-V5

FIG. 5A


Fold Induction of a luciferase reporter (over unstimulated EpoR)
15
10
5
+Ligand
EpoR(1-508)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EpoR(339-508)-V5
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-GHR(353-638)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
STAT1/2
STAT3
STAT4
STAT5
STAT1/2 STAT3
STAT1/2 STAT4
STAT1/2 STAT5
STAT3 STAT4
STAT3 STAT5
STAT4 STAT5

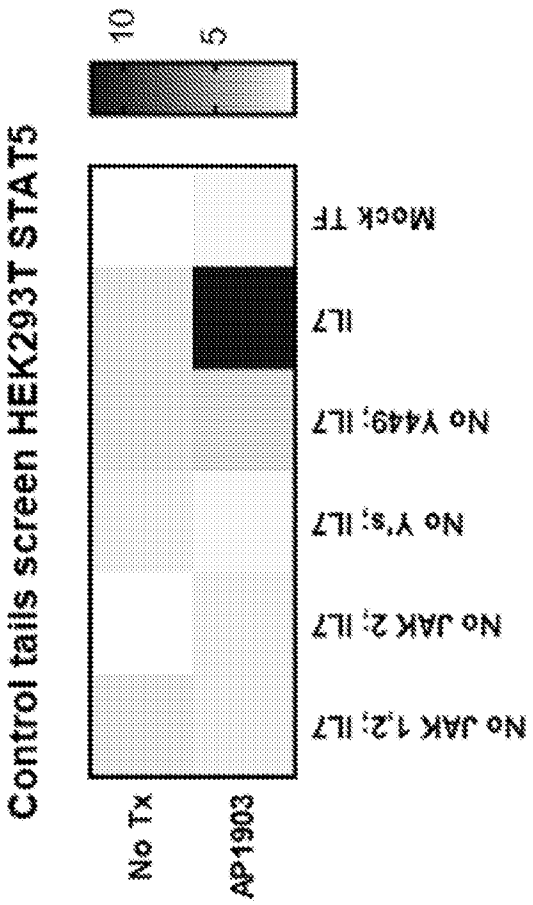
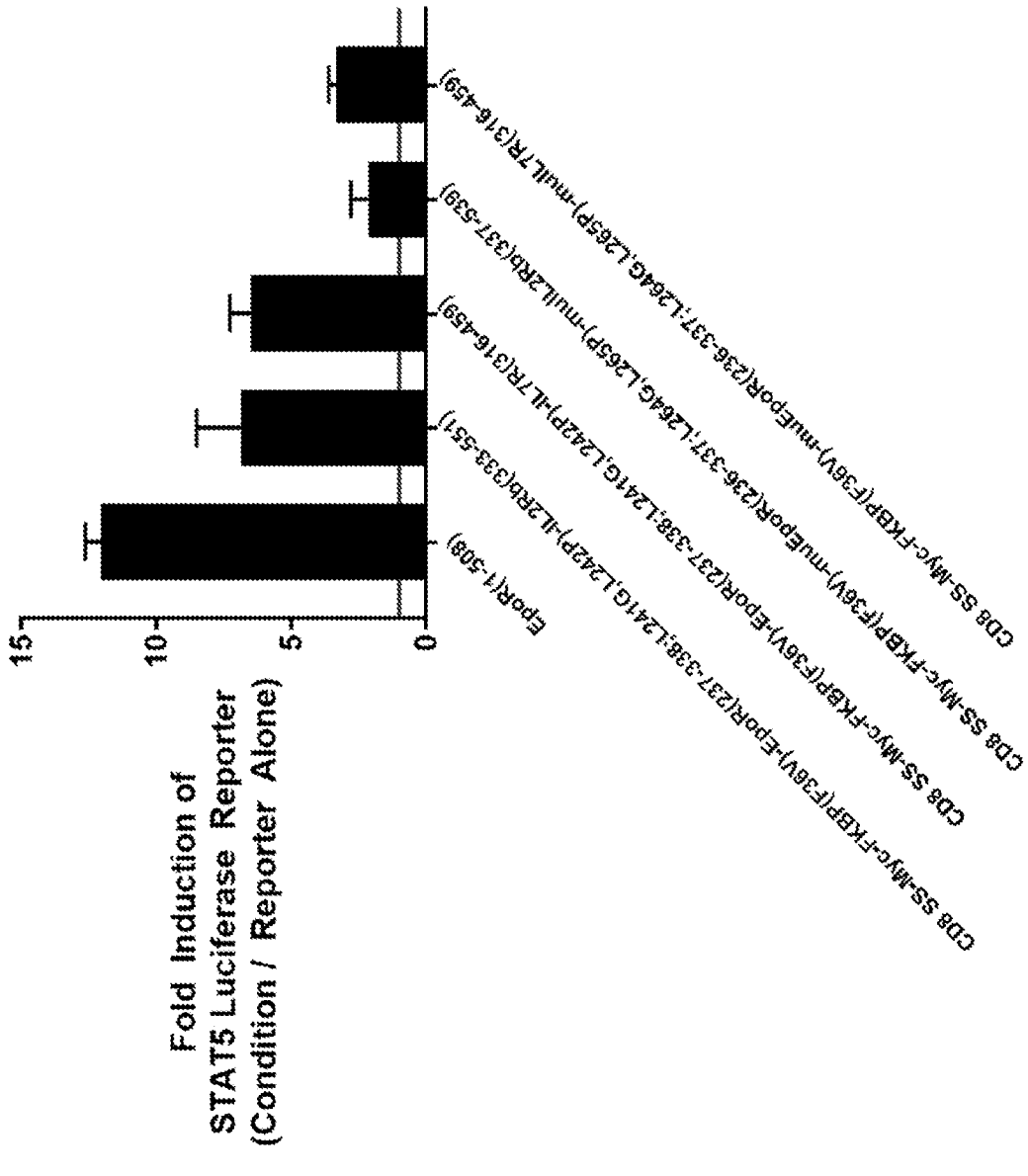

Control tails screen HEK293T STAT5
10
5
Mock TF
IL7
No Y449; IL7
No Y's; IL7
No JAK 2; IL7
No JAK 1,2; IL7
No Tx
AP1903

FIG. 5B

FIG. 6


Fold Induction of
STAT5 Luciferase Reporter
(Condition / Reporter Alone)
15
10
5
0
EpoR(1-508)
CD8 SS-MYC-FKBP(F36V)-EPOR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-MYC-FKBP(F36V)-EPOR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-MYC-FKBP(F36V)-muEPOR(236-337;L264G,L265P)-muIL2Rb(337-539)
CD8 SS-MYC-FKBP(F36V)-muEPOR(236-337;L264G,L265P)-muIL7R(316-459)

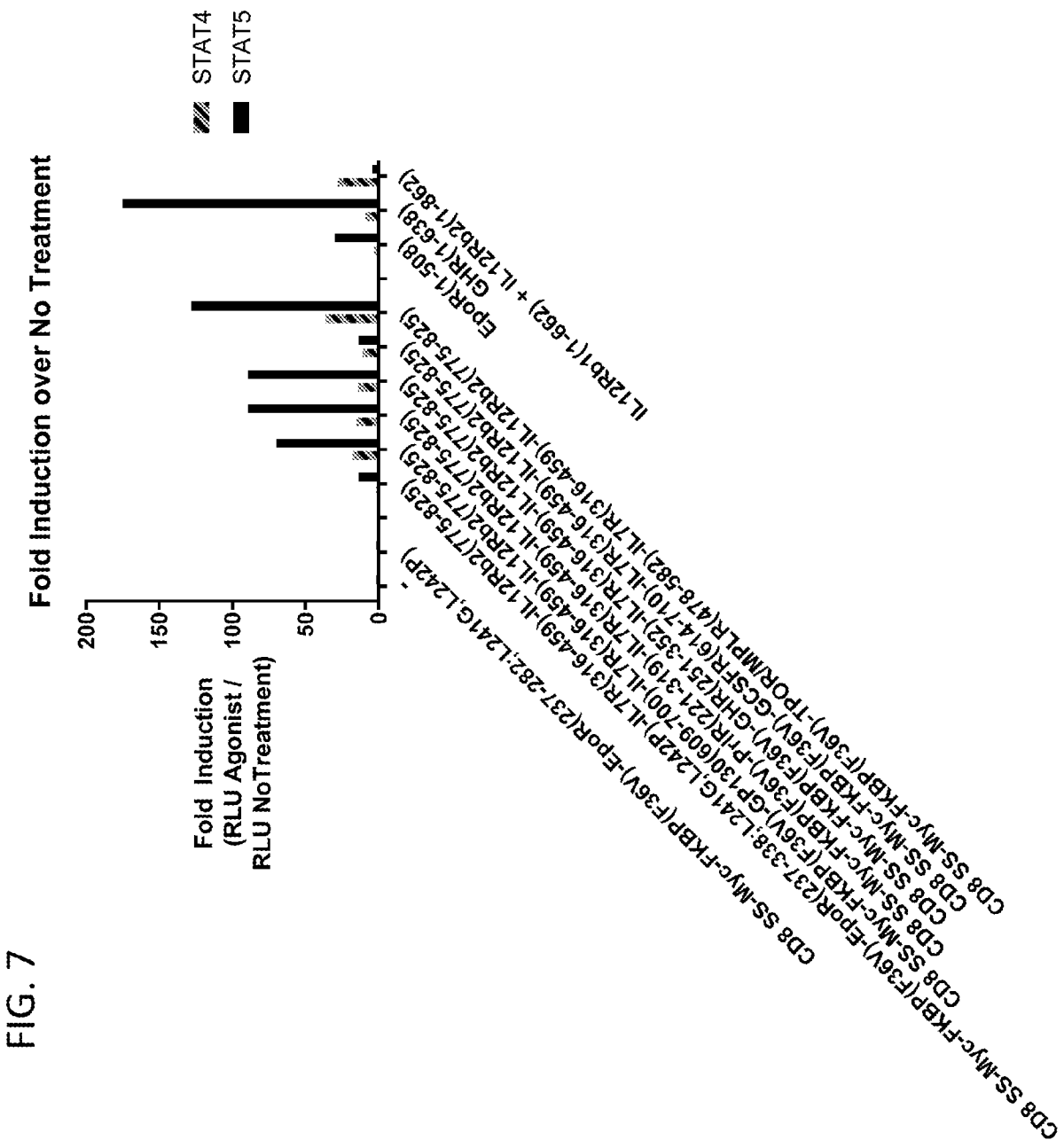
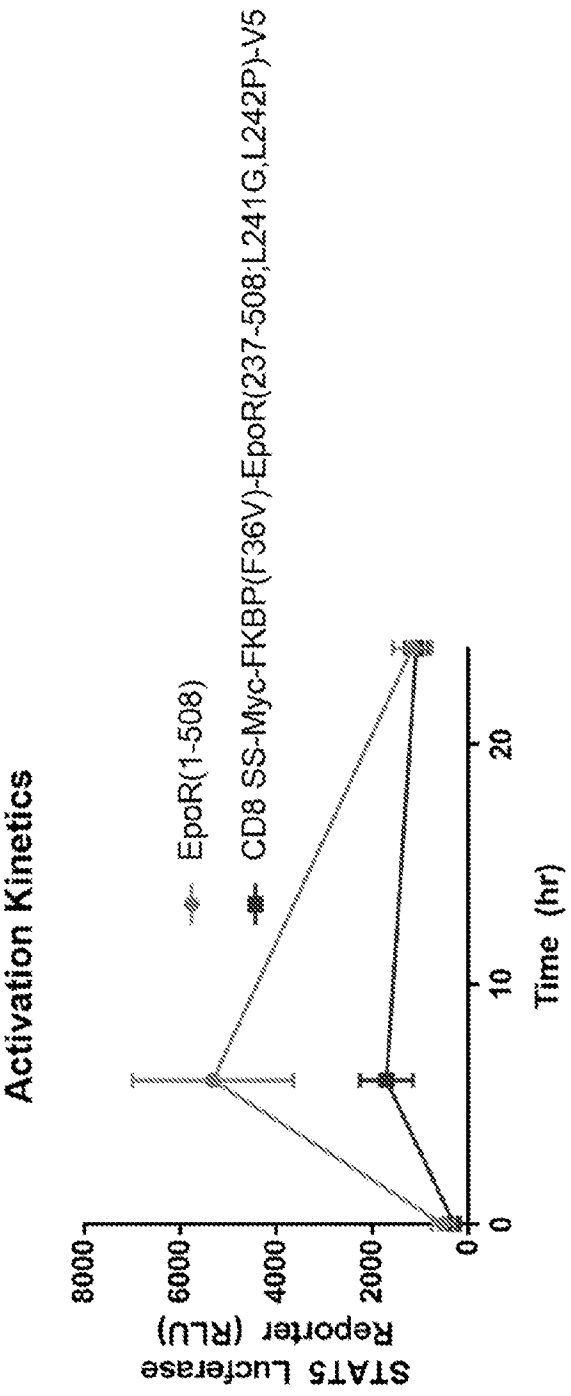

Fold Induction over No Treatment
STAT4
STAT5
Fold Induction (RLU Agonist / RLU NoTreatment)
200
150
100
50
0
-
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L24G,L24P)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24G,L24P)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GP130(609-700)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-PrlR(221-319)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GHR(251-352)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)
IL12Rb1(1-662) + IL12Rb2(1-862)
EpoR(1-508)
GHR(1-638)

FIG. 7

FIG. 8


Activation Kinetics
EpoR(1-508)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-508;L241G,L242P)-V5
STAT5 Luciferase Reporter (RLU)
8000
6000
4000
2000
0
0
10
20
Time (hr)

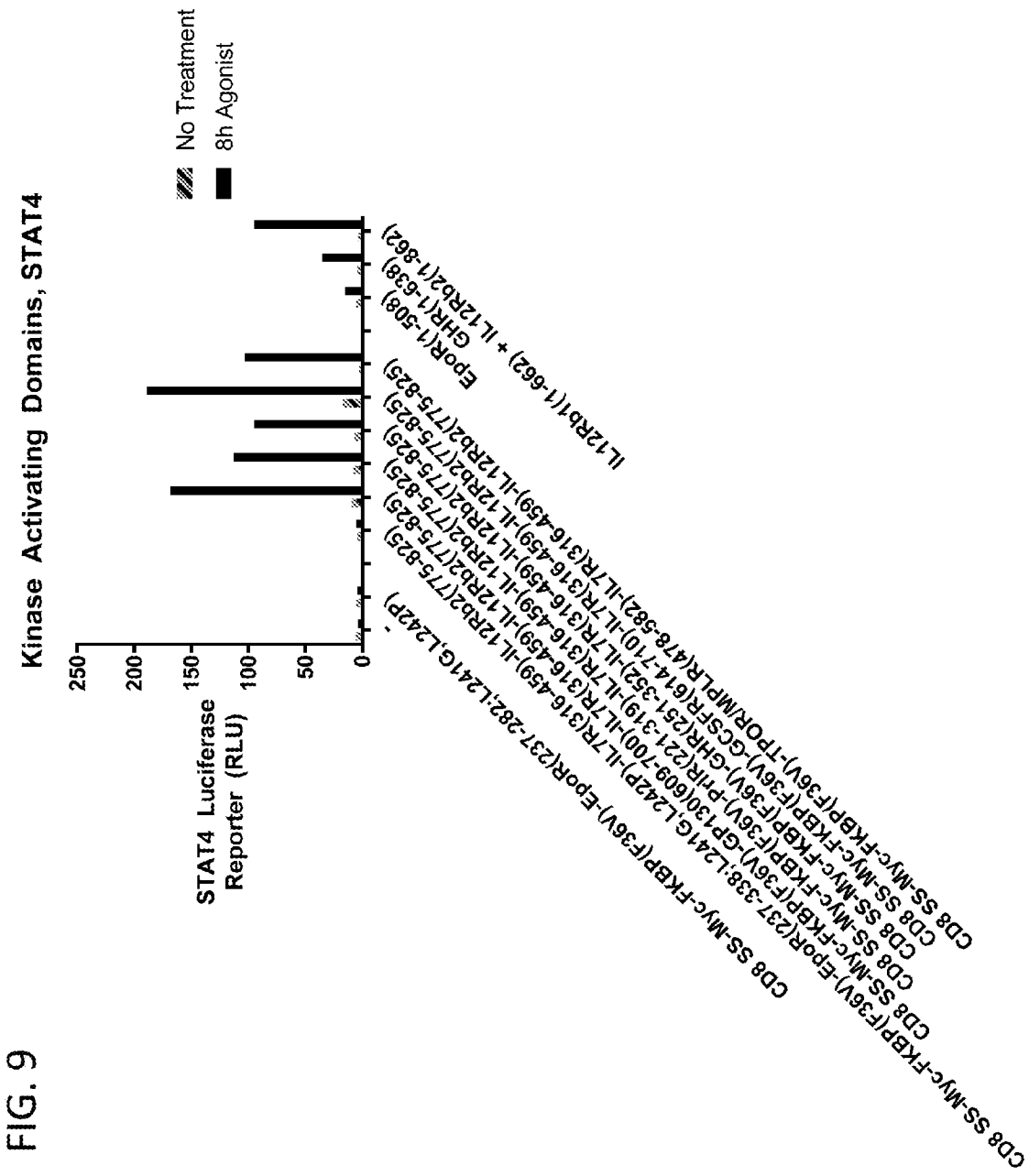

Kinase Activating Domains, STAT4
No Treatment
8h Agonist
STAT4 Luciferase Reporter (RLU)
250
200
150
100
50
0
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GP130(609-700)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-PrlR(221-319)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)
IL12Rb1(1-662) + IL12Rb2(1-862)
EpoR(1-508)
GHR(1-638)

FIG. 9

FIG. 10A

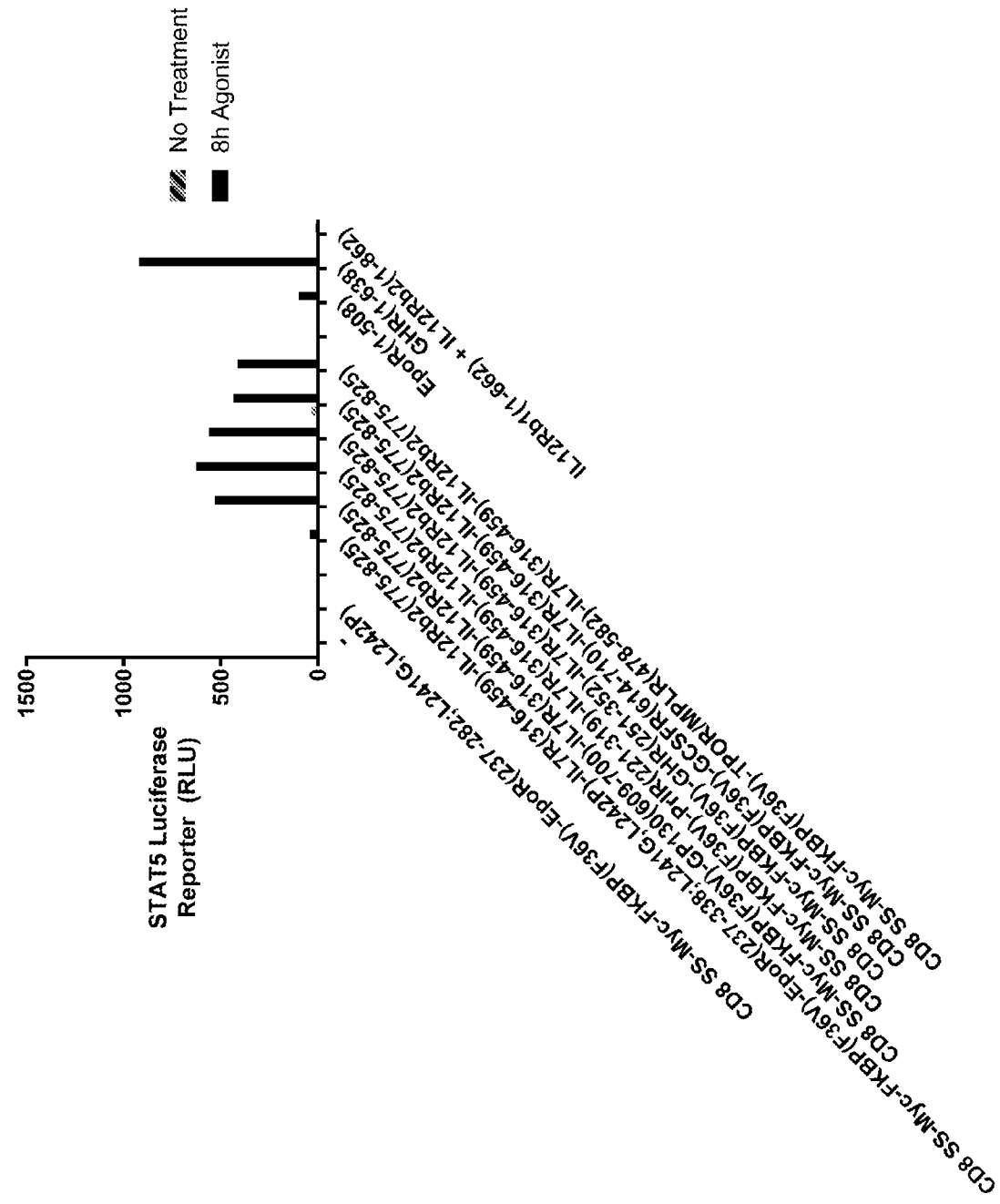
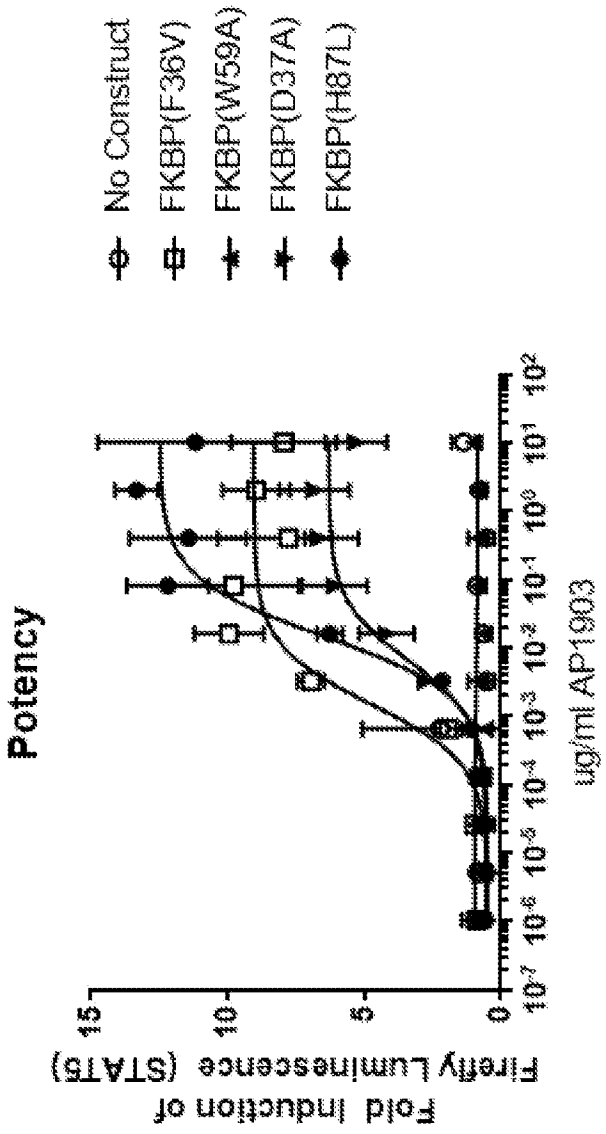

Kinase Activating Domains, STAT5
No Treatment
8h Agonist
STAT5 Luciferase Reporter (RLU)
1500
1000
500
0
-
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L24G,L24P)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24G,L24P)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GP130(609-700)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-PRLR(221-352)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GHR(251-319)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825)
CD8 SS-Myc-FKBP(F36V)-TPORMPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)
IL12Rb1(1-662) + IL12Rb2(1-862)
EpoR(1-508)
GHR(1-638)

FIG. 10B


Potency
No Construct
FKBP(F36V)
FKBP(W59A)
FKBP(D37A)
FKBP(H87L)
Fold Induction of
Firefly Luminescence (STAT5)
15
10
5
0
10-7 10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
ug/ml AP1903

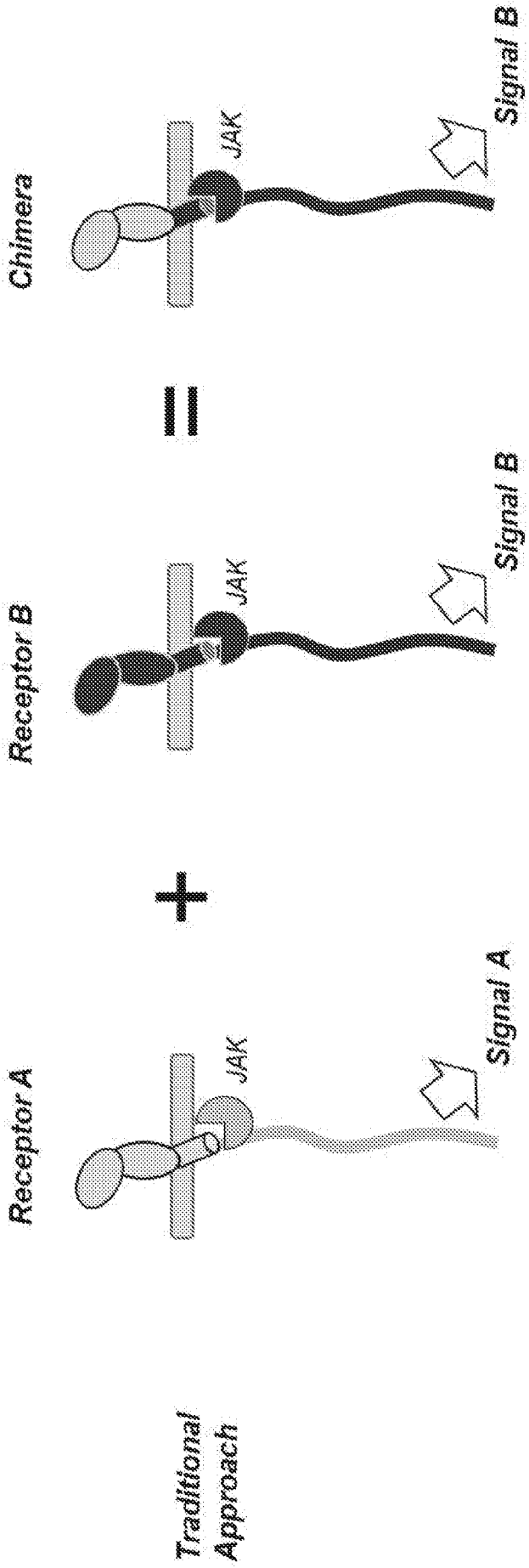

Traditional Approach
Receptor A
JAK
Signal A
Receptor B
JAK
Signal B
Chimera
JAK
Signal B

FIG. 10C

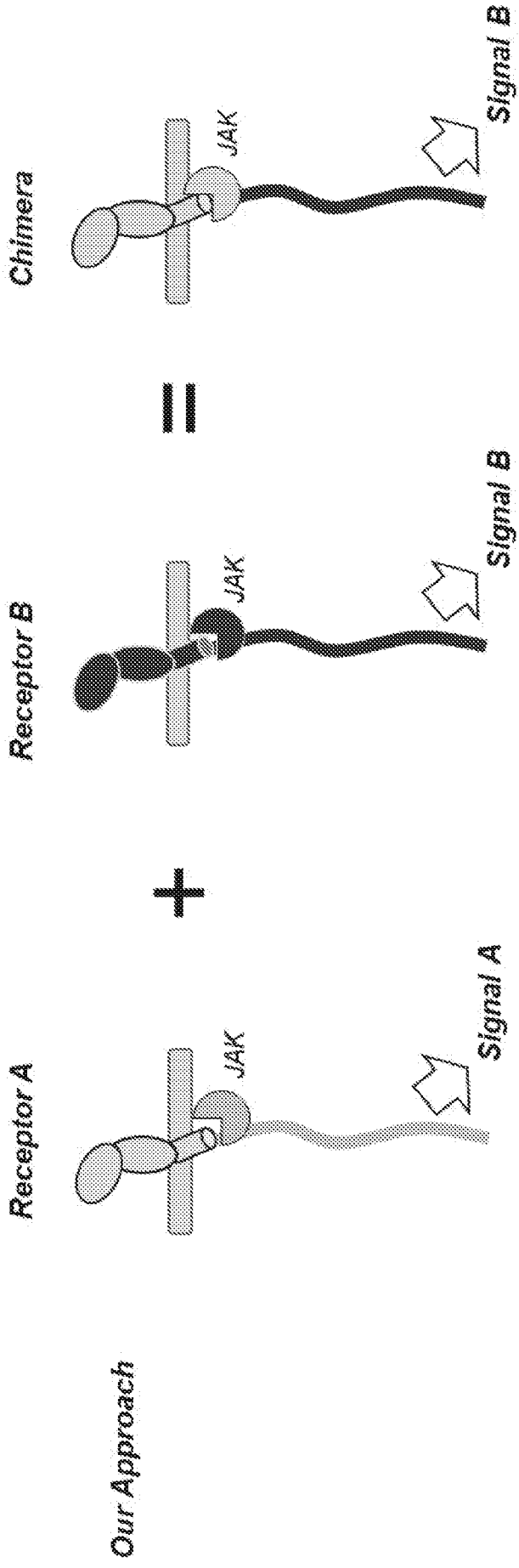

Our Approach
Receptor A
JAK
Signal A
+
Receptor B
JAK
Signal B
=
Chimera
JAK
Signal B

FIG. 10D

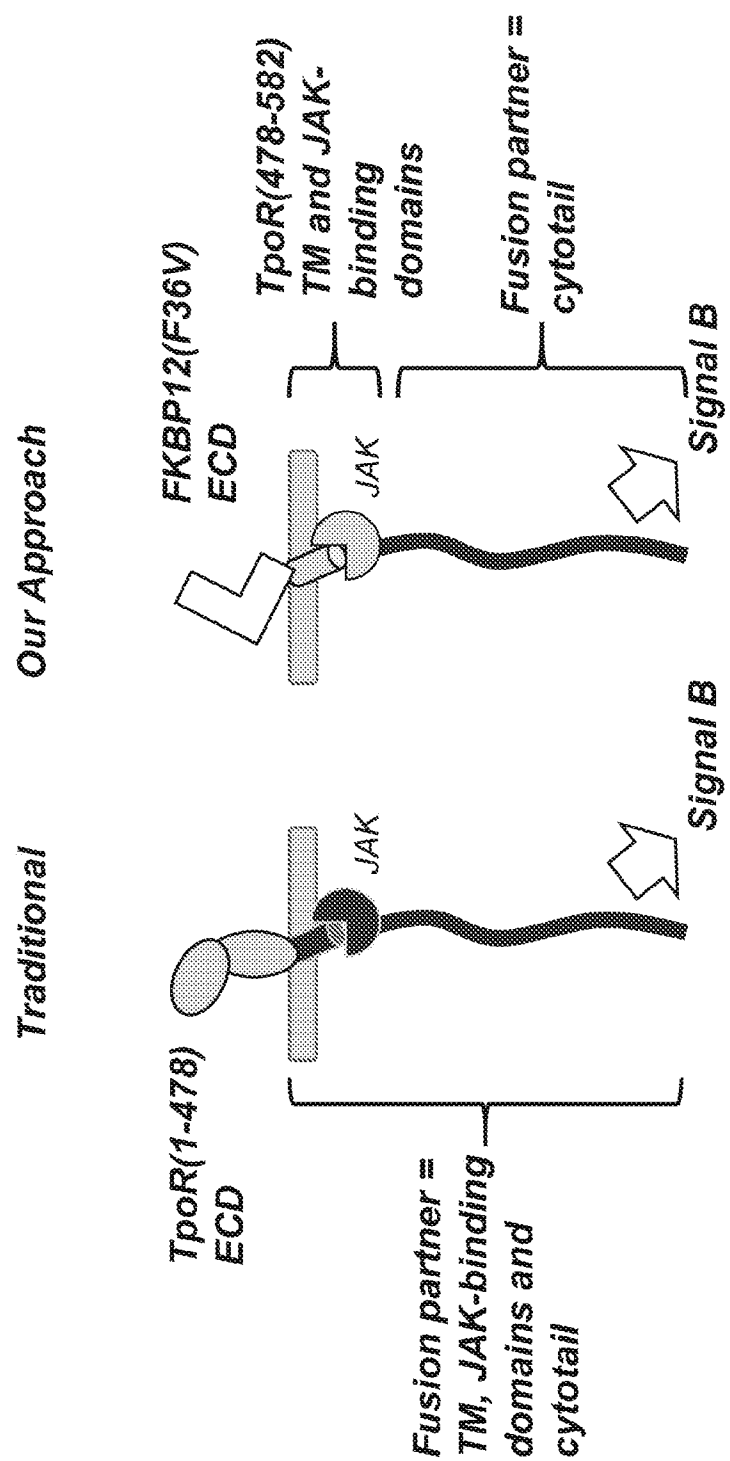

Traditional
TpoR(1-478)
ECD
JAK
Signal B
Fusion partner =
TM, JAK-binding
domains and
cytotail
Our Approach
FKBP12(F36V)
ECD
TpoR(478-582)
TM and JAK-
binding
domains
JAK
Fusion partner =
cytotail
Signal B

FIG. 10E

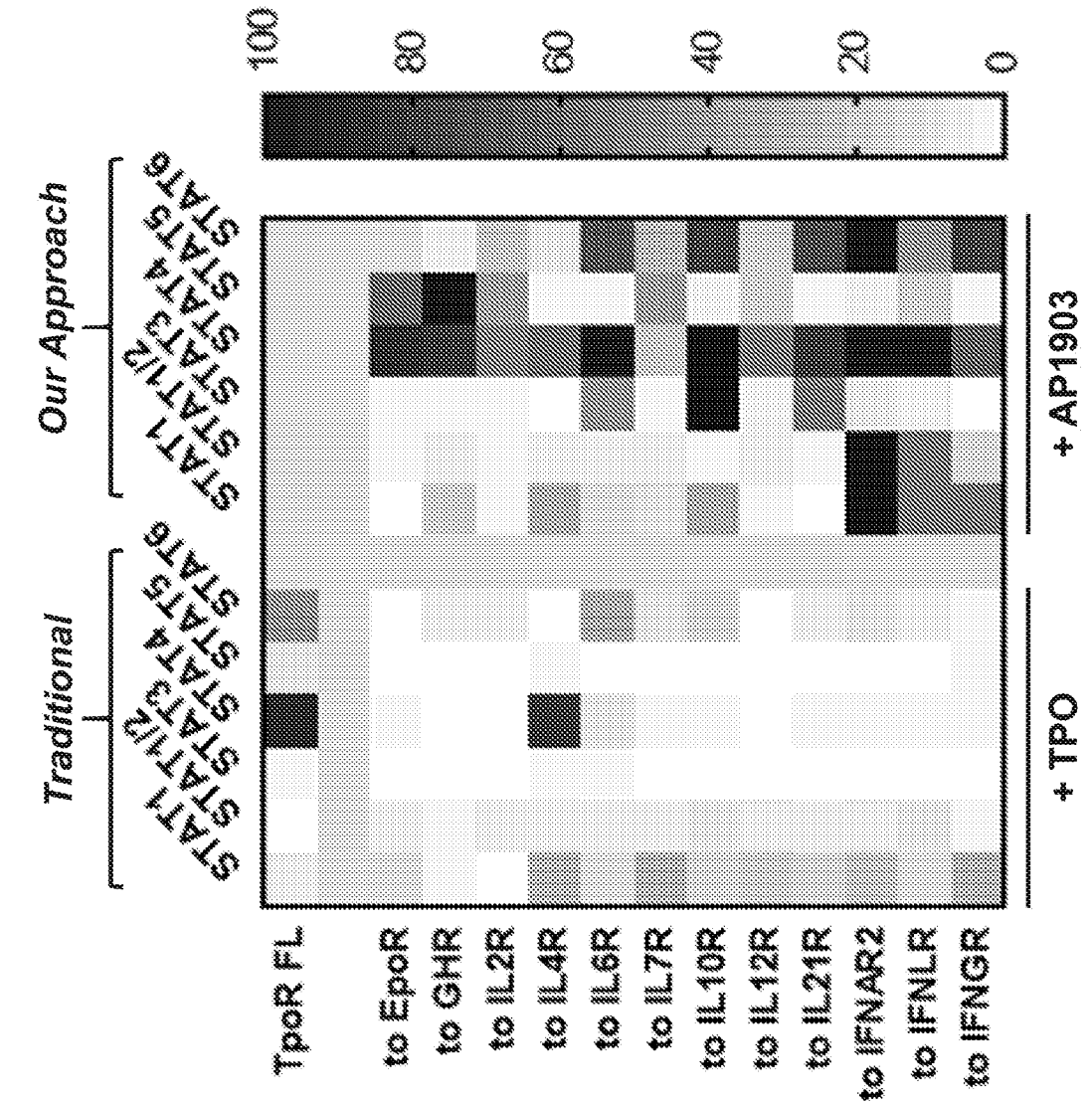
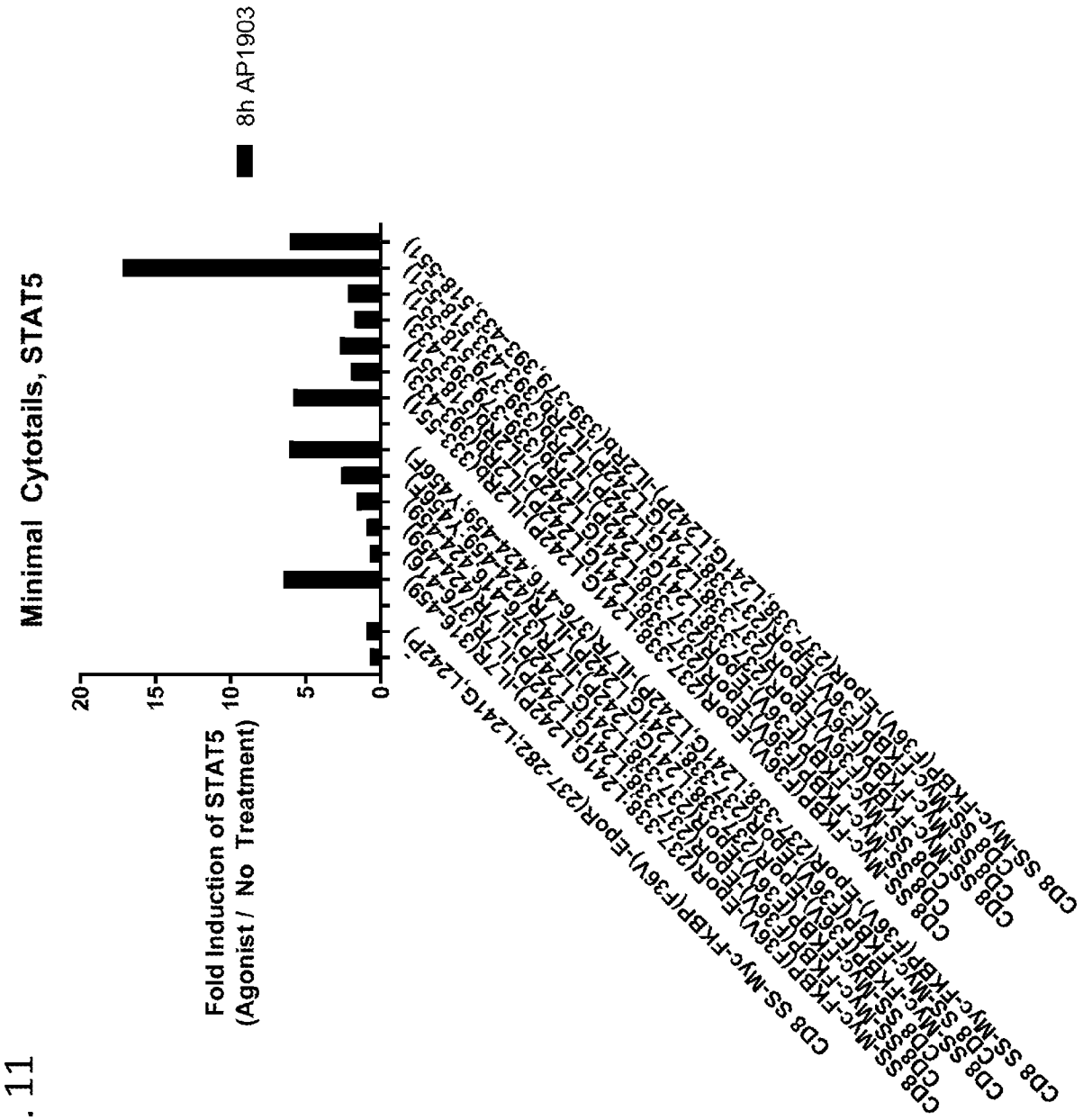

100
80
60
40
20
0
TpoR FL
to EpoR
to GHR
to IL2R
to IL4R
to IL6R
to IL7R
to IL10R
to IL12R
to IL21R
to IFNAR2
to IFNLR
to IFNGR
+ TPO
+ AP1903
Traditional
STAT1/2
STAT1/3
STAT3
STAT5
STAT6
Our Approach
STAT1/2
STAT1/3
STAT3
STAT5
STAT6

FIG. 10F

FIG. 11


Minimal Cytotails, STAT5
8h AP1903
Fold Induction of STAT5
(Agonist / No Treatment)
0
5
10
15
20
CD8 SS-Myc-FKBP(F36V)-EPOR(237-282:L241G,L242P)-IL7R(376-459)
CD8 SS-Myc-FKBP(F36V)-EPOR(237-338:L241G,L242P)-IL7R(376-459)
CD8 SS-Myc-FKBP(F36V)-EPOR(237-338:L241G,L242P)-IL7R(376-424,459,V456F)
CD8 SS-Myc-FKBP(F36V)-EPOR(237-338:L241G,L242P)-IL7R(376-424,459,V456F)
CD8 SS-Myc-FKBP(F36V)-EPOR(237-338:L241G,L242P)-IL2Rb(339-379,393-433,518-551

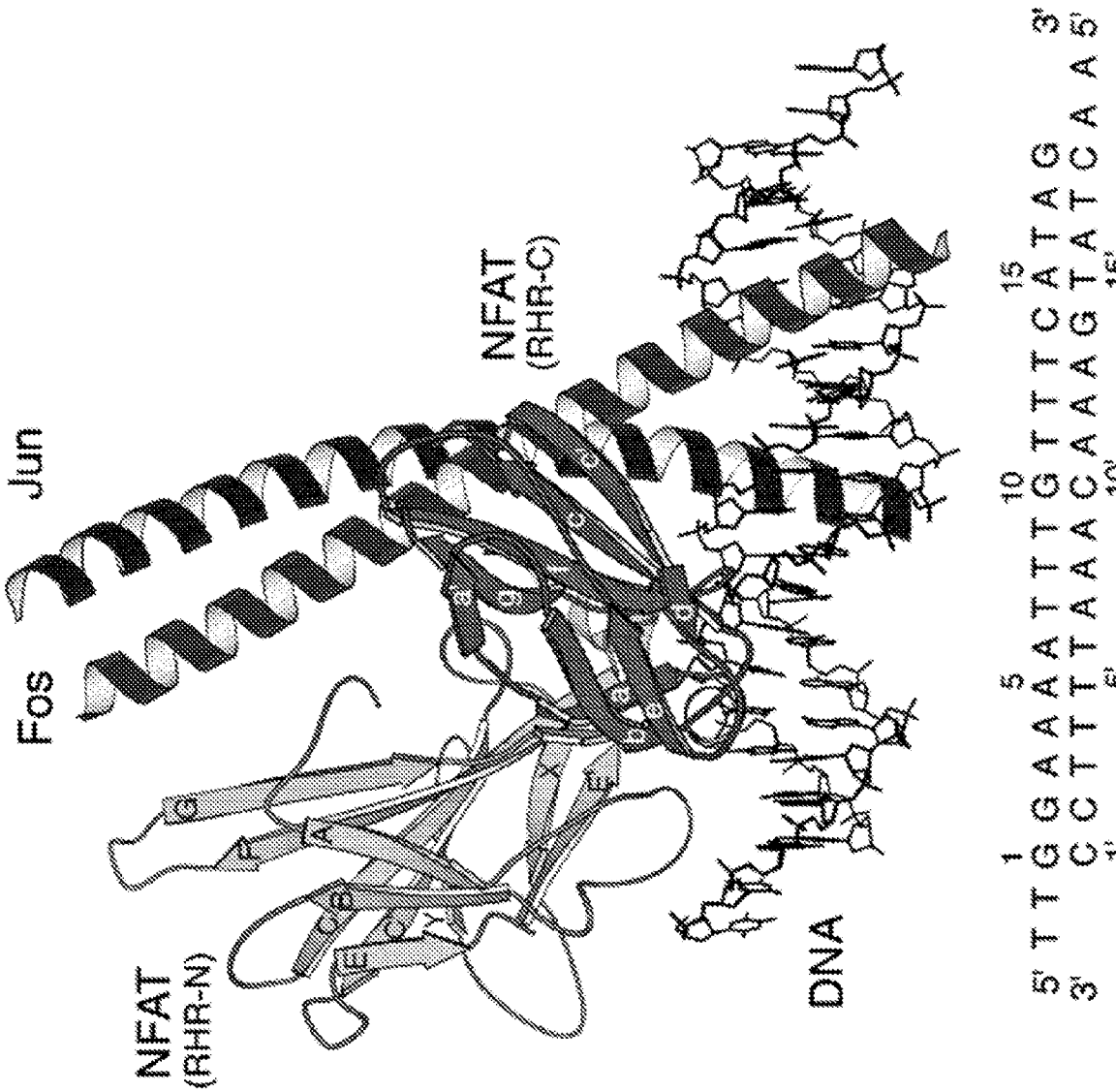

Jun
Fos
NFAT
(RHR-C)
NFAT
(RHR-N)
DNA
5' T T G G A A A T T T G T T T C A T A G 3'
3' C C T T T A A A C A A A G T A T C A A 5'
1 5 10 15
1' 5' 10' 15'

FIG. 12

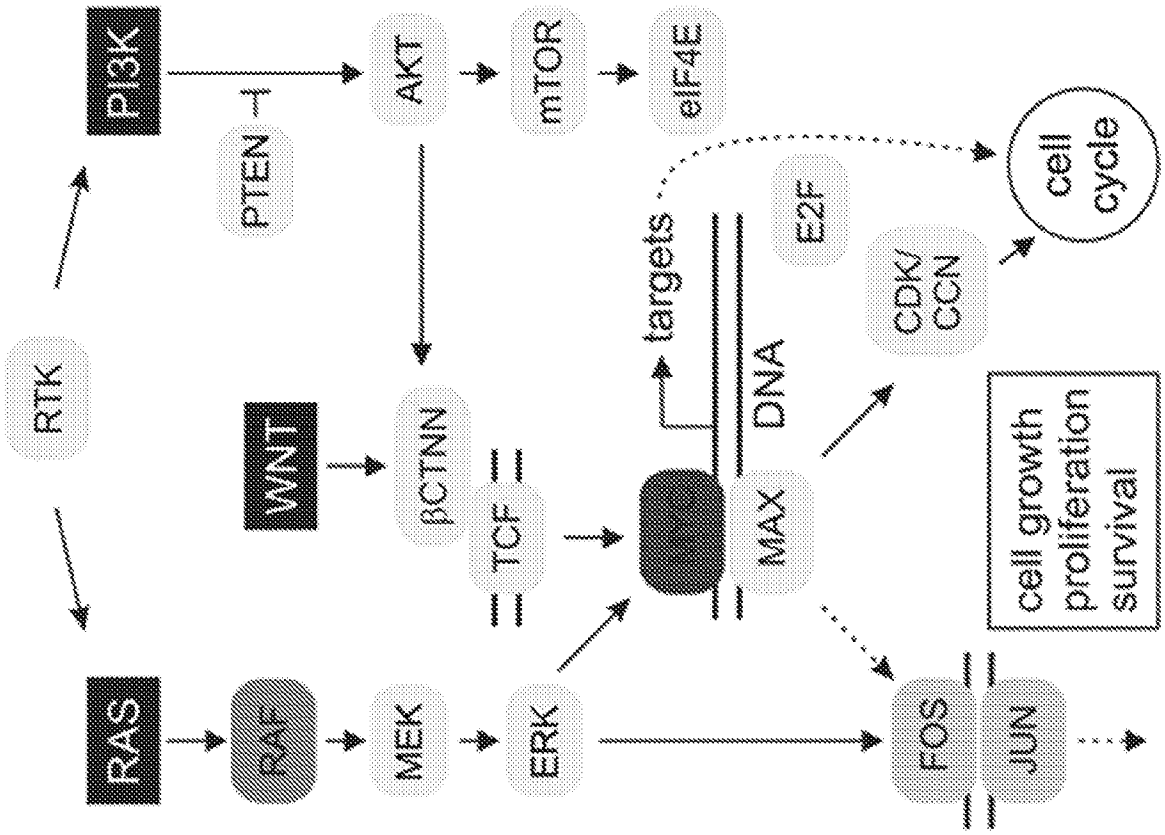
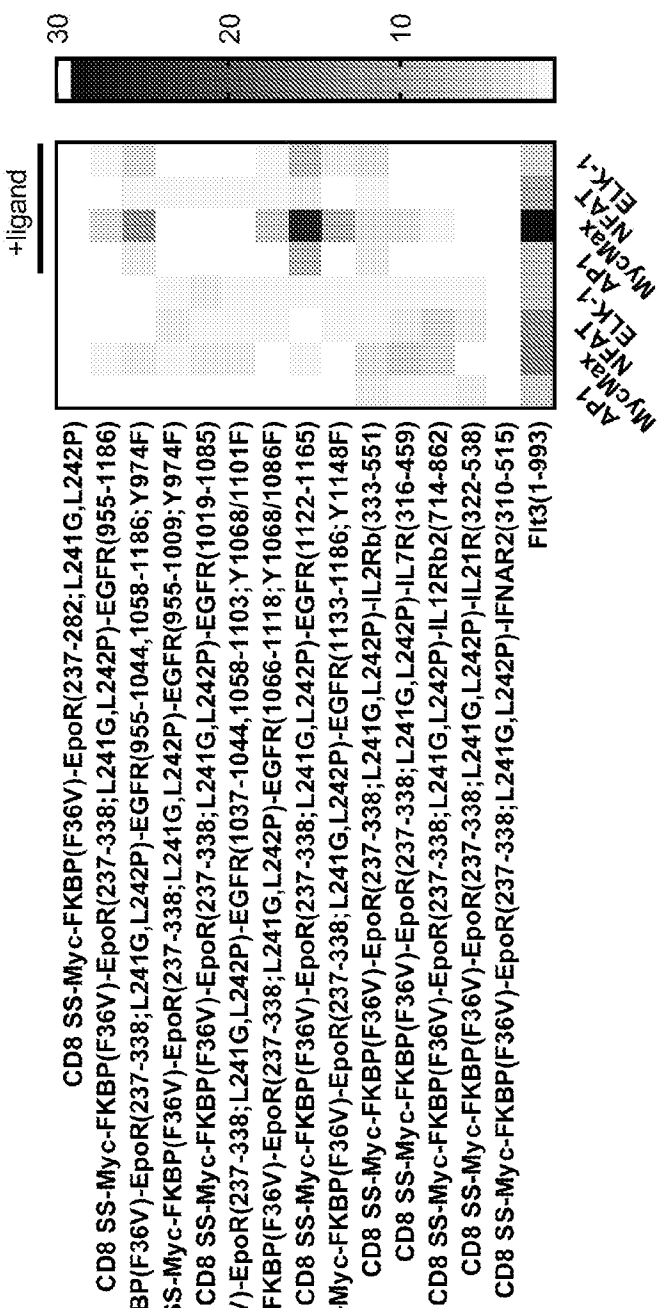

RTK
PI3K
PTEN
AKT
mTOR
eIF4E
WNT
βCTNN
TCF
targets
DNA
MAX
E2F
CDK/
CCN
cell
cycle
RAS
RAF
MEK
ERK
FOS
JUN
cell growth
proliferation
survival

FIG. 13

FIG. 14


30
20
10
+ligand
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1186)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1044,1058-1186;Y974F)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(955-1009;Y974F)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1019-1085)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1037-1044,1058-1103;Y1068/1101F)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1066-1118;Y1068/1086F)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1122-1165)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-EGFR(1133-1186;Y1148F)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
Flt3(1-993)
AP1
MycMax
NFAT
ELK-1
AP1
MycMax
NFAT
ELK-1

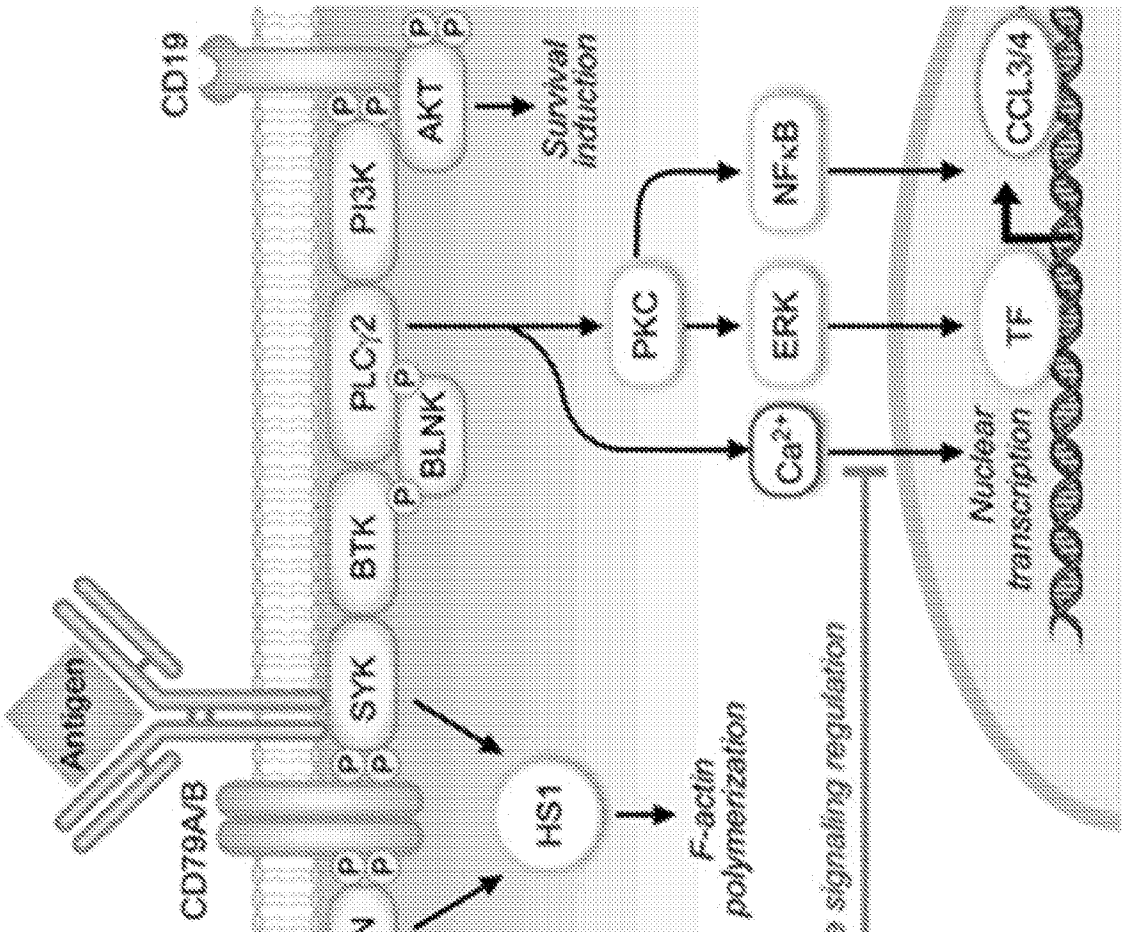
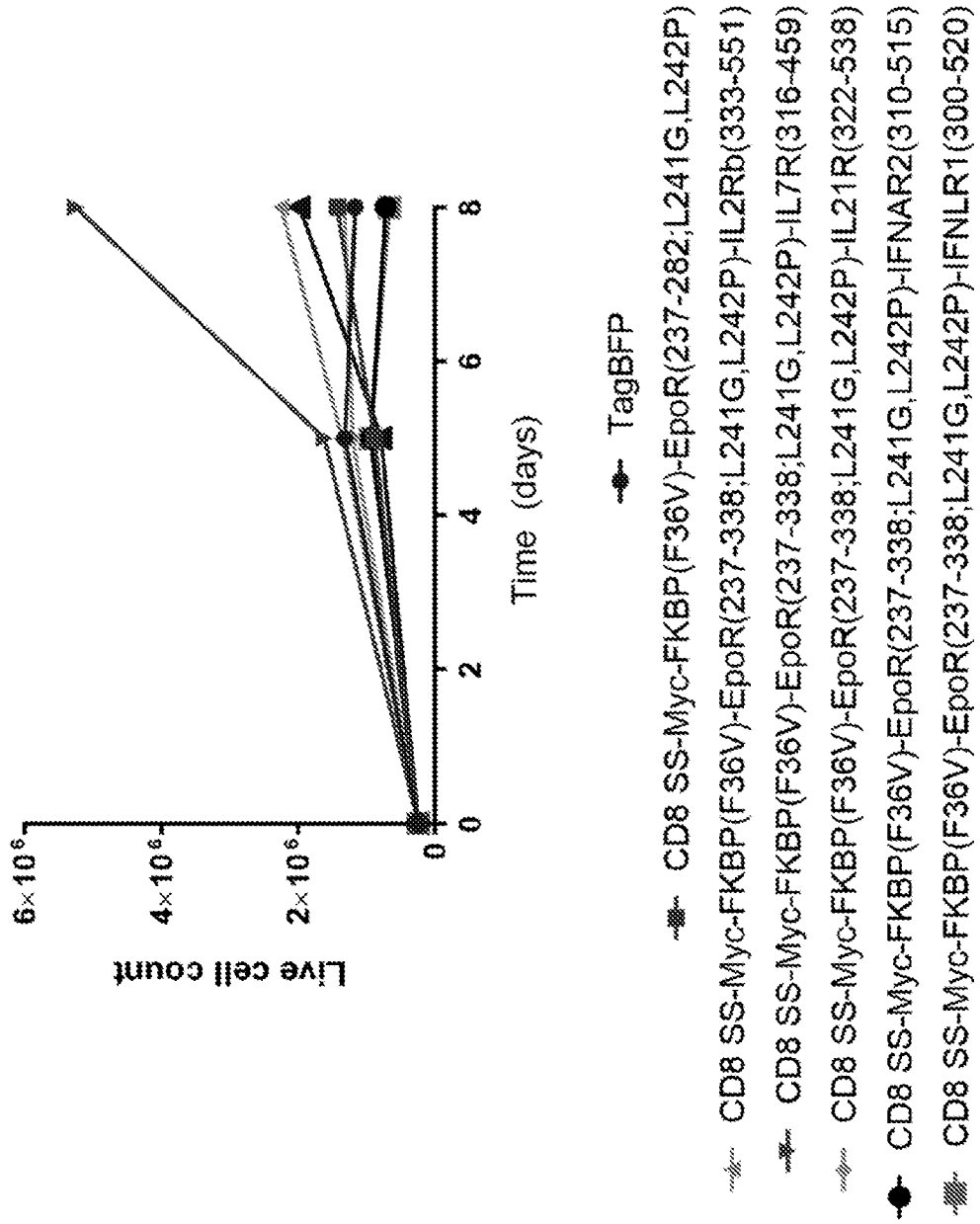

Antigen
CD79A/B
CD19
SYK
BTK
BLNK
PLCγ2
PI3K
AKT
Survival induction
HS1
F-actin polymerization
PKC
ERK
NFκB
Ca2+
Nuclear transcription
TF
CCL3/4
signaling regulation

FIG. 15

FIG. 16


Proliferation with AP1903
Live cell count
6×10^6
4×10^6
2×10^6
0
0
2
4
6
8
Time (days)
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
GoCART

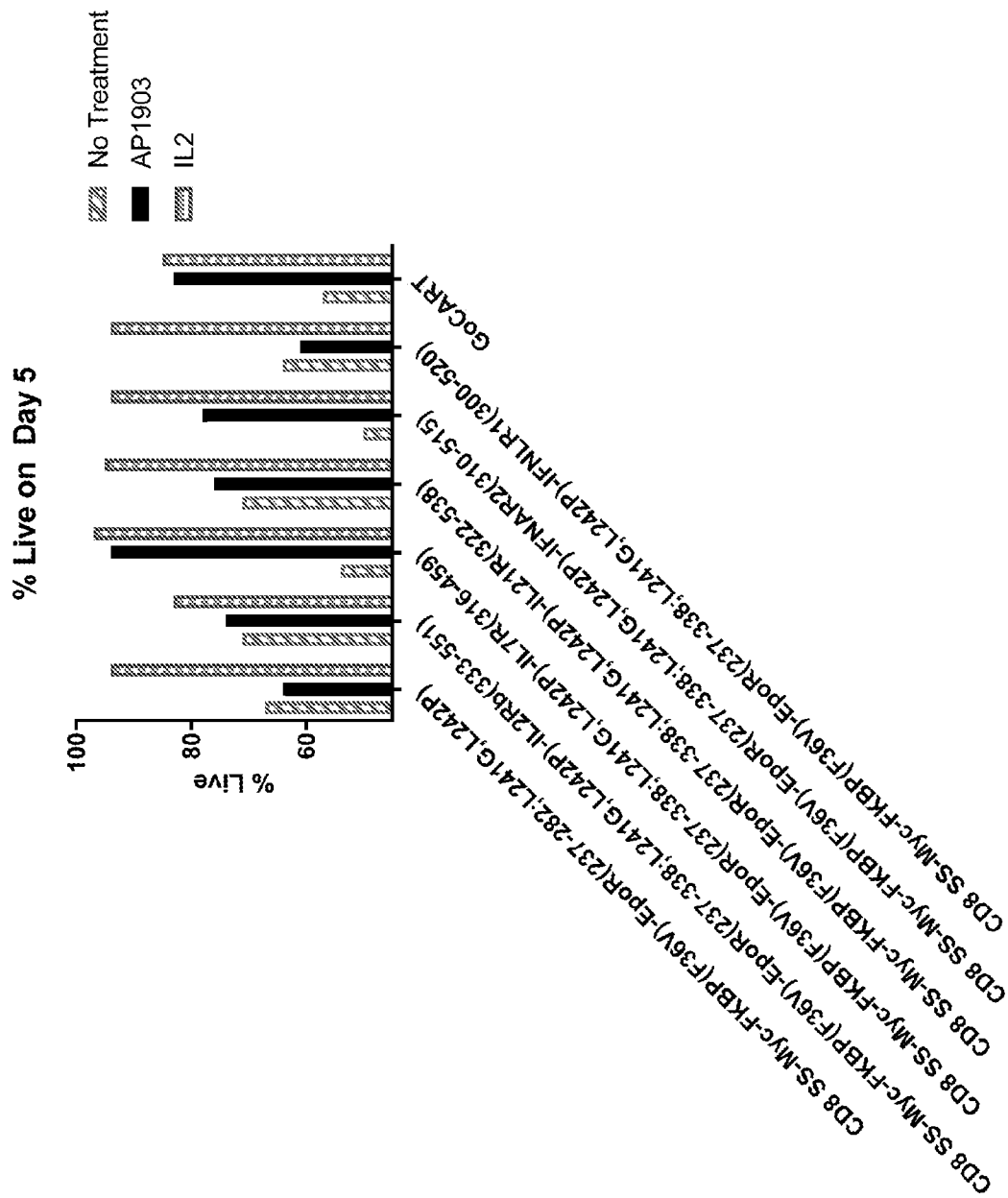

% Live on Day 5
% Live
100
80
60
No Treatment
AP1903
IL2
GoCART
CD8 SS-Myc-FKBP(F36V)-IFNLR1(300-520)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7Rb(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)

FIG. 17

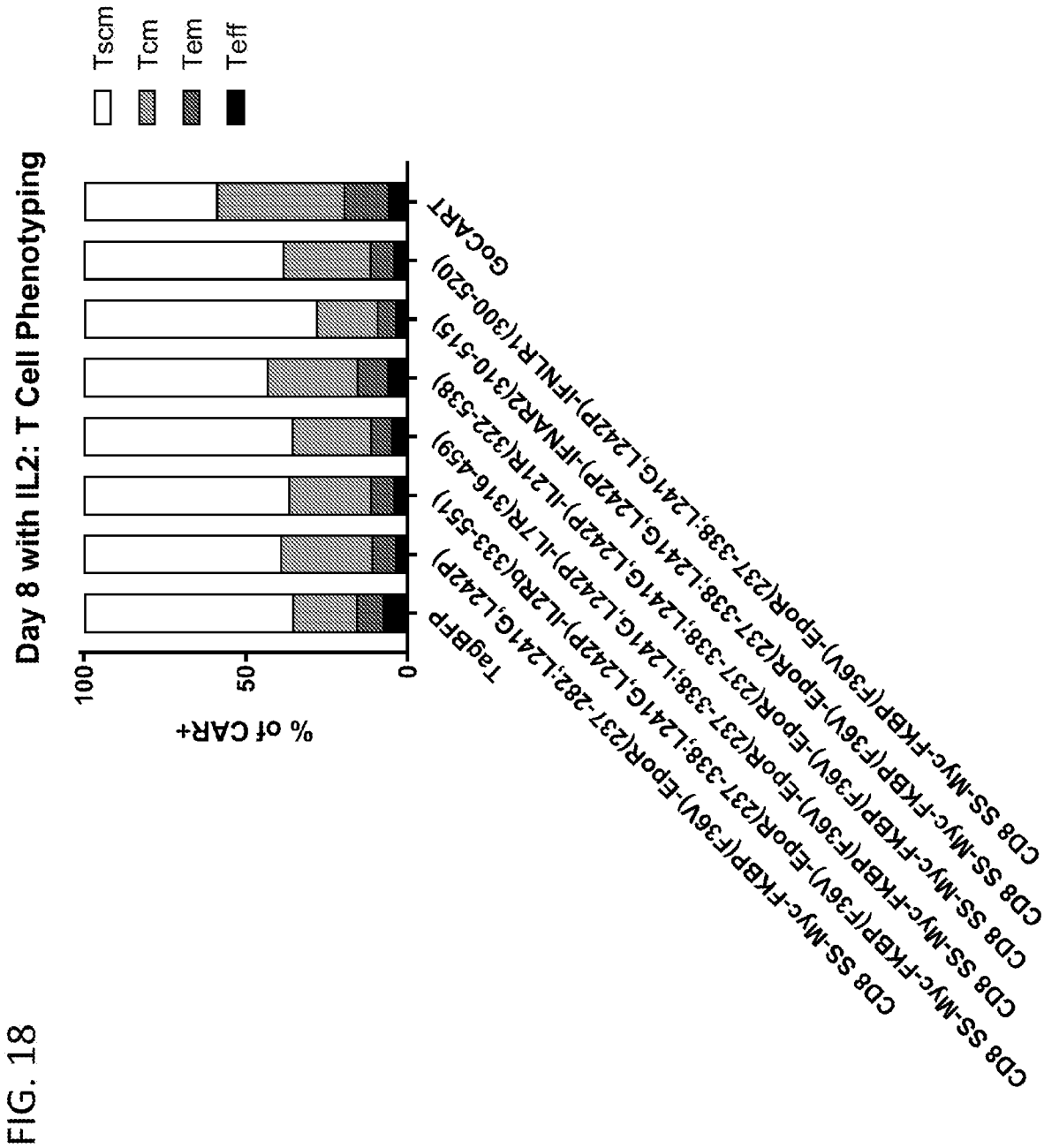

Day 8 with IL2: T Cell Phenotyping
Tscm
Tcm
Tem
Teff
% of CAR+
100
50
0
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L24G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24G,L242P)-IFNLR1(300-520)
GoCART

FIG. 18

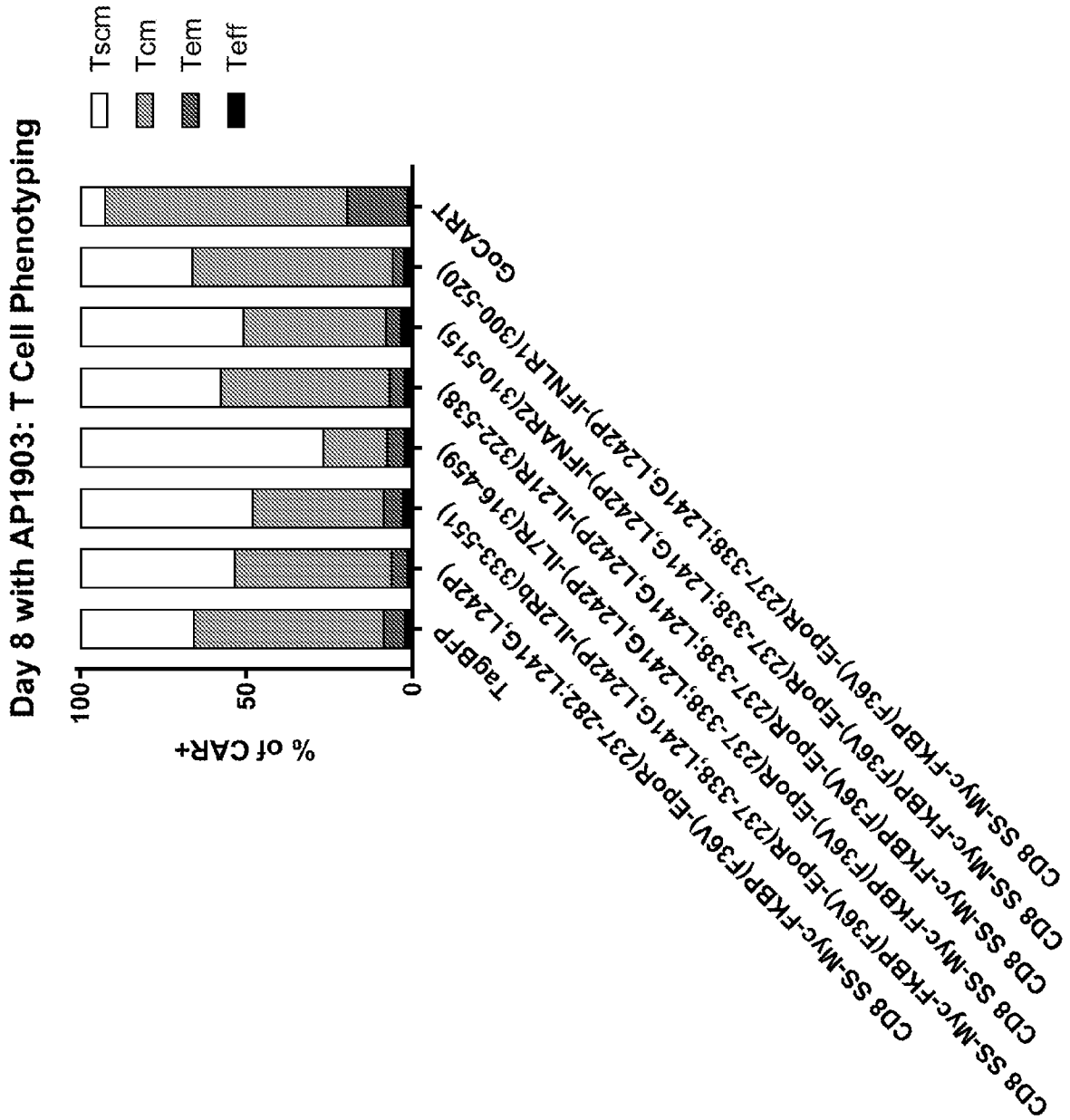

Day 8 with AP1903: T Cell Phenotyping
Tscm
Tcm
Tem
Teff
% of CAR+
100
50
0
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L24IG,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24IG,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24IG,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24IG,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24IG,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L24IG,L242P)-IFNLR1(300-520)
GoCART

FIG. 19

FIG. 20

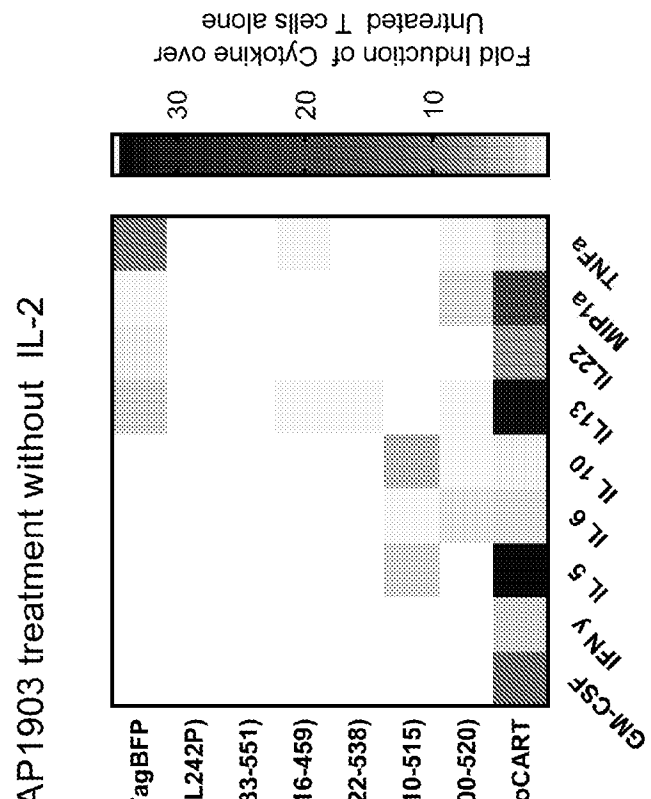

2 Days of AP1903 treatment without IL-2
Fold Induction of Cytokine over Untreated T cells alone
30
20
10
GM-CSF
IFNγ
IL 5
IL 6
IL 10
IL13
IL22
MIP1a
TNFa
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
GoCART

FIG. 21

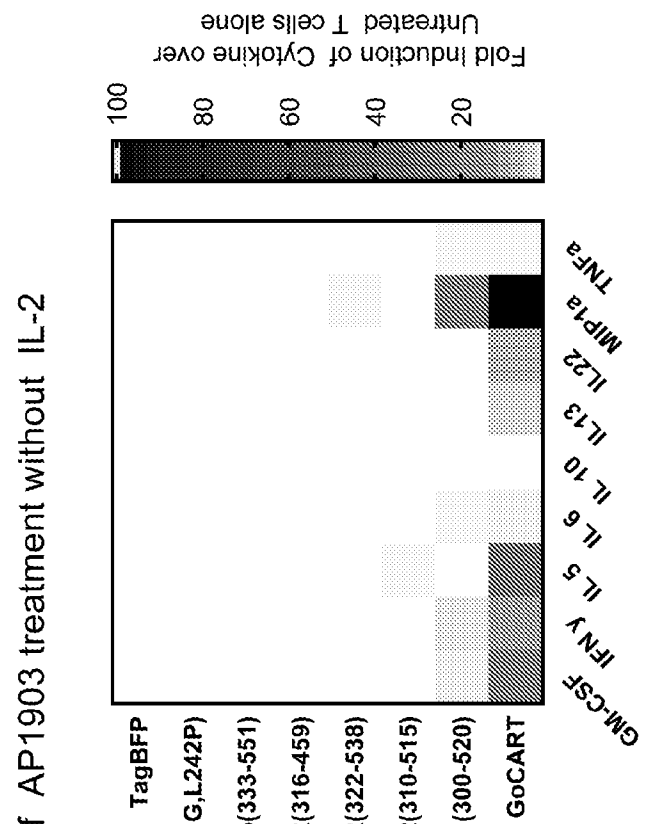

8 Days of AP1903 treatment without IL-2
Fold Induction of Cytokine over Untreated T cells alone
100
80
60
40
20
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
GoCART
GM-CSF
IFNγ
IL-5
IL-6
IL-10
IL-13
IL-22
MIP1a
TNFa

FIG. 22

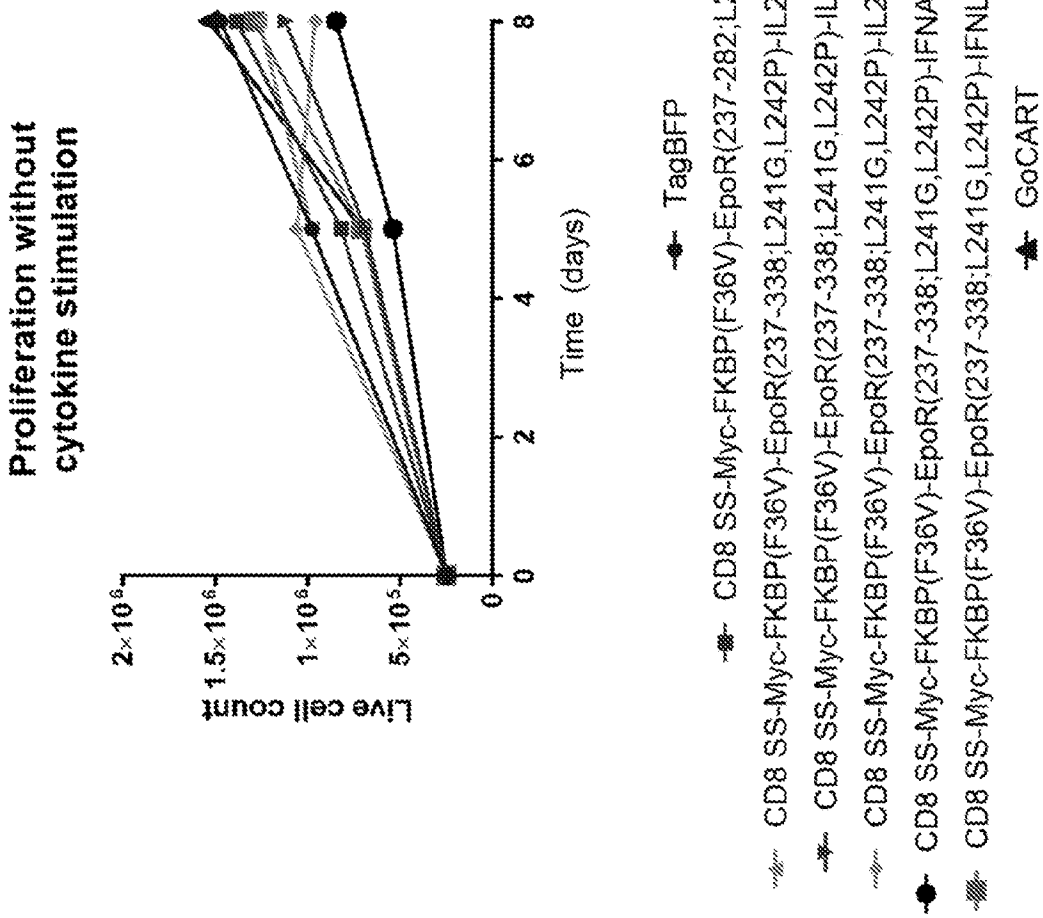

Proliferation without cytokine stimulation
Live cell count
2×10^6
1.5×10^6
1×10^6
5×10^5
0
0
2
4
6
8
Time (days)
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
GoCART

FIG. 23

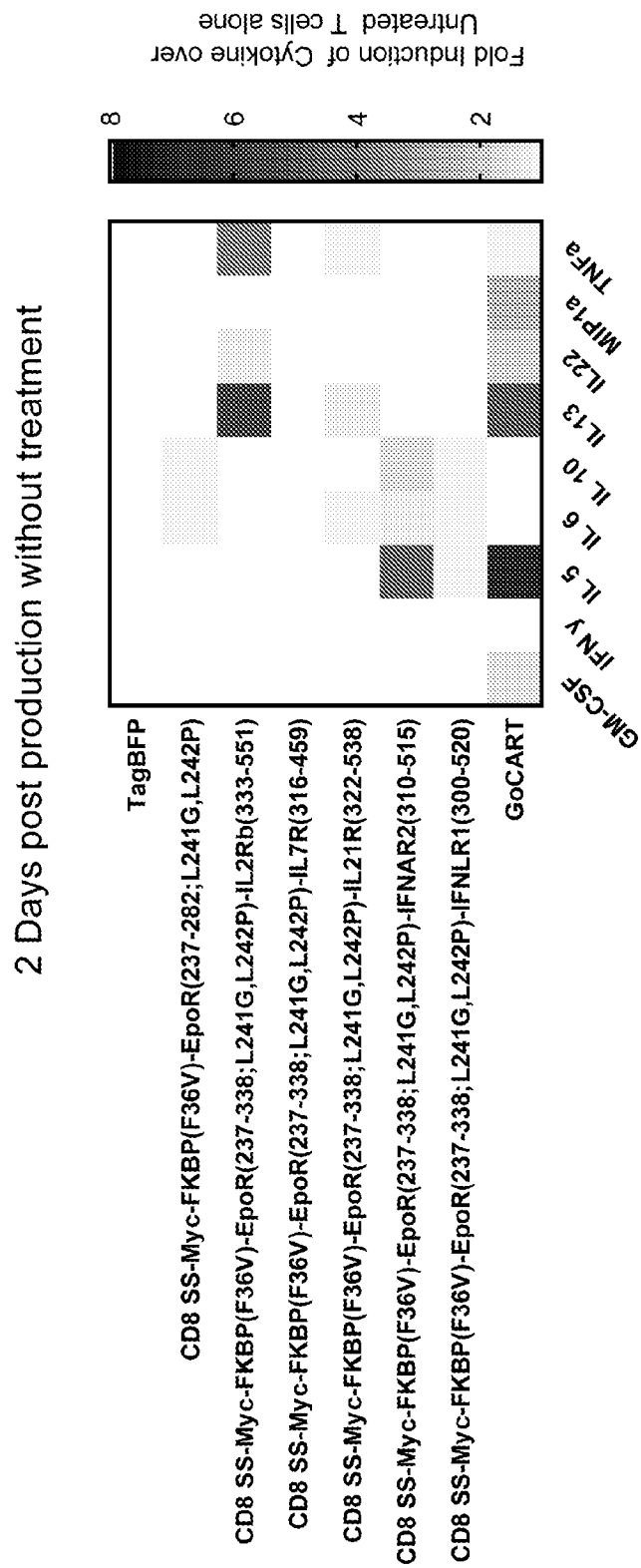

2 Days post production without treatment
Fold Induction of Cytokine over Untreated T cells alone
8
6
4
2
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
GoCART
GM-CSF
IFNγ
IL-5
IL-6
IL-10
IL-13
IL-22
MIP1a
TNFa

FIG. 24

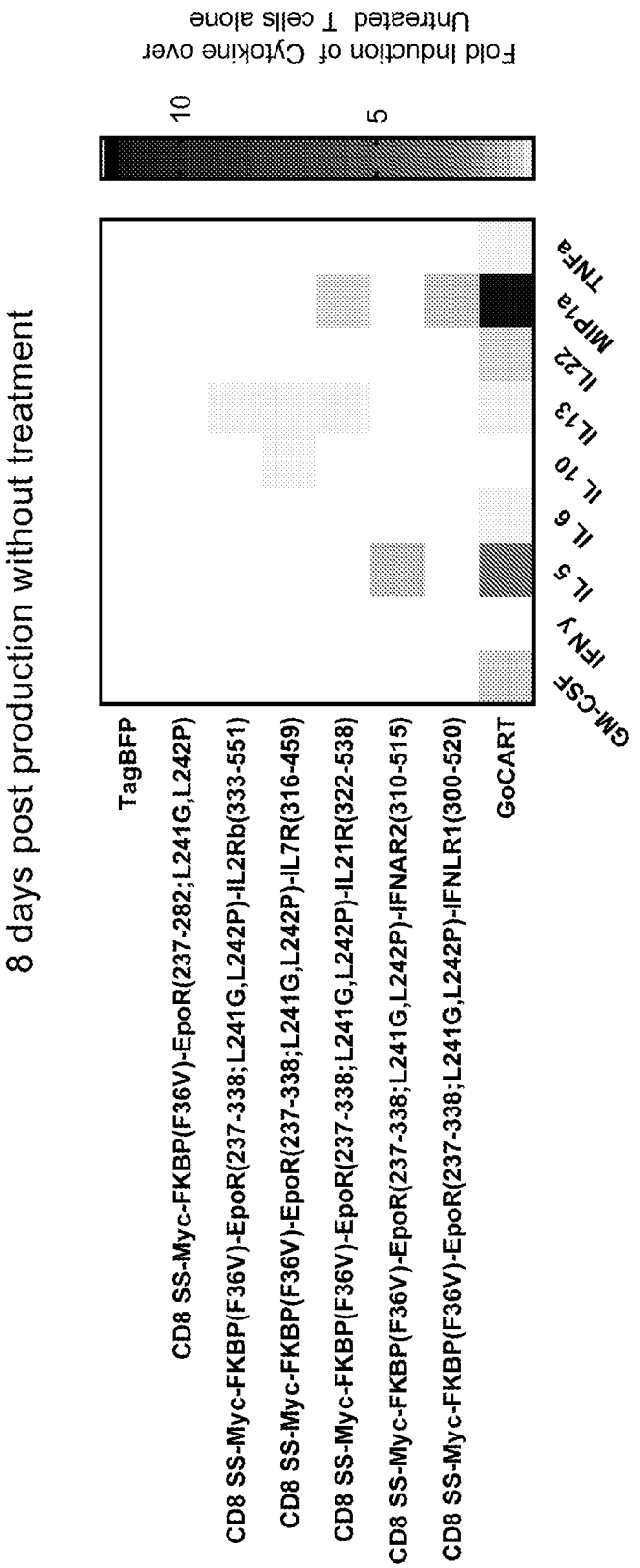

8 days post production without treatment
Fold Induction of Cytokine over Untreated T cells alone
10
5
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
GoCART
GM-CSF
IFN γ
IL 5
IL 6
IL 10
IL 13
IL22
MIP1a
TNFa

FIG. 25

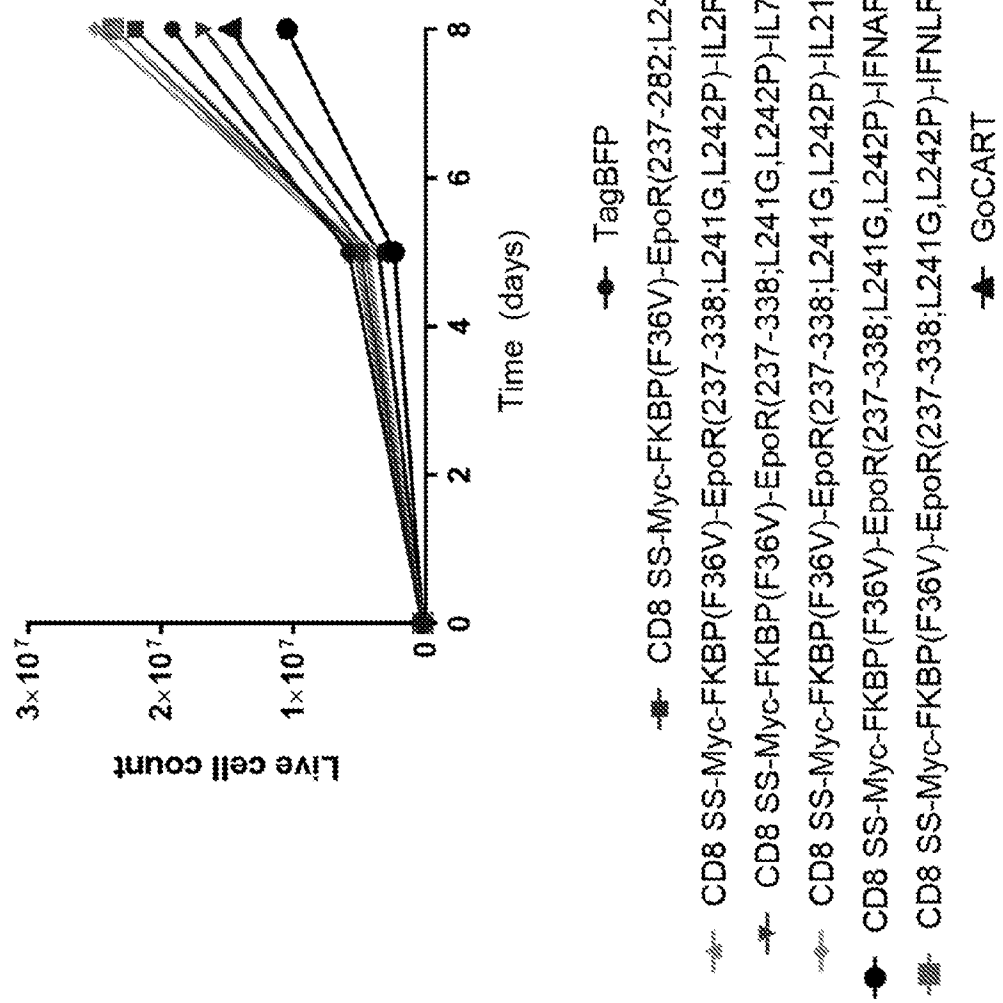
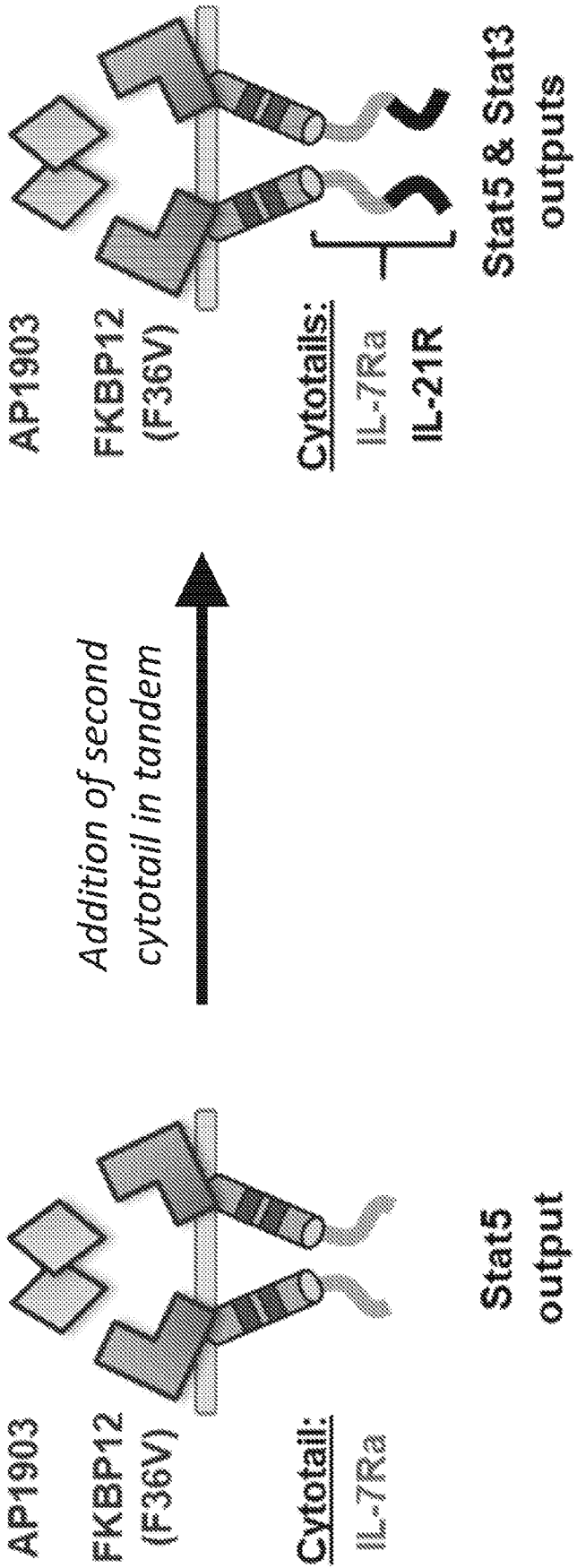

Proliferation with IL2
Live cell count
3×10^7
2×10^7
1×10^7
0
0
2
4
6
8
Time (days)
TagBFP
CD8 SS-Myc-FKBP(F36V)-EpoR(237-282;L241G,L242P)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)
CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNLR1(300-520)
GoCART

FIG. 26


AP1903
FKBP12
(F36V)
Cytotail:
IL-7Rα
Stat5
output
Addition of second
cytotail in tandem
AP1903
FKBP12
(F36V)
Cytotails:
IL-7Rα
IL-21R
Stat5 & Stat3
outputs

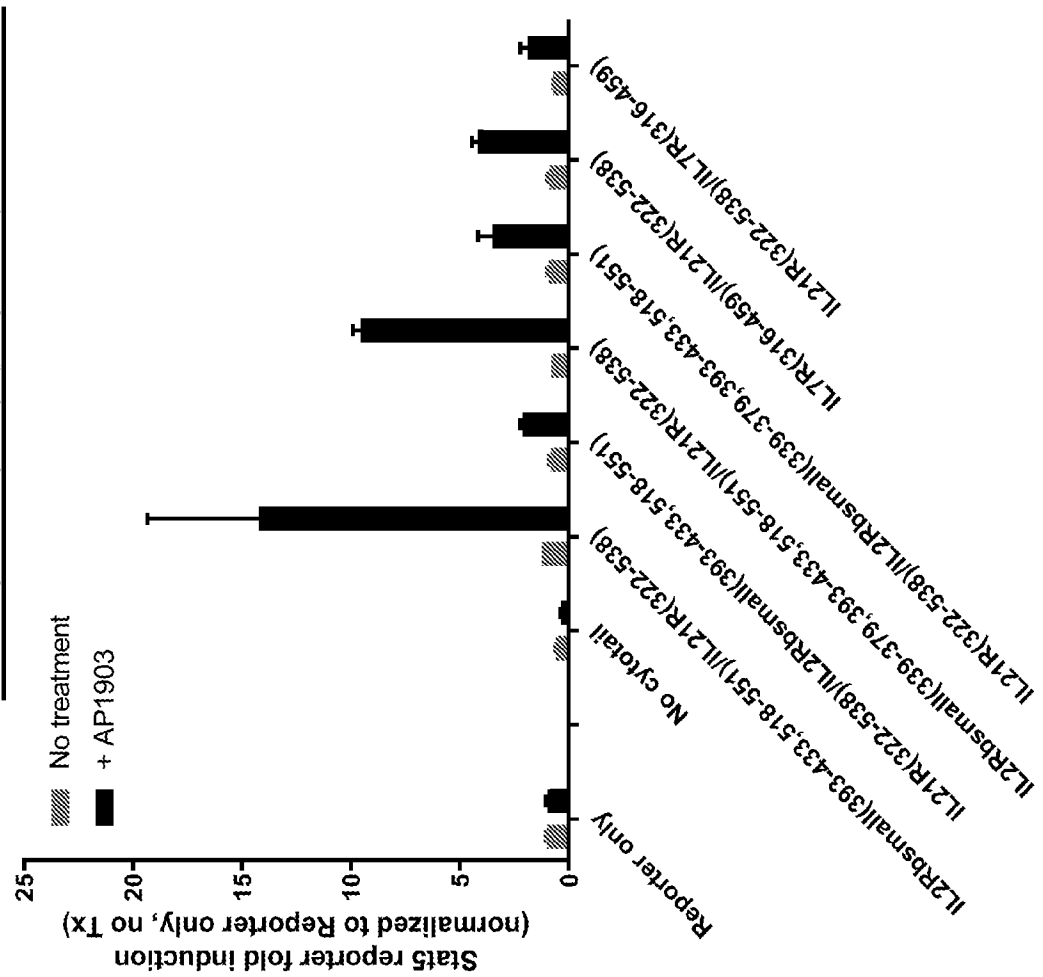

SS-Myc-FKBP(F36V)-TpoR(478-582)-CYTOTAILS
No treatment
+ AP1903
Stat5 reporter fold induction
(normalized to Reporter only, no Tx)
25
20
15
10
5
0
Reporter only
No cytotail
IL2Rbsmall(393-433,518-551)/IL21R(322-538)
IL21R(322-538)/IL2Rbsmall(393-433,518-551)
IL2Rbsmall(339-379,393-433,518-551)/IL21R(322-538)
IL7R(316-459)/IL21R(322-538)
IL21R(322-538)/IL7R(316-459)

FIG. 27A

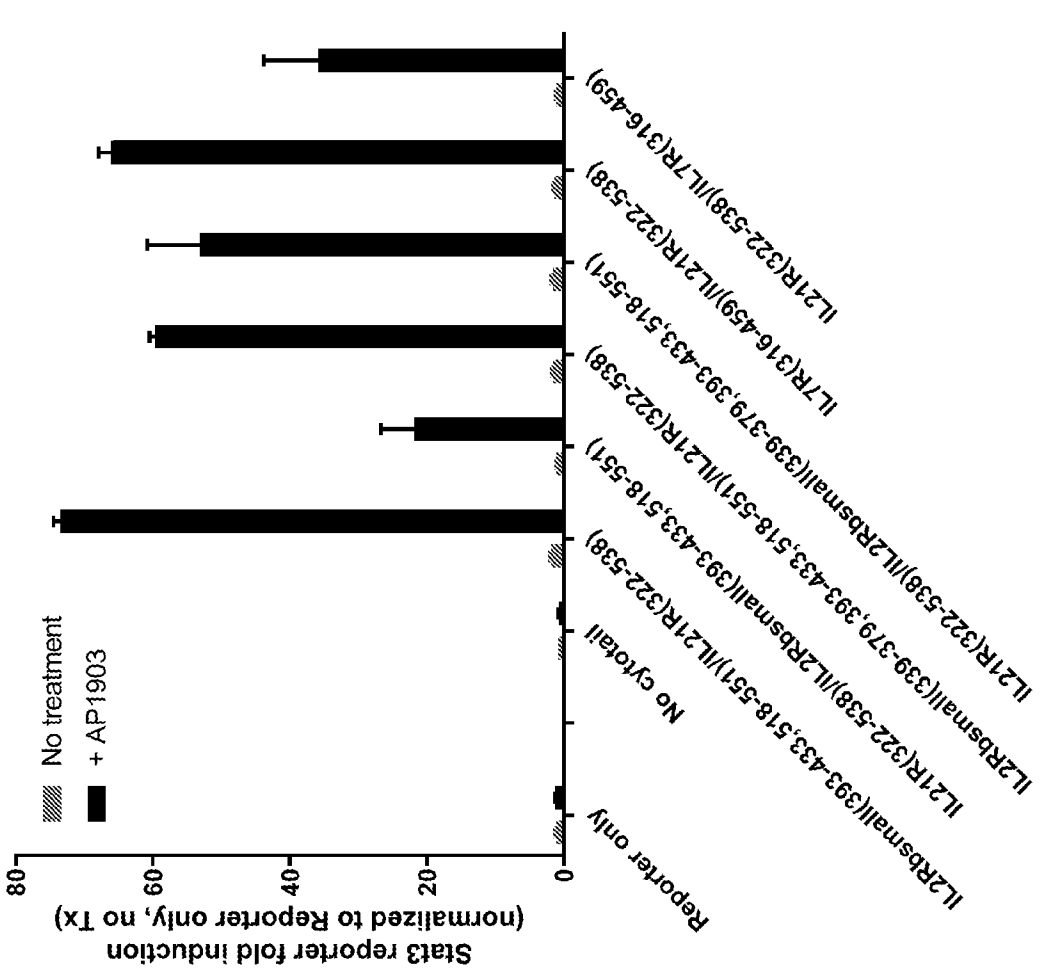

SS-Myc-FKBP(F36V)-TpoR(478-582)-CYTOTAILS
No treatment
+ AP1903
Stat3 reporter fold induction
(normalized to Reporter only, no Tx)
0
20
40
60
80
Reporter only
No cytotail
IL2Rbsmall(393-433,518-551)/IL21R(322-538)
IL21R(322-538)/IL2Rbsmall(393-433,518-551)
IL2Rbsmall(339-379,393-433,518-551)/IL21R(322-538)
IL2Rbsmall(339-379,393-433,518-551)
IL7R(316-459)/IL21R(322-538)
IL21R(322-538)/IL7R(316-459)

FIG. 27B

FIG. 28A

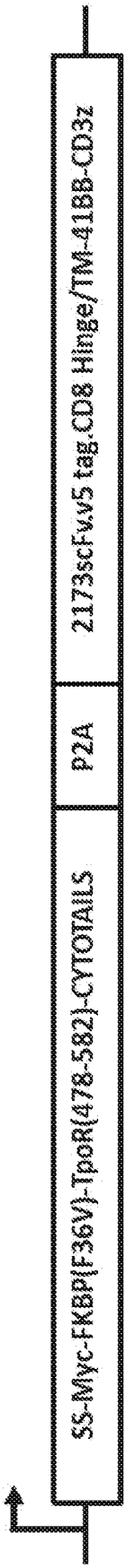


FIG. 28B

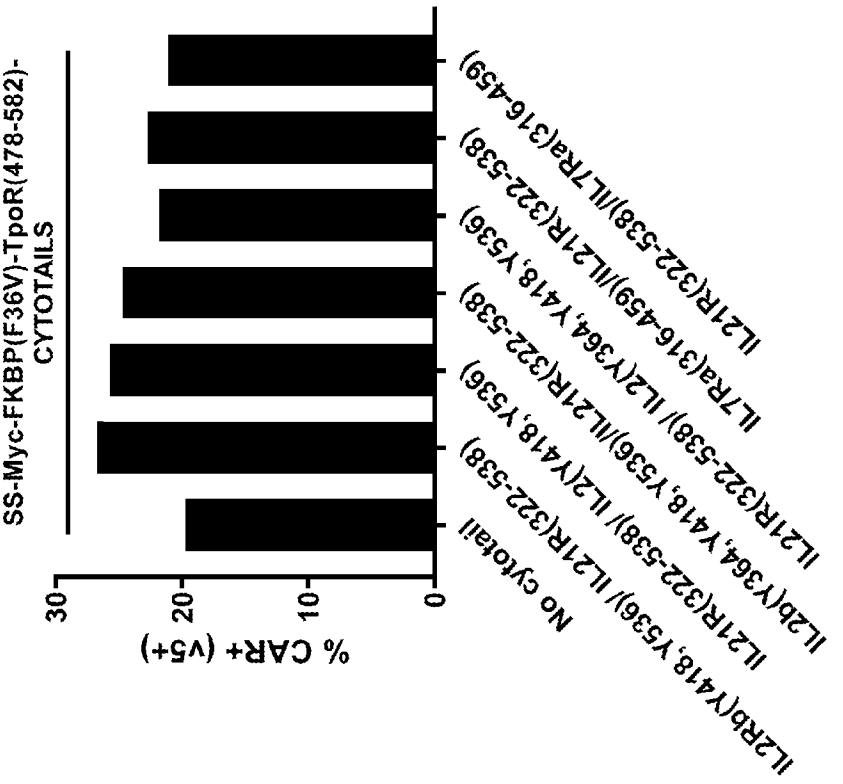
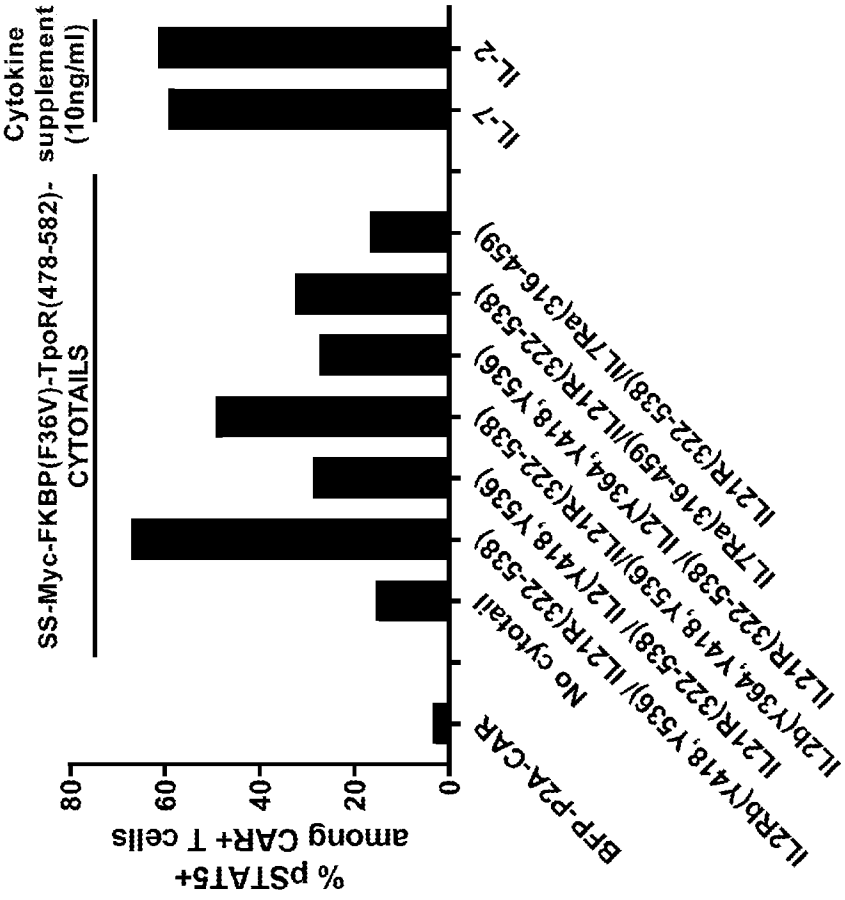


FIG. 28C



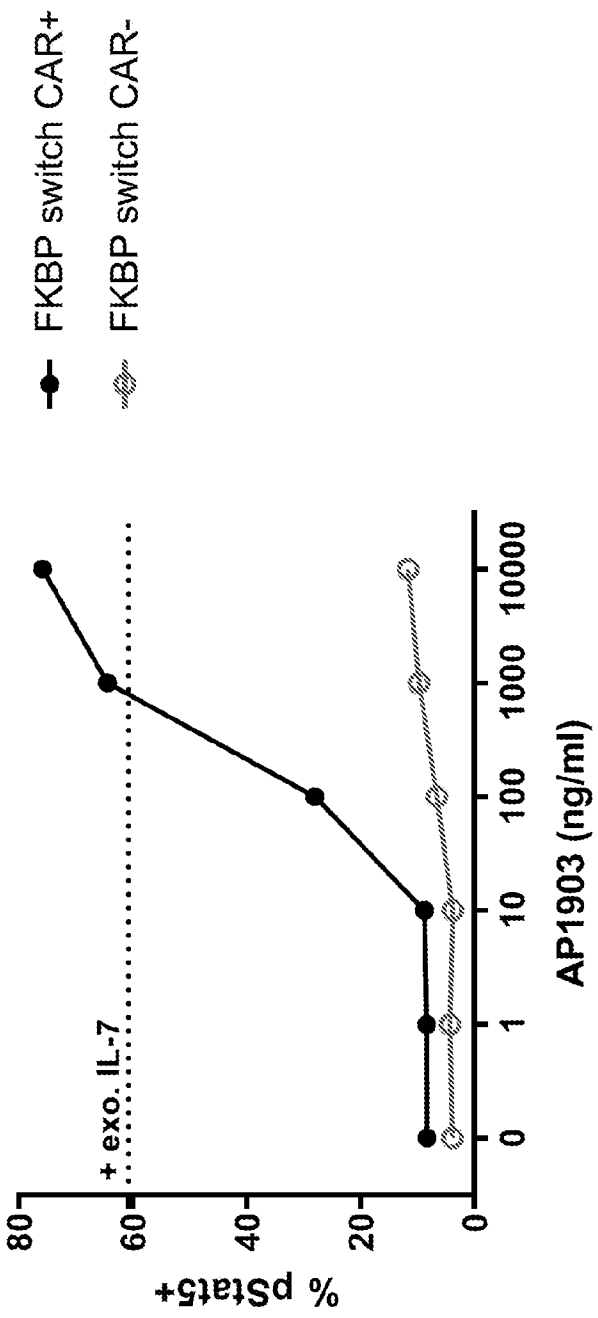

FKBP switch CAR+
FKBP switch CAR-
+ exo. IL-7
% pStat5+
0
20
40
60
80
0
1
10
100
1000
10000
AP1903 (ng/ml)

FIG. 29

FIG. 30A

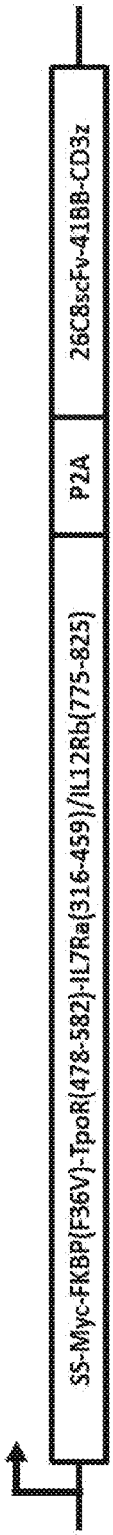


FIG. 30B

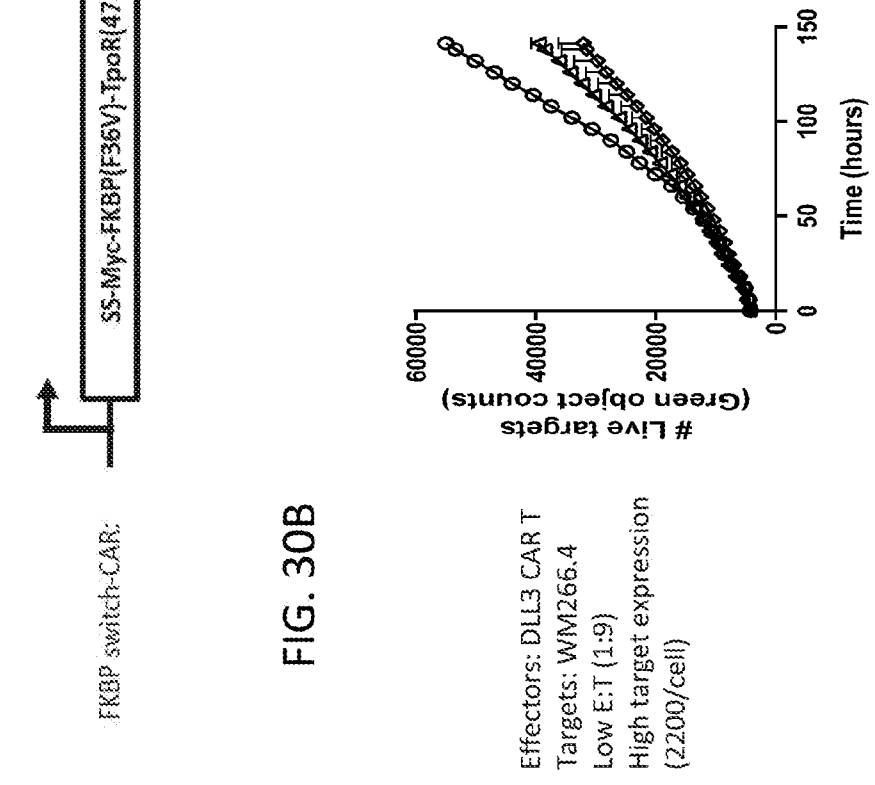


FIG. 30C

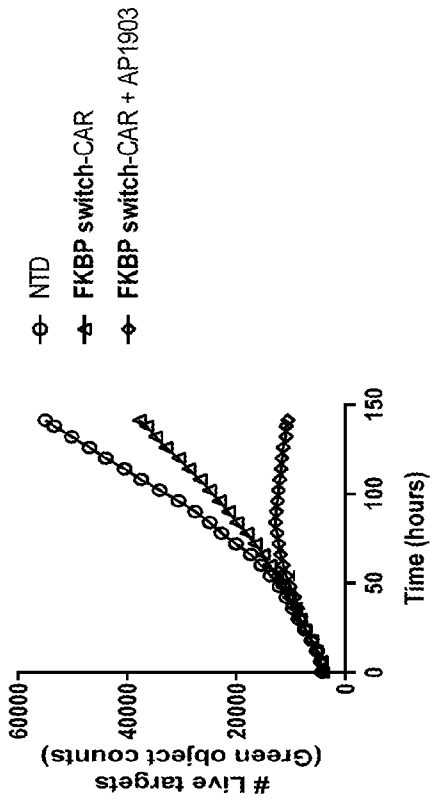


FIG. 30D

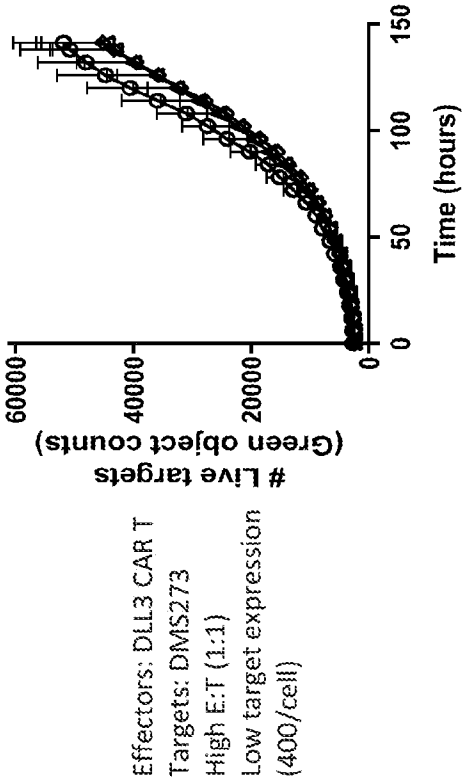


FIG. 30E

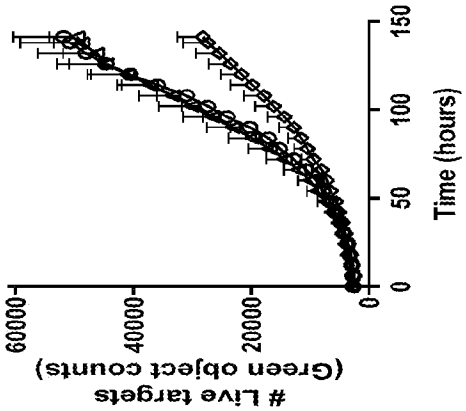


FIG. 31A

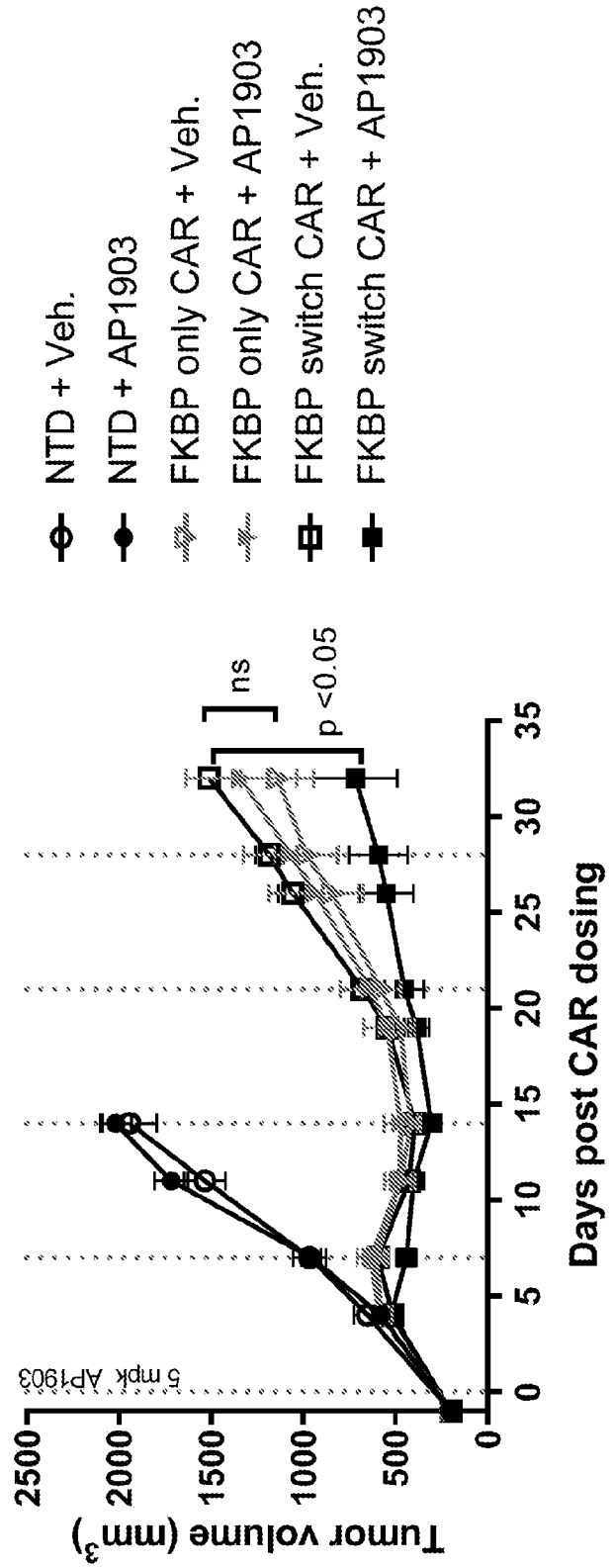

NTD + Veh.
NTD + AP1903
FKBP only CAR + Veh.
FKBP only CAR + AP1903
FKBP switch CAR + Veh.
FKBP switch CAR + AP1903
ns
p <0.05
5 mpk AP1903
Tumor volume (mm3)
2500
2000
1500
1000
500
0
0
5
10
15
20
25
30
35
Days post CAR dosing

FIG. 31B

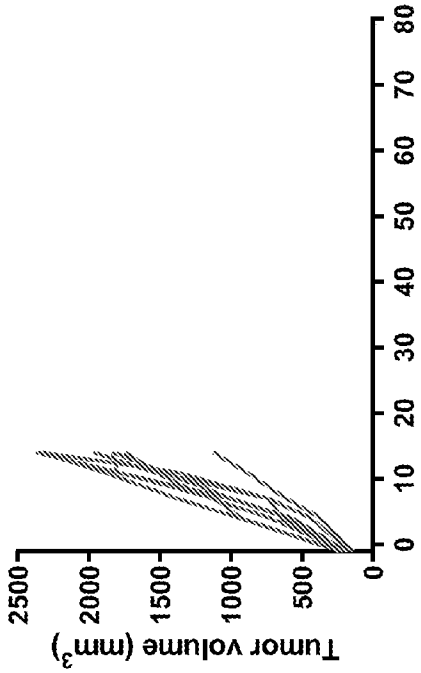
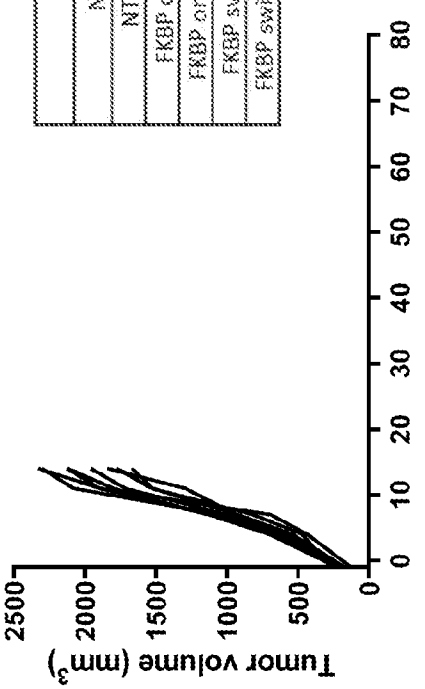


FIG. 31C



Group	% tumor-free
NTD + Veh.	0%
NTD + AP1903	0%
FKBP only CAR + Veh.	25%
FKBP only CAR + AP1903	0%
FKBP switch CAR + Veh.	0%
FKBP switch CAR + AP1903	62.5%

FIG. 31D

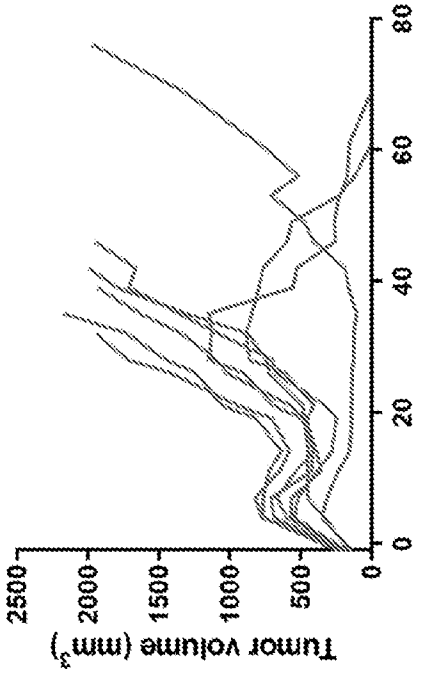


FIG. 31E

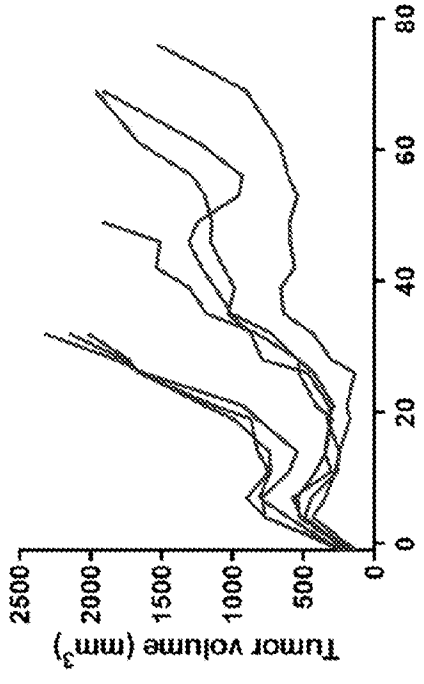


FIG. 31F

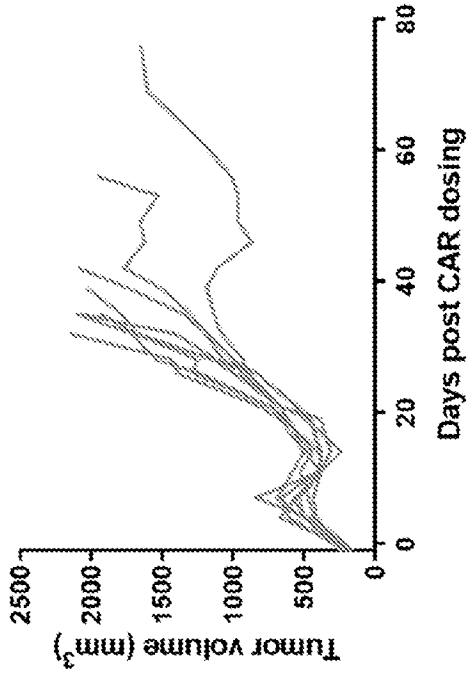
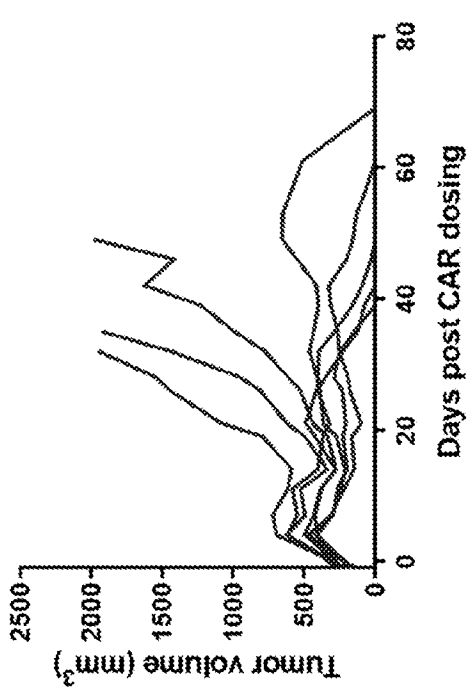


FIG. 31G



Group	% tumor-free
NTD + Veh.	0%
NTD + AP1903	0%
FKBP only CAR + Veh.	25%
FKBP only CAR + AP1903	0%
FKBP switch CAR + Veh.	0%
FKBP switch CAR + AP1903	62.5%

FIG. 31H

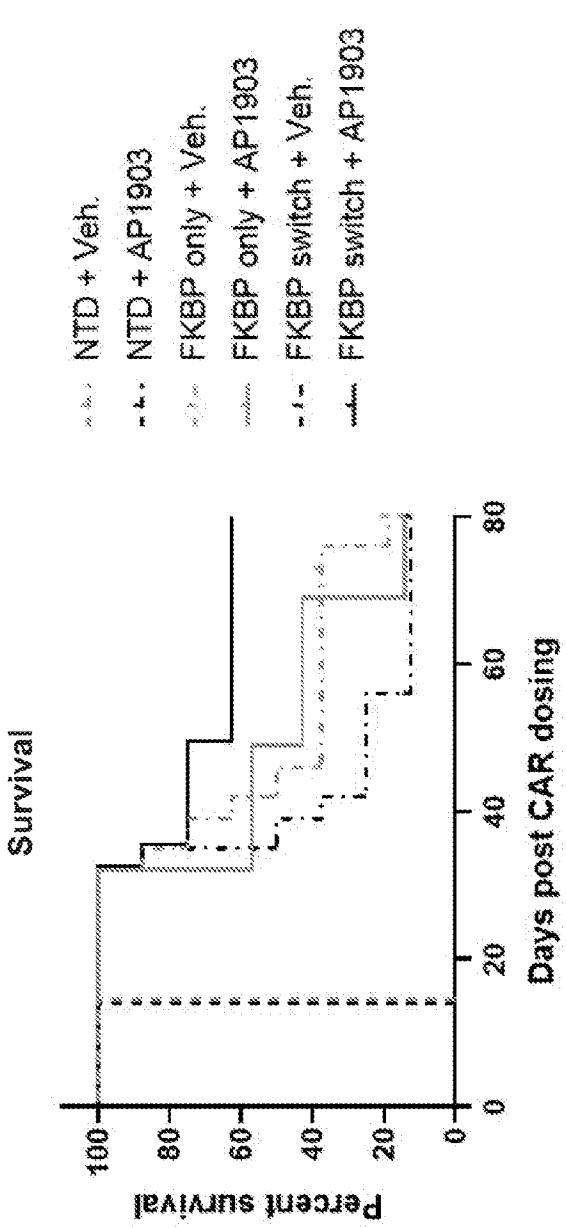

Survival
NTD + Veh.
NTD + AP1903
FKBP only + Veh.
FKBP only + AP1903
FKBP switch + Veh.
FKBP switch + AP1903
Percent survival
100
80
60
40
20
0
0
20
40
60
80
Days post CAR dosing

FIG. 32A

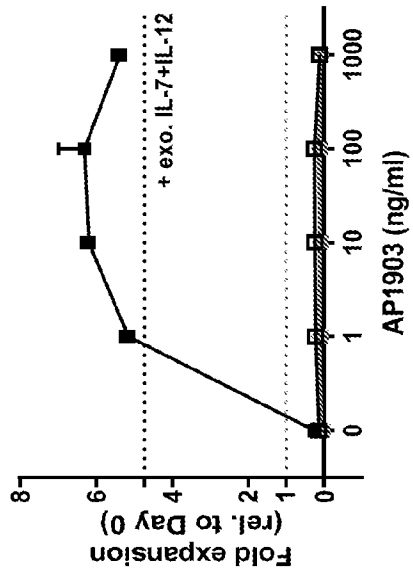


FIG. 32B

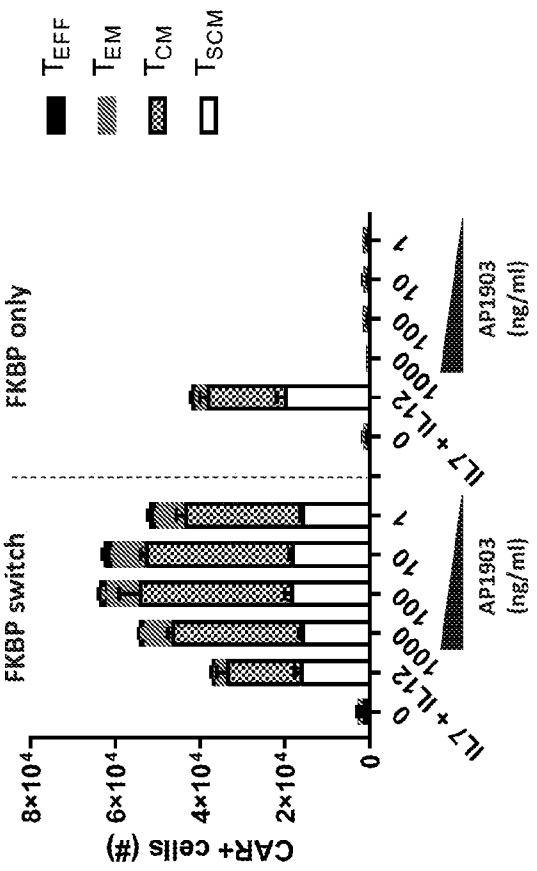
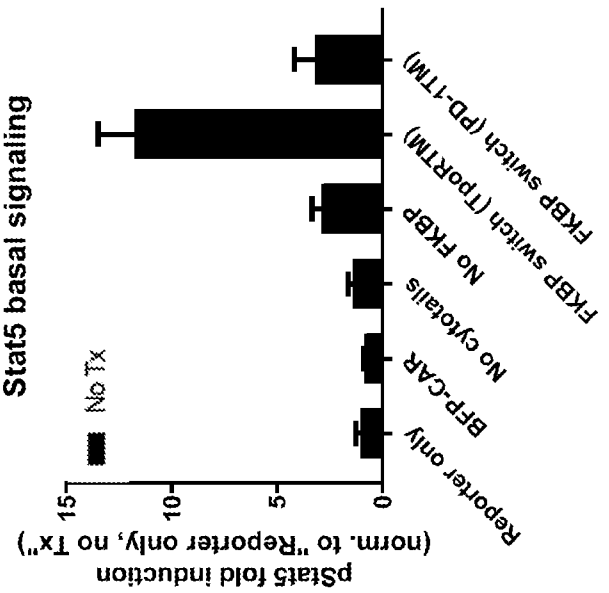


FIG. 33A



Label	Inducible chimeric cytokine receptor
BFP-CAR	None
No cytotails	SS-Myc-FKBP(F36V)-TpoR(478-482) (No cytotails)
No FKBP	SS-Myc-TpoR(478-482)-IL7Ra(316-459)/IL12Rb2(393-433,518-551) (No FKBP)
FKBP switch (TporRTM)	SS-Myc-FKBP(F36V)-TpoR(478-482)-IL7Ra(316-459)/IL12Rb2(393-433,518-551)
FKBP switch (PD-1TM)	SS-Myc-FKBP(F36V)-PD1(156-191).TpoR(514-582)-IL7Ra(316-459)/IL12Rb2(393-433,518-551)

FIG. 33B

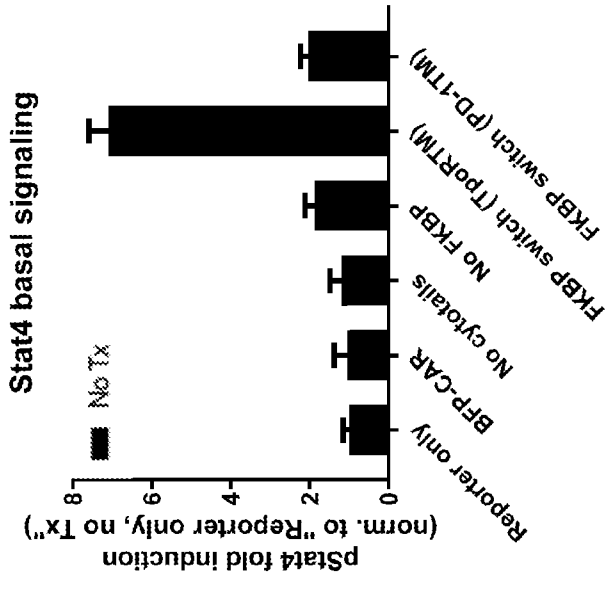


FIG. 33C

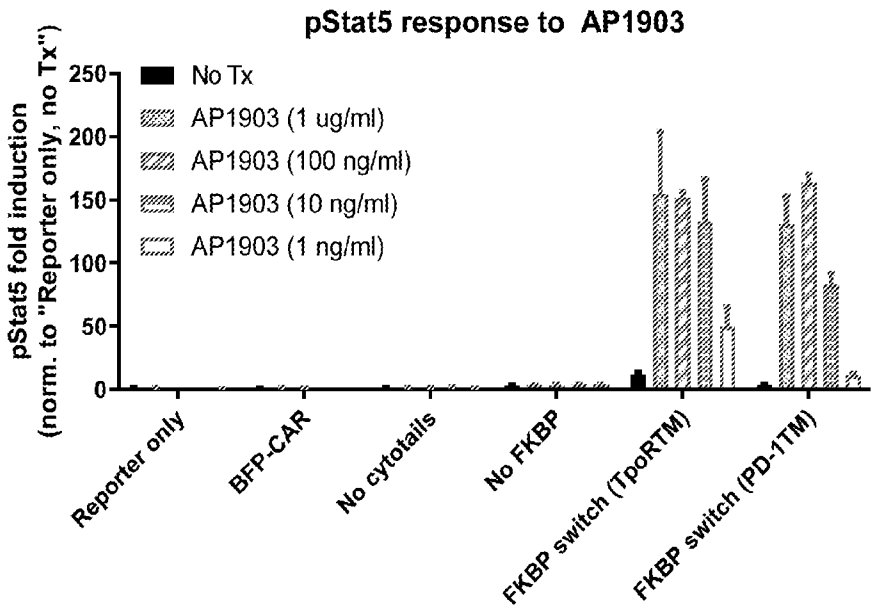
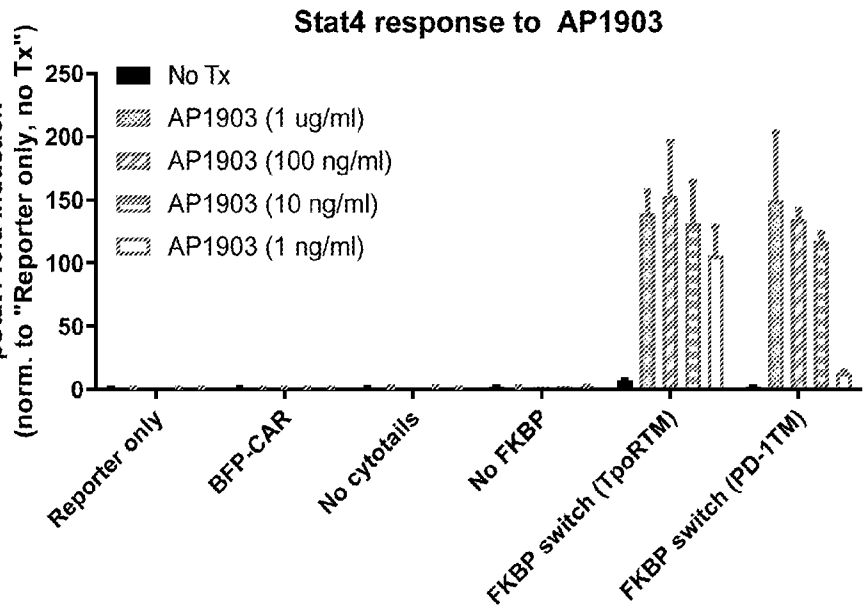


FIG. 33D



Label	Inducible chimeric cytokine receptor
BFP-CAR	None
No cytotails	SS-Myc-FKBP(F36V)-TpoR(478-482) (No cytotails)
No FKBP	SS-Myc-TpoR(478-482)-IL7Ra(316-459)/IL12Rb2(393-433,518-551) (No FKBP)
FKBP switch (TpoRTM)	SS-Myc-FKBP(F36V)-TpoR(478-482)-IL7Ra(316-459)/IL12Rb2(393-433,518-551)
FKBP switch (PD-1TM)	SS-Myc-FKBP(F36V)-PD1(156-191).TpoR(514-582)-IL7Ra(316-459)/IL12Rb2(393-433,518-551)

FIG. 34A

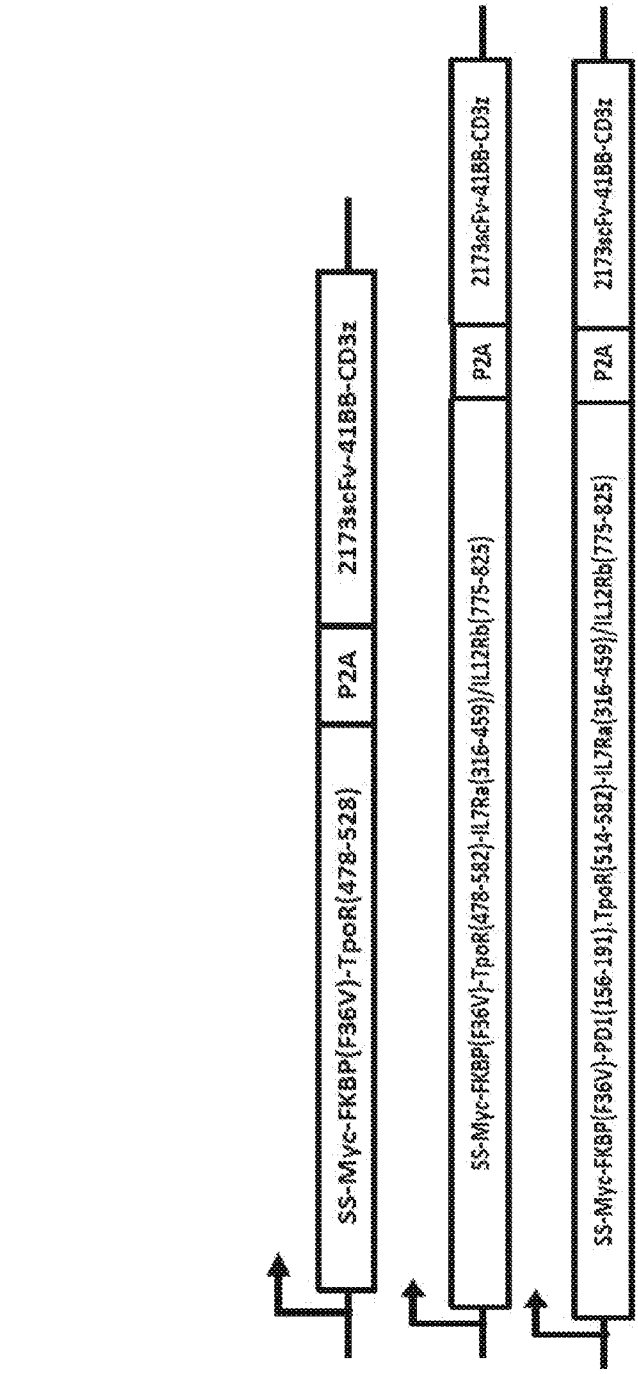

FKBP only Control CAR:
SS-Myc-FKBP(F36V)-TpoR(478-528)
P2A
2173scFv-4188-CD3z
FKBP switch (TpoR TM) CAR:
SS-Myc-FKBP(F36V)-TpoR(478-582)-IL7Ra(316-459)/IL12Rb(775-825)
P2A
2173scFv-4188-CD3z
FKBP switch (PD1 TM) CAR:
SS-Myc-FKBP(F36V)-PD1(156-191)-TpoR(514-582)-IL7Ra(316-459)/IL12Rb(775-825)
P2A
2173scFv-4188-CD3z

FIG. 34B

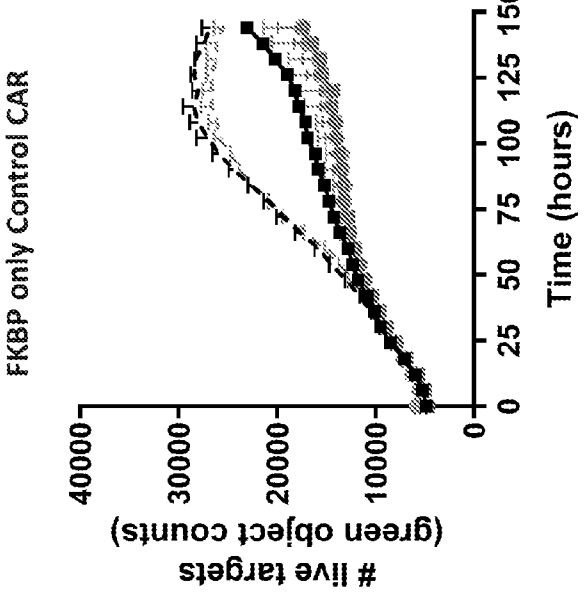


FIG. 34C

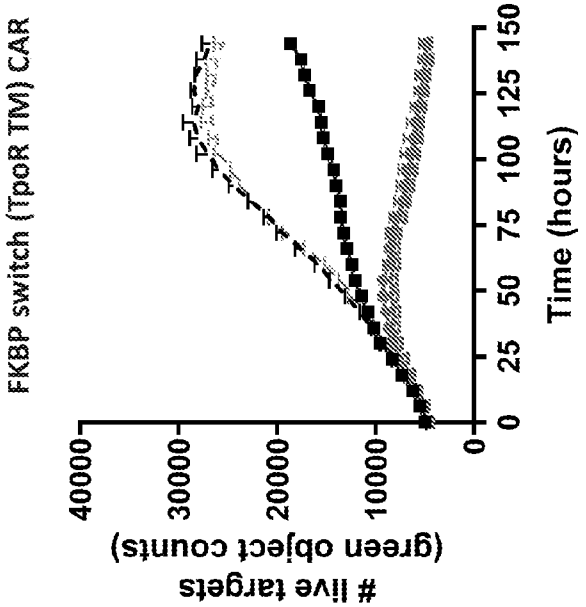


FIG. 34D

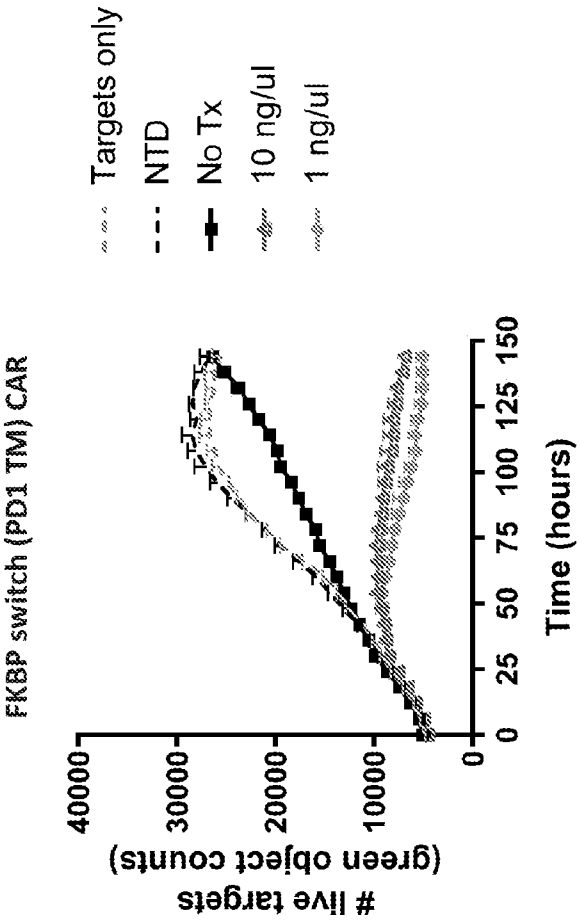


FIG. 34E

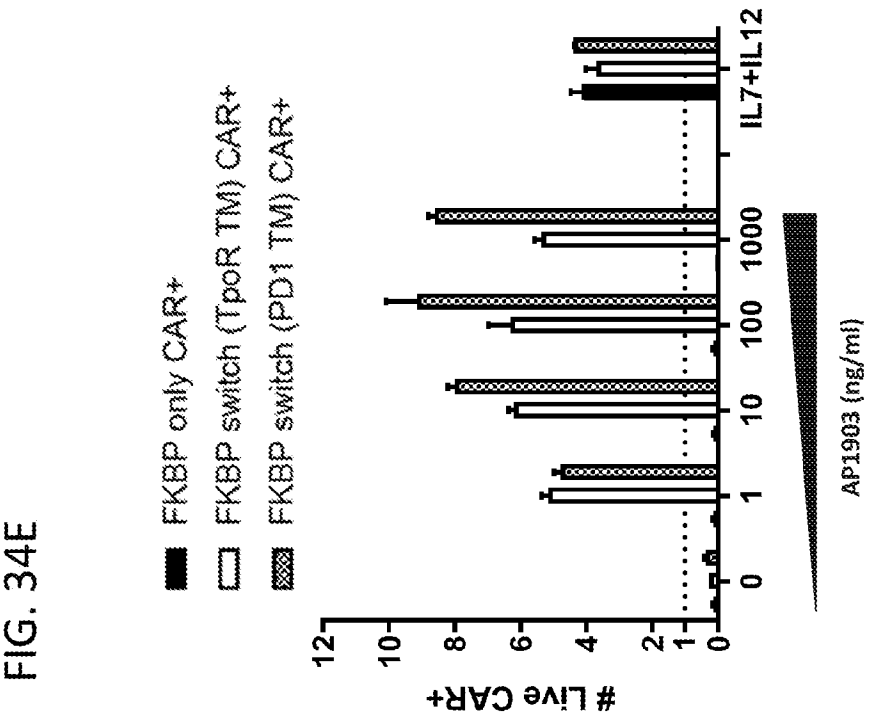


FIG. 34F

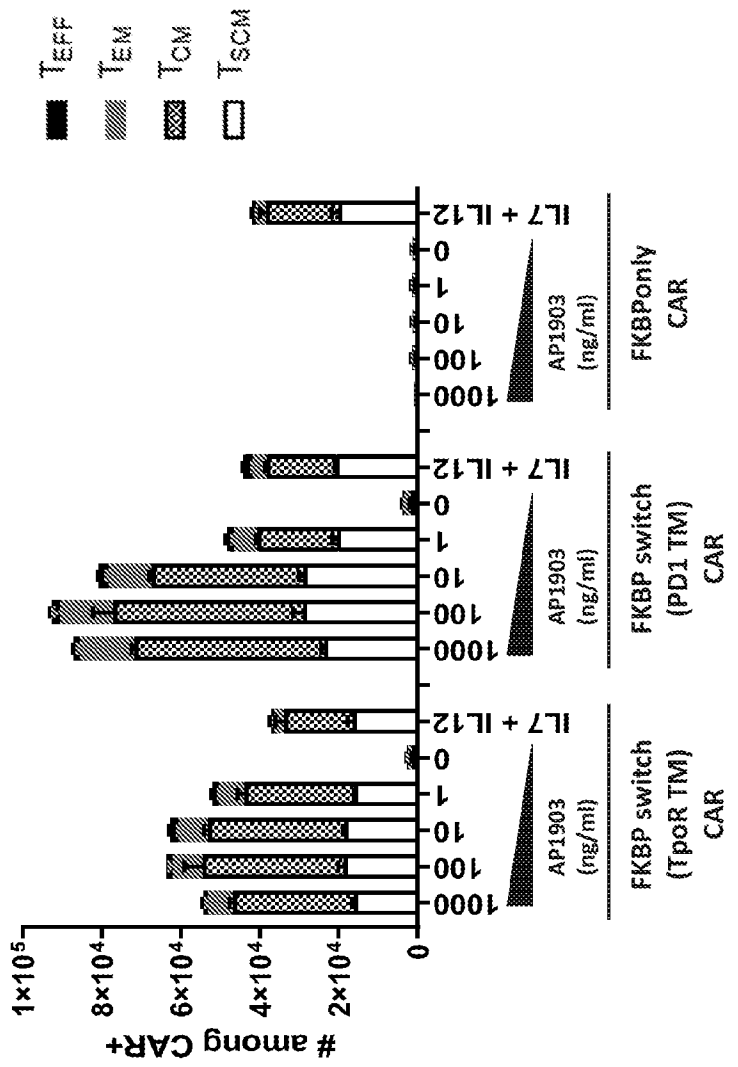


FIG. 35A

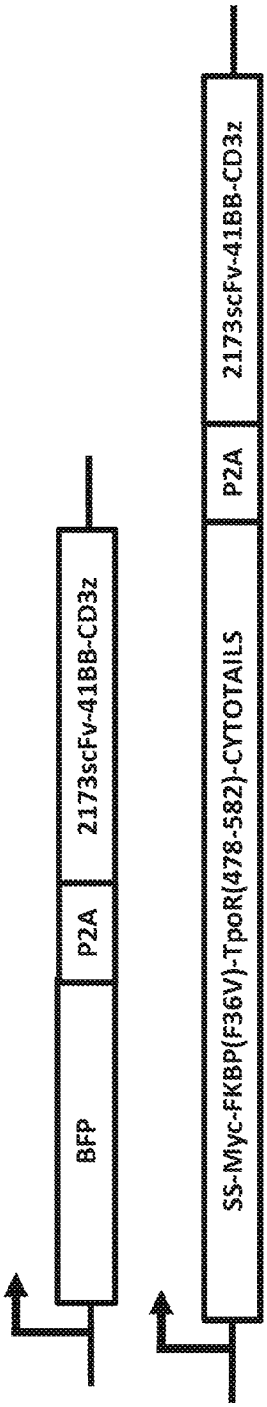


FIG. 35B

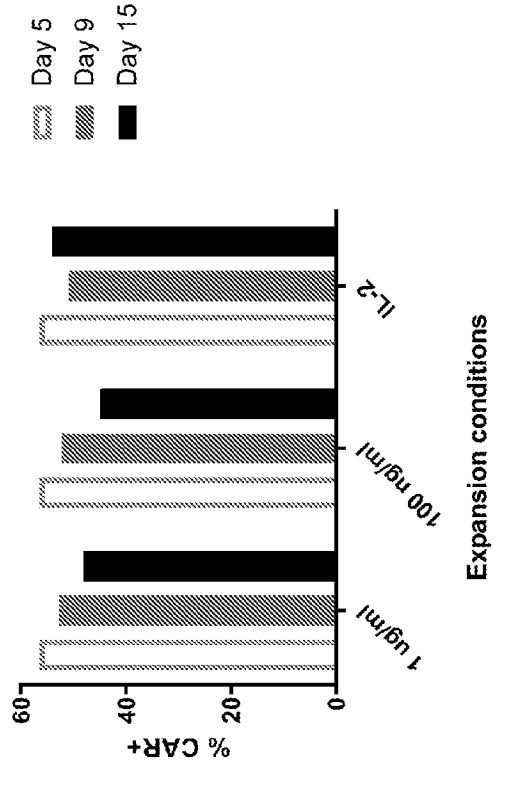


FIG. 35C

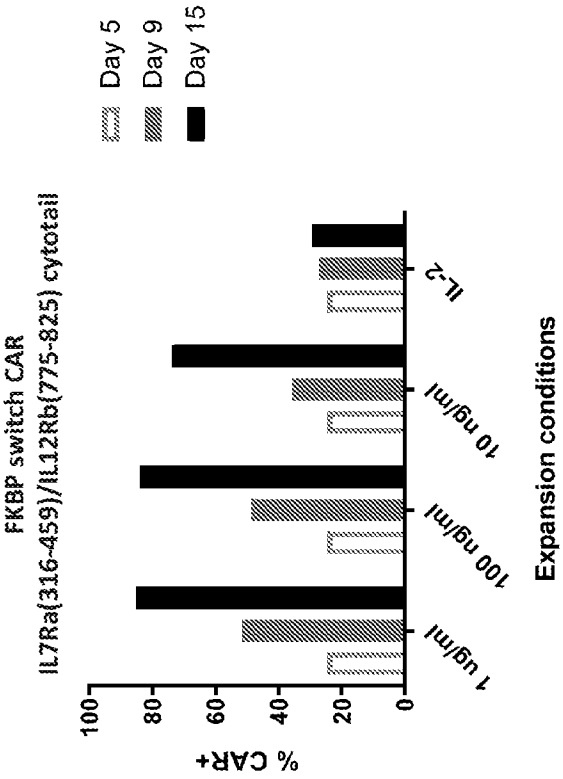


FIG. 35D

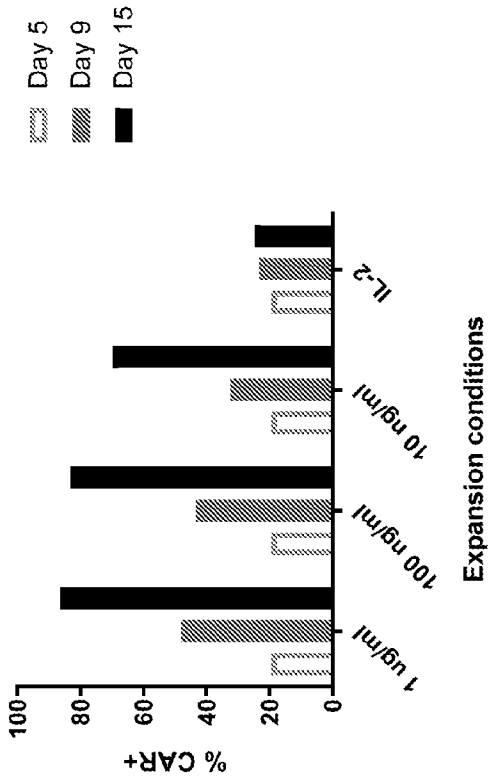


FIG. 35E

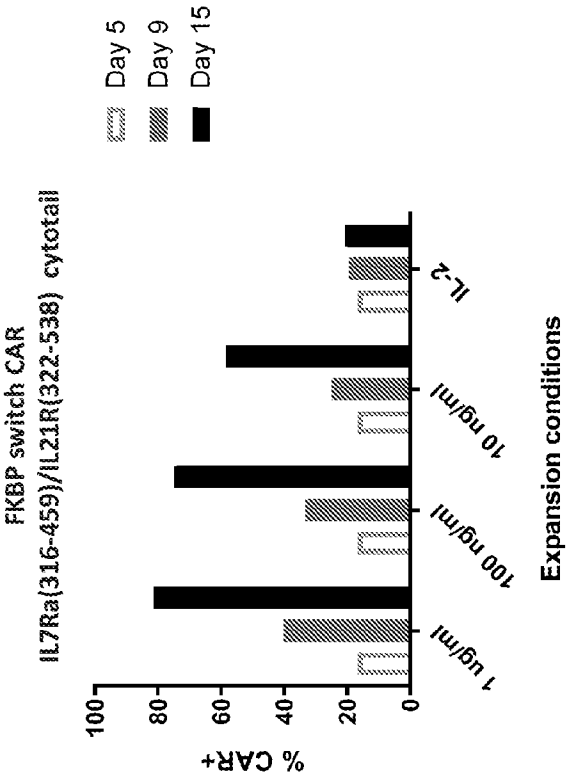


FIG. 36A

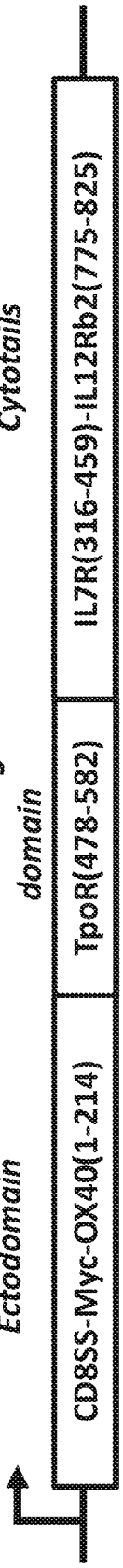


FIG. 36B

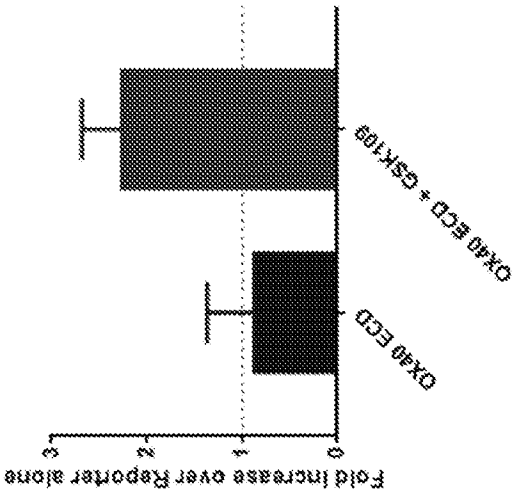


FIG. 36C

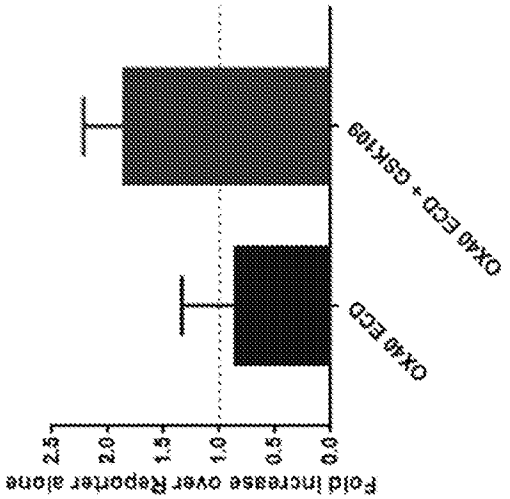


FIG. 37A

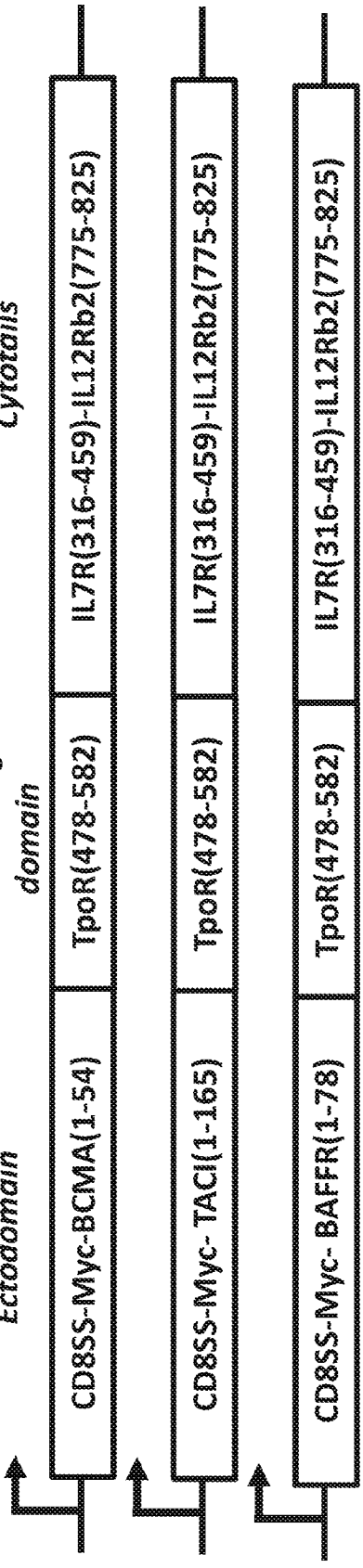
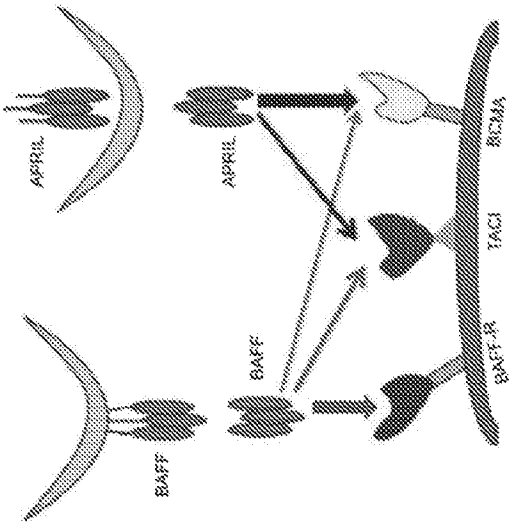


FIG. 37B



Drug Des Devel Ther. 2015 Jan 7;9:333-47.

FIG. 37C

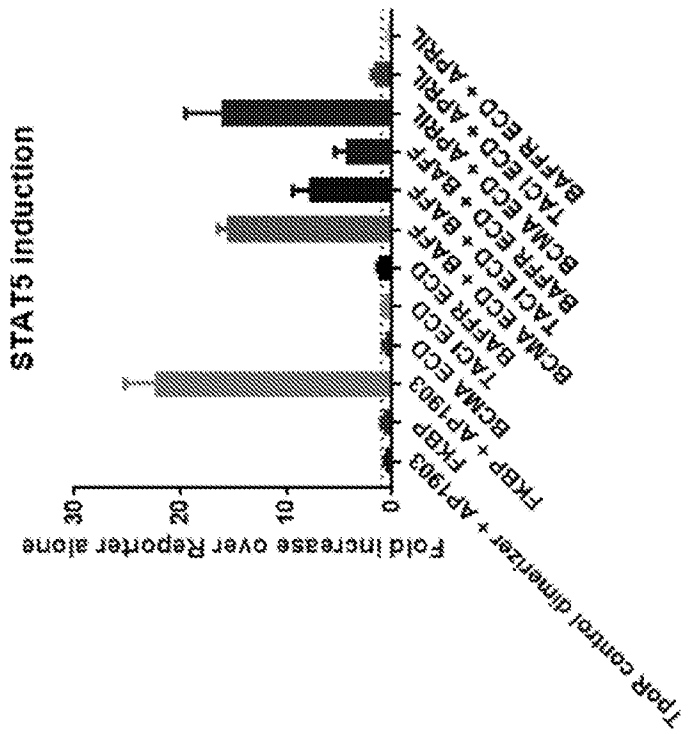


FIG. 37D

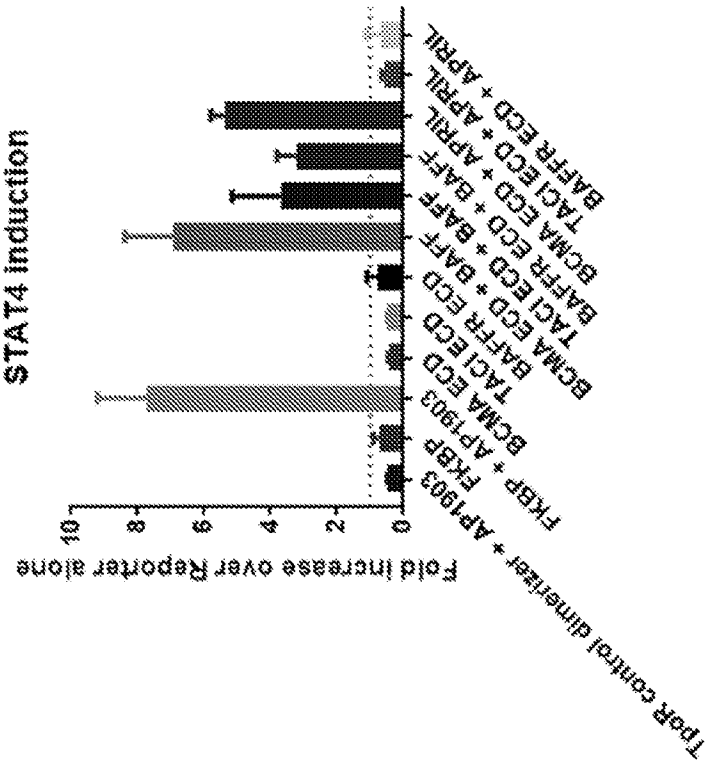


FIG. 38A

Underlined: wildtype TpoR TM region
Bold: means insertion

```
Template:   SDPTRVETATETAWISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL (4138 - 4302 bp)
N-1:        SDPTRVETATET-WISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-2:        SDPTRVETATET--ISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-2+1:      SDPTRVETATET-LISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-3:        SDPTRVETATET---SLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-4:        SDPTRVETATET----LVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-4+1:      SDPTRVETATET---ILVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-5:        SDPTRVETATET-----VTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-6:        SDPTRVETATET------TALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-7:        SDPTRVETATET-------ALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-8:        SDPTRVETATET--------LHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N-9:        SDPTRVETATET---------HLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
```

FIG. 38B

```
Template:   SDPTRVETATETAW--------ISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL (4138 - 4302 bp)
N+1:        SDPTRVETATETAW-------LISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N+2:        SDPTRVETATETAW------VLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N+3:        SDPTRVETATETAW-----LVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N+4:        SDPTRVETATETAW----ILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N+5:        SDPTRVETATETAW---LILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N+6:        SDPTRVETATETAW--LLILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N+7:        SDPTRVETATETAW-VLLILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
N+8:        SDPTRVETATETAWLVLLILVLISLVTALHLVLGLSAVLGLLLLRWQFPAHYRRLRHALWPSL
```

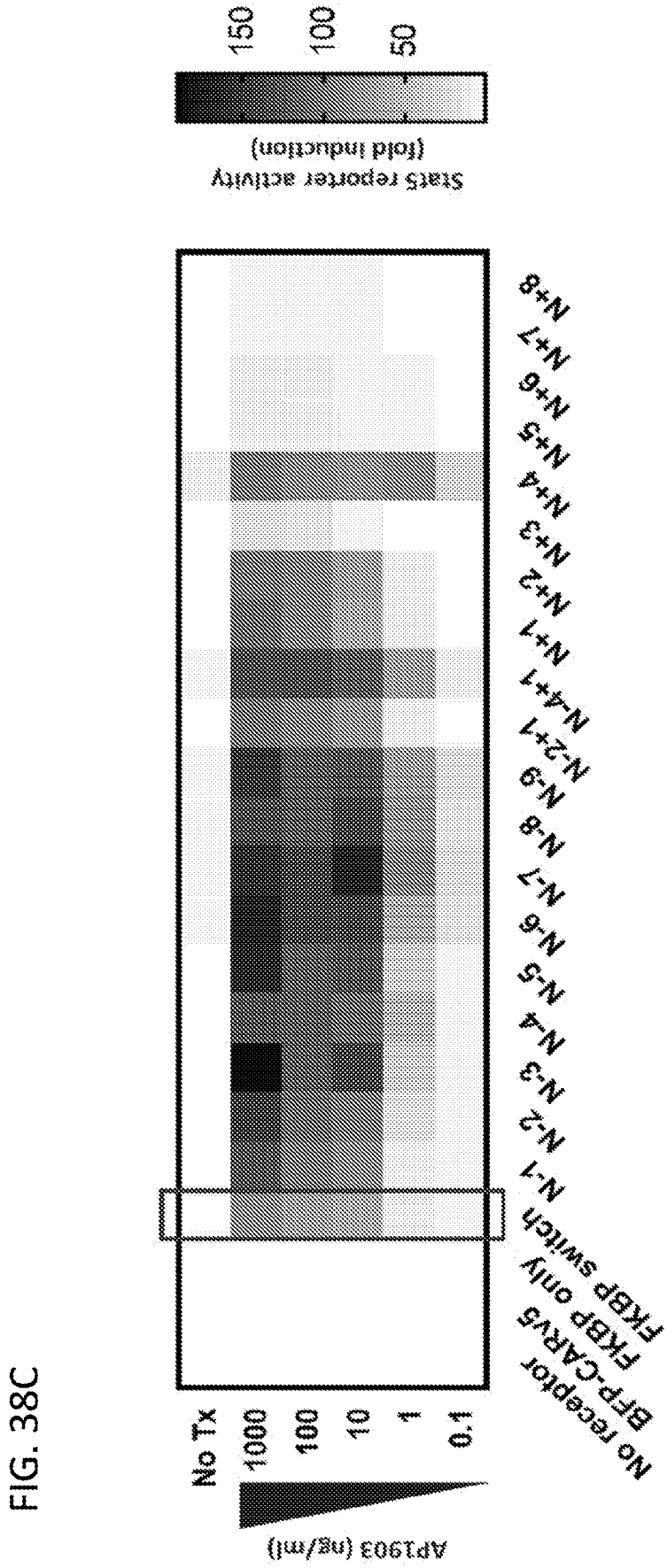

150
100
50
Stat5 reporter activity
(fold induction)
N+8
N+7
N+6
N+5
N+4
N+3
N+2
N+1
N+1
N-2+1
N-9
N-8
N-7
N-6
N-5
N-4
N-3
N-2
N-1
No receptor
BFP-CAR.v5
FKBP only
FKBP switch
No Tx
1000
100
10
1
0.1
AP1903 (ng/ml)

FIG. 38C

FIG. 39A

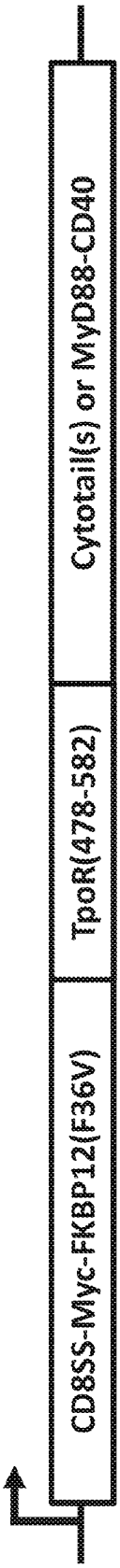


FIG. 39B

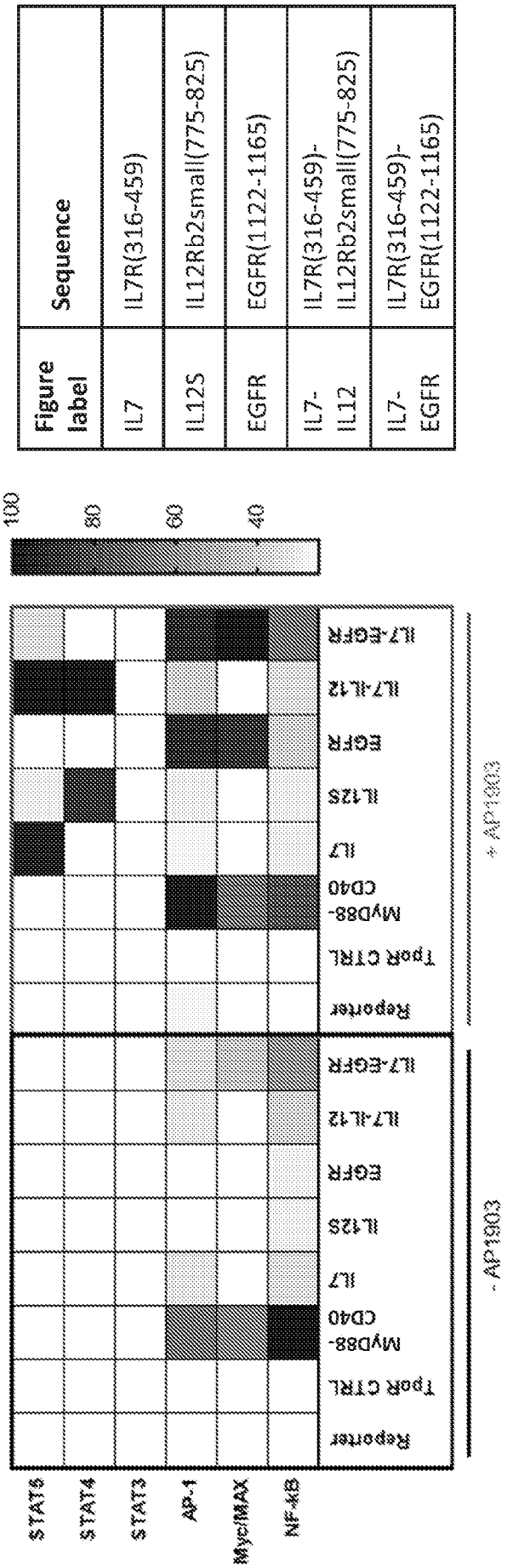


Figure label	Sequence
IL7	IL7R(316-459)
IL12S	IL12Rb2small(775-825)
EGFR	EGFR(1122-1165)
IL7-IL12	IL7R(316-459)-IL12Rb2small(775-825)
IL7-EGFR	IL7R(316-459)-EGFR(1122-1165)

FIG. 40A

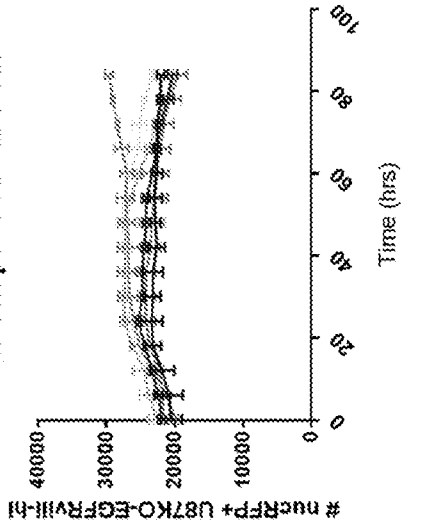


FIG. 40B

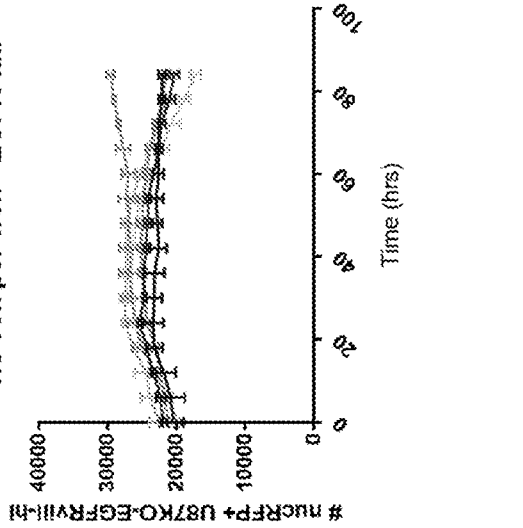


FIG. 40C

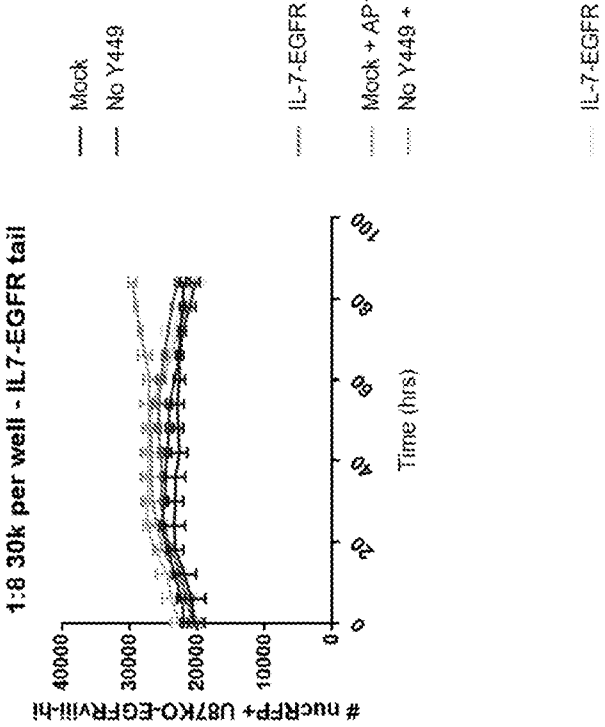


FIG. 40D

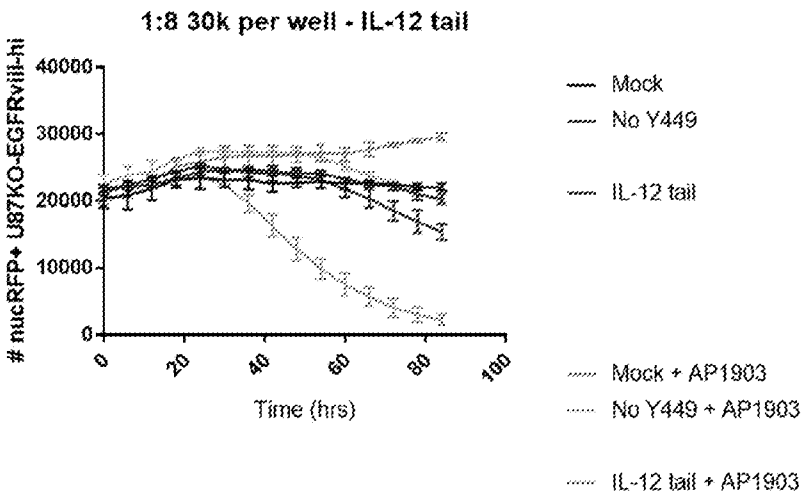


FIG. 40E

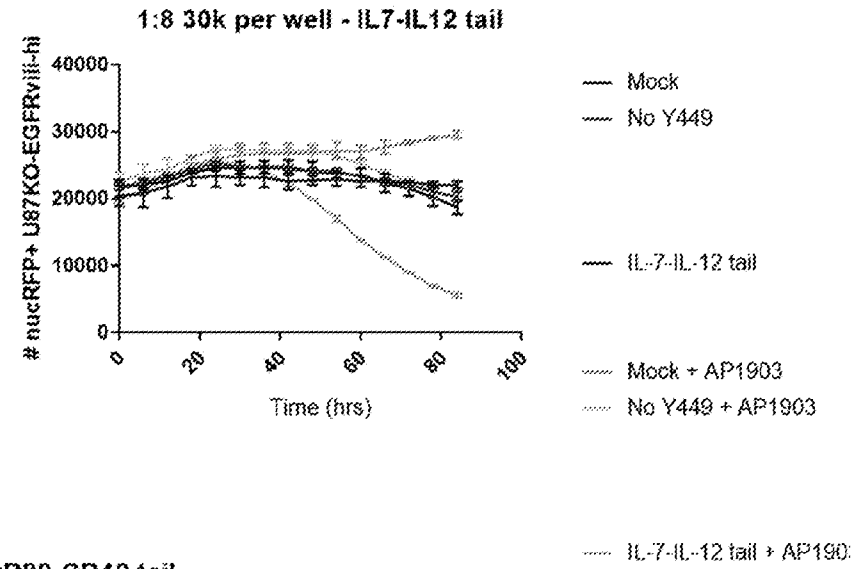


FIG. 40F

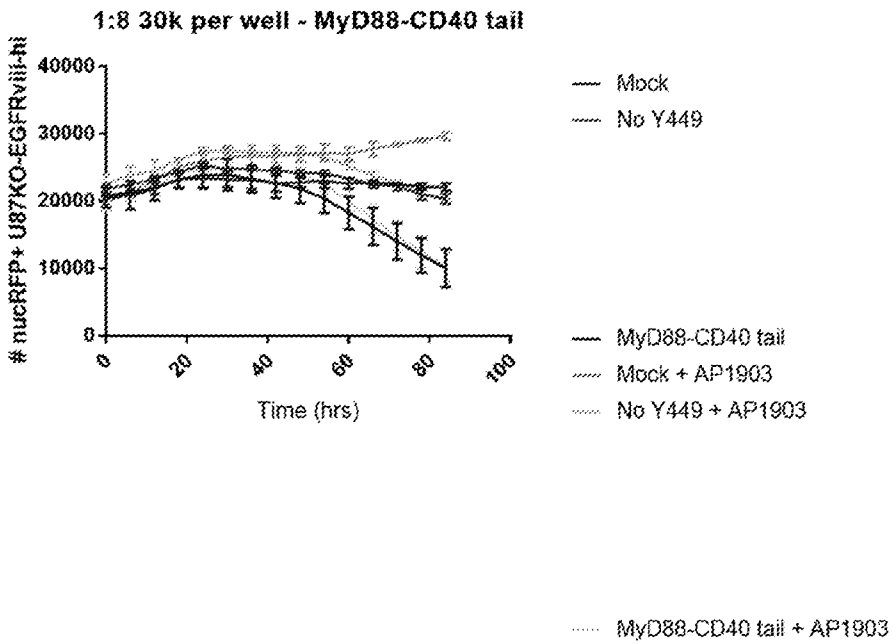


FIG. 41A

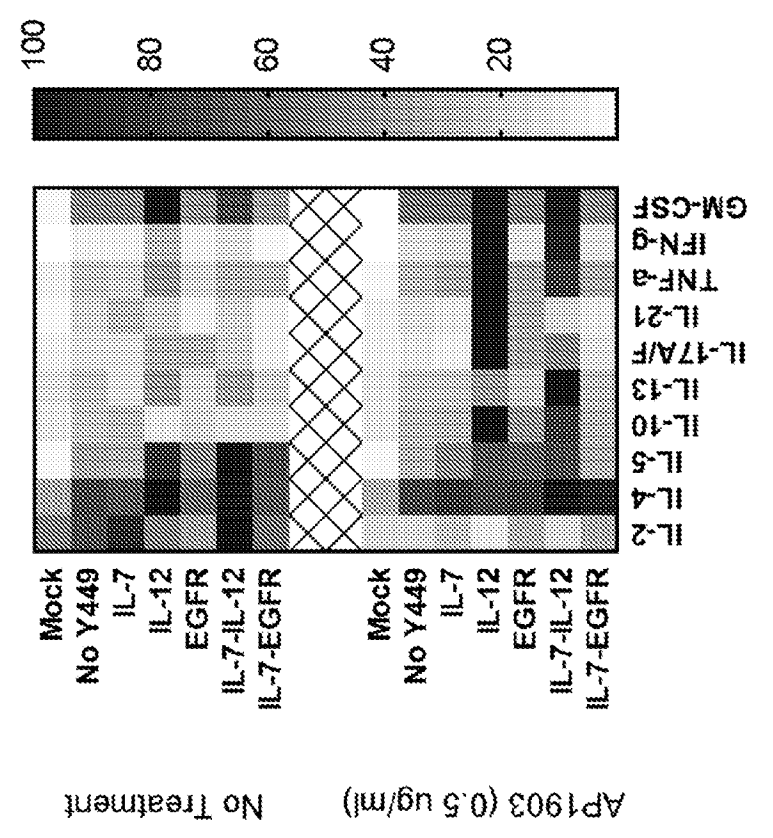
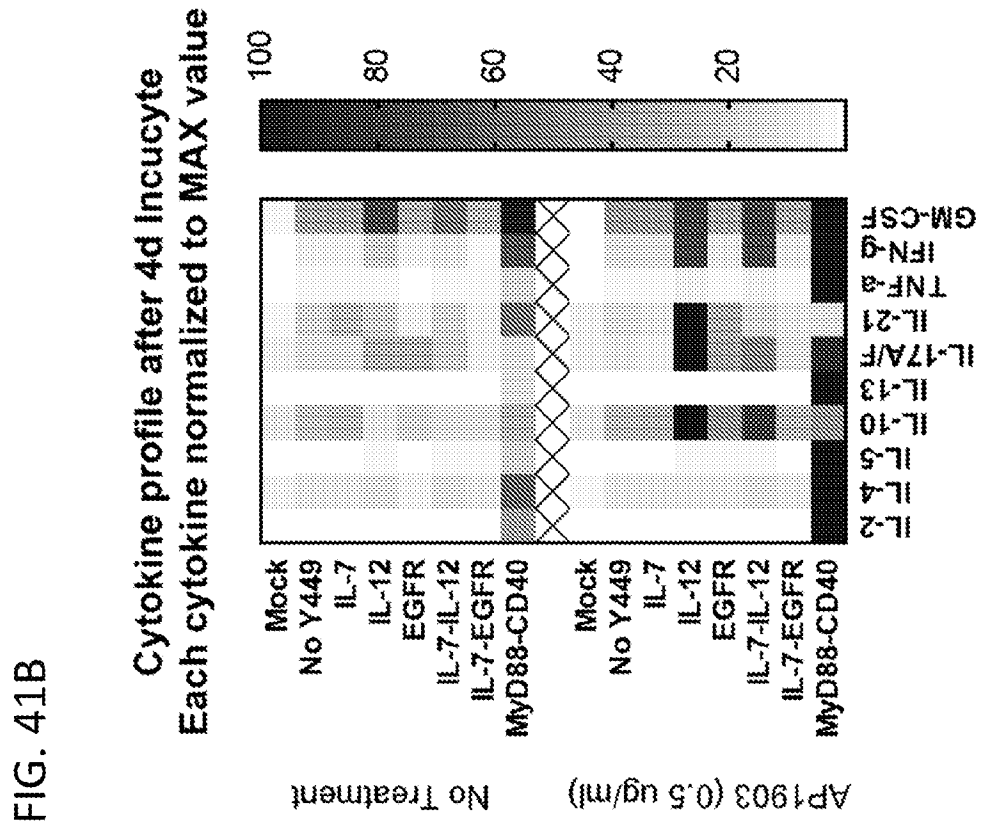

Cytokine profile after 4d Incucyte
Each cytokine normalized to MAX value
MAX values for each cytokine (ng/ml):
IL-2: 1280 (IL7-EGFR)
IL-4: 392 (IL7-IL12)
IL-5: 3664 (IL7-IL12)
IL-10: 1839 (IL12)
IL-13: 1073 (IL7-IL12)
IL-17A/F: 2236 (IL12)
IL-21: 1918 (IL12)
TNF-a: 2557 (IL12)
IFN-g: 815086 (IL12)
GM-CSF: 1761695 (IL12)
100
80
60
40
20
IL-2
IL-4
IL-5
IL-10
IL-13
IL-17A/F
IL-21
TNF-a
IFN-g
GM-CSF
Mock
No Y449
IL-7
IL-12
EGFR
IL-7-IL-12
IL-7-EGFR
No Treatment
AP1903 (0.5 ug/ml)

FIG. 41B



MAX values for each cytokine (ng/ml):

- IL-2: 577948 (MyD88-CD40)
- IL-4: 3308 (MyD88-CD40)
- IL-5: 260012 (MyD88-CD40)
- IL-10: 1839 (IL12)
- IL-13: 252817 (MyD88-CD40)
- IL-17A/F: 2236 (IL12)
- IL-21: 1918 (IL12)
- TNF-a: 38345 (MyD88-CD40)
- IFN-g: 1059627 (MyD88-CD40)
- GM-CSF: 2313205 (MyD88-CD40)

FIG. 42A

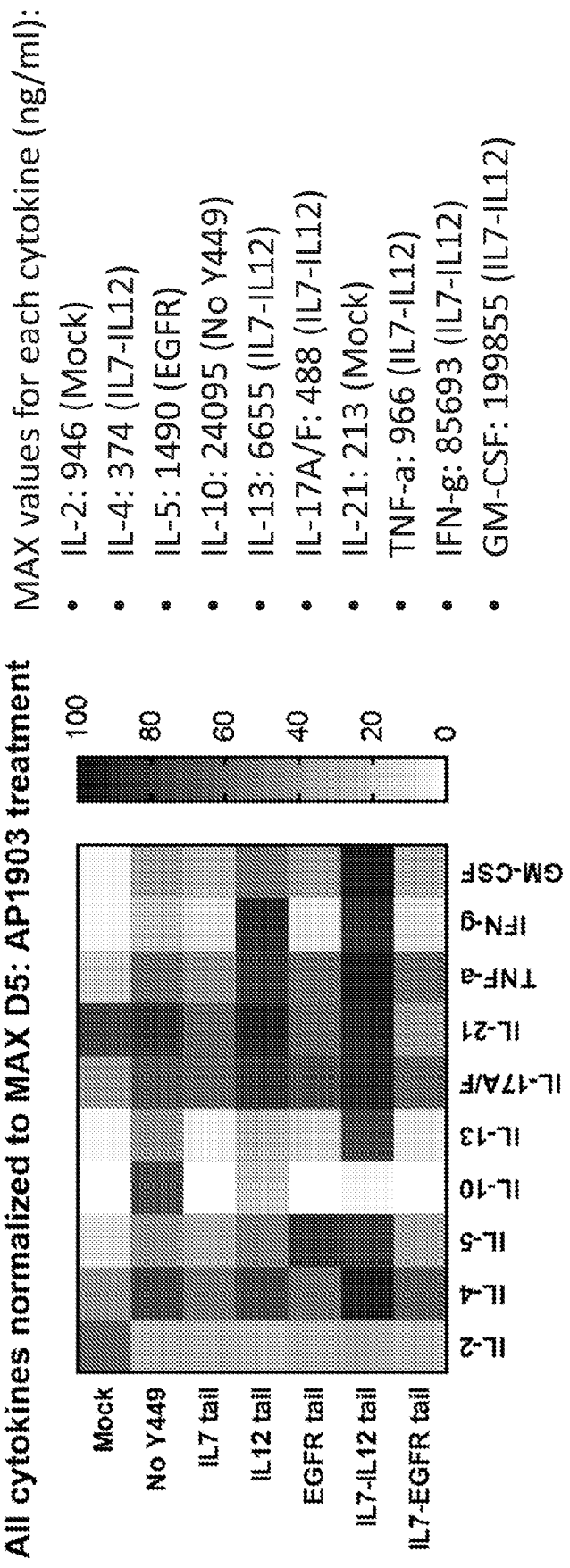
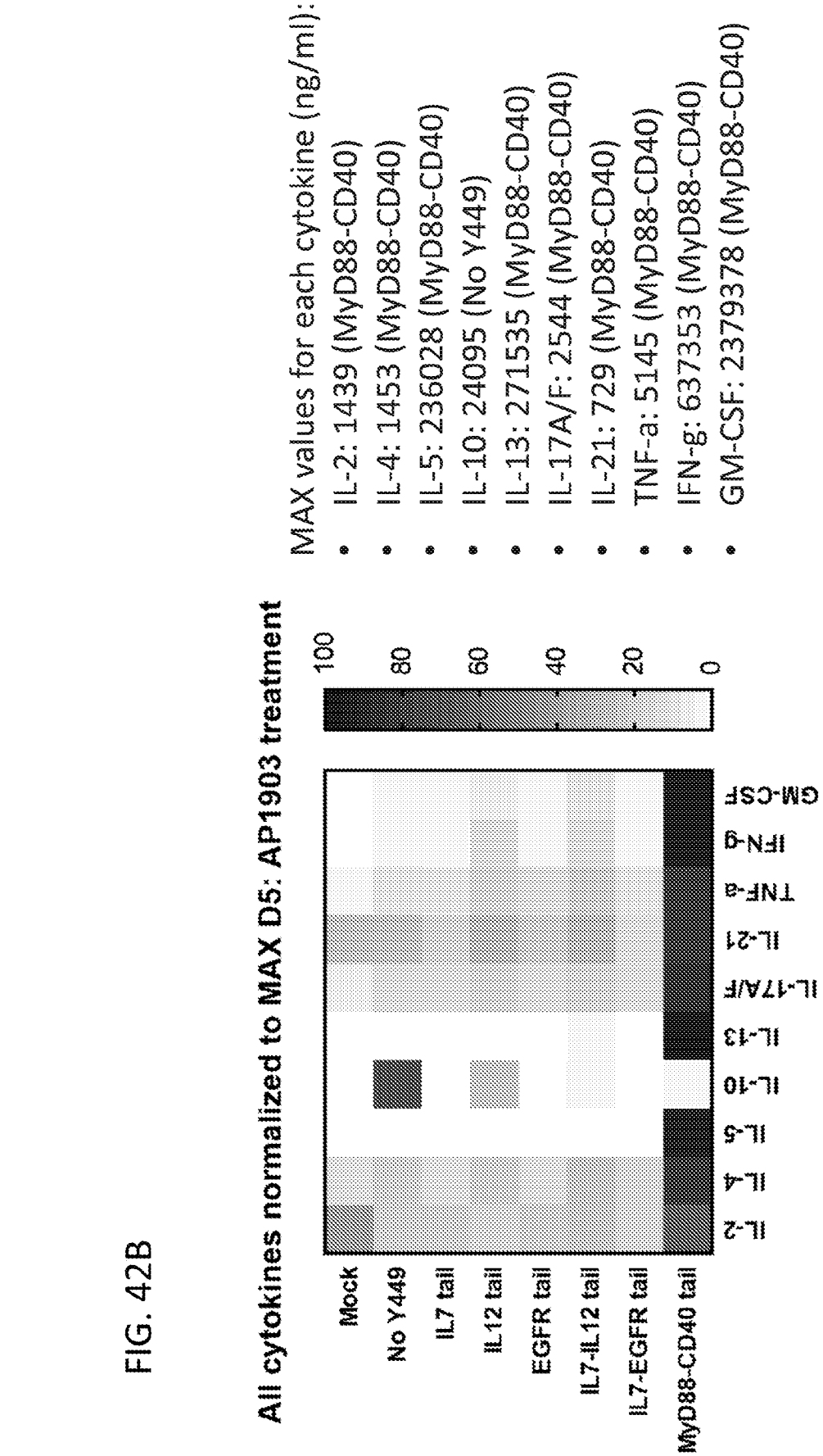

All cytokines normalized to MAX D5: AP1903 treatment
MAX values for each cytokine (ng/ml):
• IL-2: 946 (Mock)
• IL-4: 374 (IL7-IL12)
• IL-5: 1490 (EGFR)
• IL-10: 24095 (No Y449)
• IL-13: 6655 (IL7-IL12)
• IL-17A/F: 488 (IL7-IL12)
• IL-21: 213 (Mock)
• TNF-a: 966 (IL7-IL12)
• IFN-g: 85693 (IL7-IL12)
• GM-CSF: 199855 (IL7-IL12)
100
80
60
40
20
0
Mock
No Y449
IL7 tail
IL12 tail
EGFR tail
IL7-IL12 tail
IL7-EGFR tail
IL-2
IL-4
IL-5
IL-10
IL-13
IL-17A/F
IL-21
TNF-a
IFN-g
GM-CSF

FIG. 42B


All cytokines normalized to MAX D5: AP1903 treatment
Mock
No Y449
IL7 tail
IL12 tail
EGFR tail
IL7-IL12 tail
IL7-EGFR tail
MyD88-CD40 tail
IL-2
IL-4
IL-5
IL-10
IL-13
IL-17A/F
IL-21
TNF-a
IFN-g
GM-CSF
100
80
60
40
20
0
MAX values for each cytokine (ng/ml):
IL-2: 1439 (MyD88-CD40)
IL-4: 1453 (MyD88-CD40)
IL-5: 236028 (MyD88-CD40)
IL-10: 24095 (No Y449)
IL-13: 271535 (MyD88-CD40)
IL-17A/F: 2544 (MyD88-CD40)
IL-21: 729 (MyD88-CD40)
TNF-a: 5145 (MyD88-CD40)
IFN-g: 637353 (MyD88-CD40)
GM-CSF: 2379378 (MyD88-CD40)

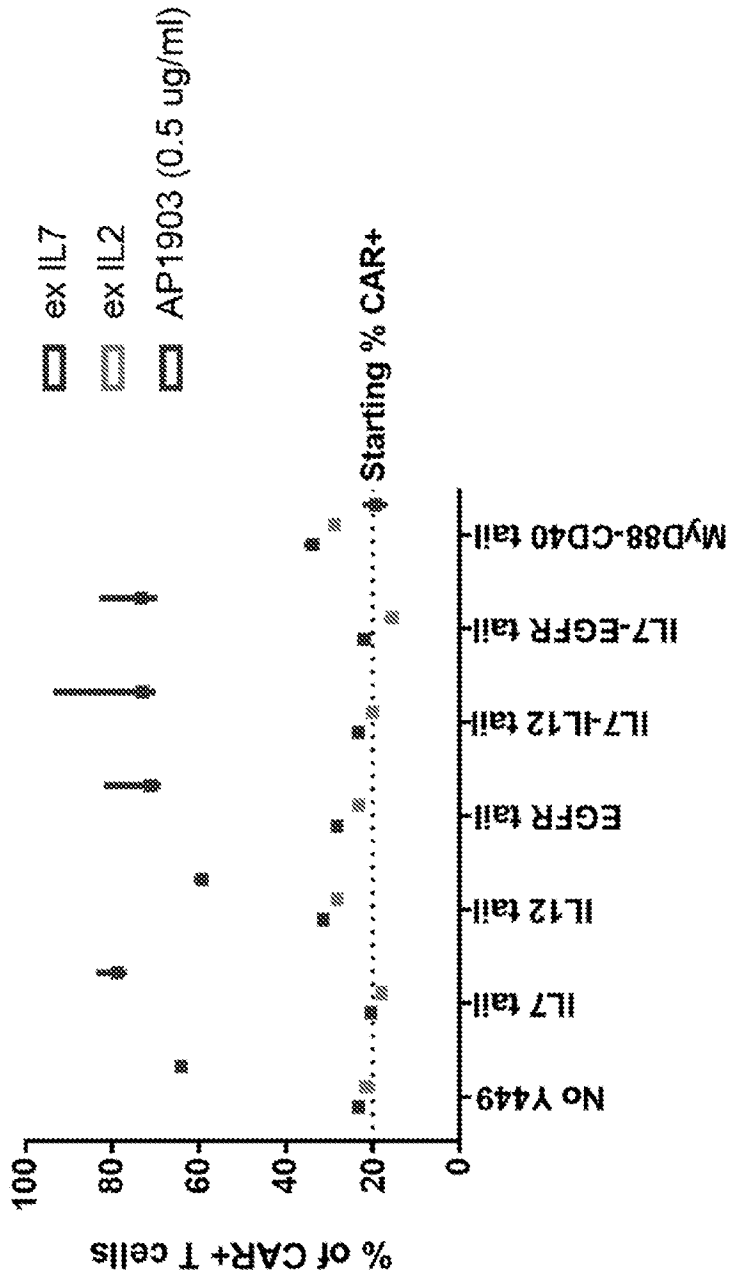

CAR-T enrichment D14 growth
ex IL7
ex IL2
AP1903 (0.5 ug/ml)
% of CAR+ T cells
100
80
60
40
20
0
Starting % CAR+
No Y449
IL7 tail
IL12 tail
EGFR tail
IL7-IL12 tail
IL7-EGFR tail
MyD88-CD40 tail

FIG. 43

FIG. 44A

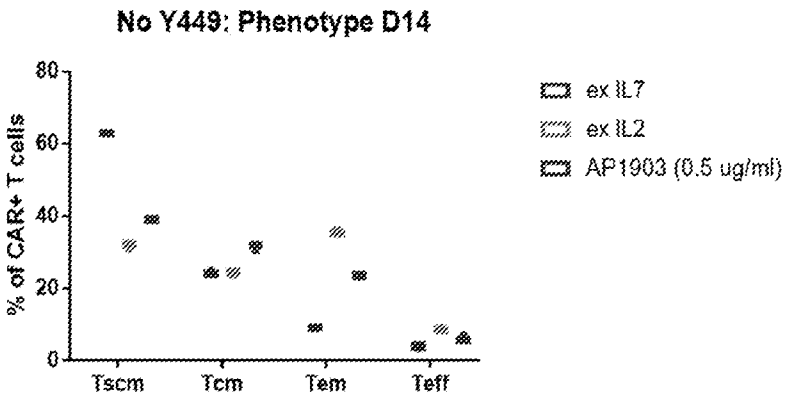


FIG. 44B

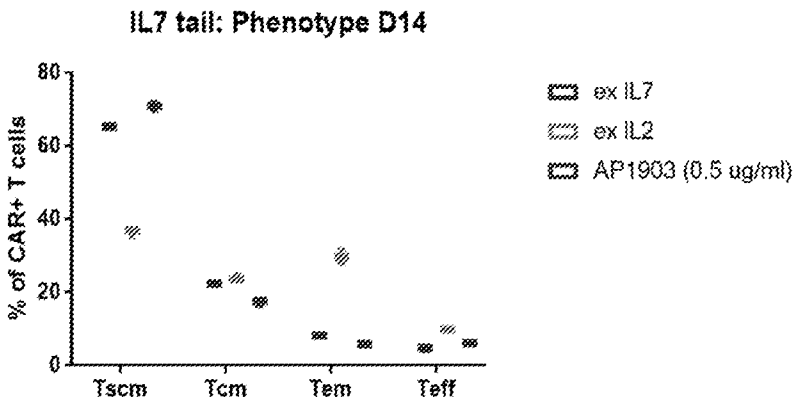


FIG. 44C

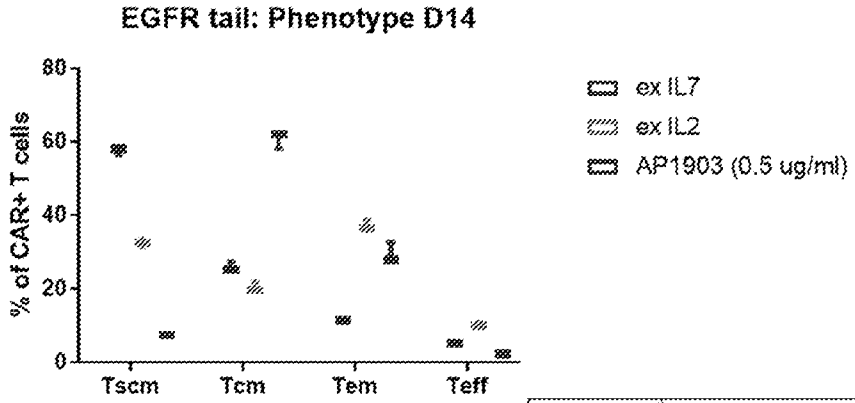


FIG. 44D

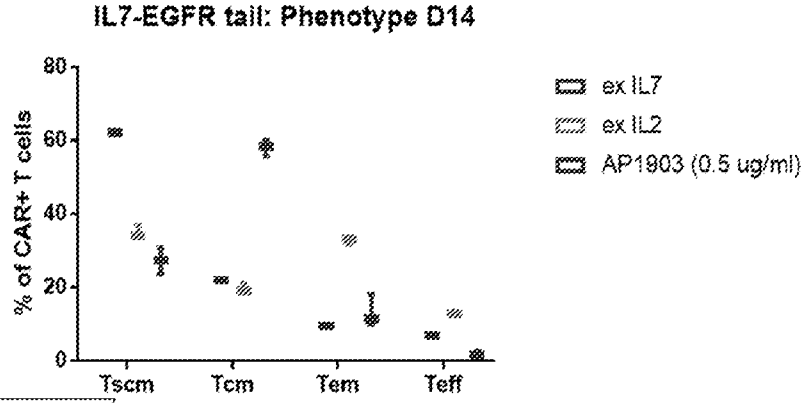


Figure label	Sequence
Y449	IL7R(424-459;Y456F)
IL7	IL7R(316-459)
IL12S	IL12Rb2small(775-825)
EGFR	EGFR(1122-1165)
IL7-IL12	IL7R(316-459)-IL12Rb2small(775-825)
IL7-EGFR	IL7R(316-459)-EGFR(1122-1165)

FIG. 44E

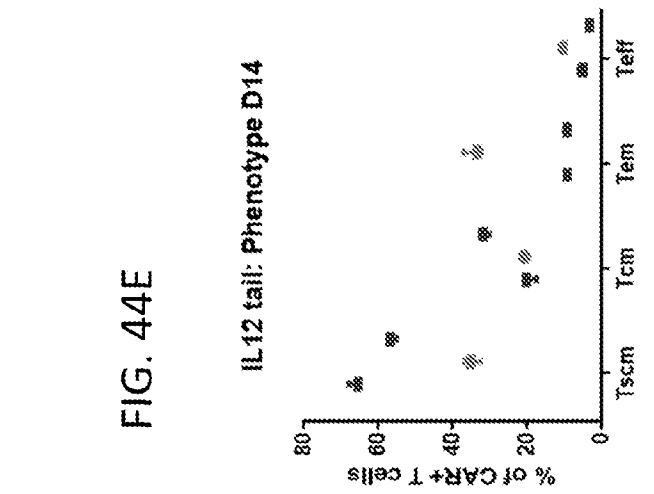


FIG. 44F

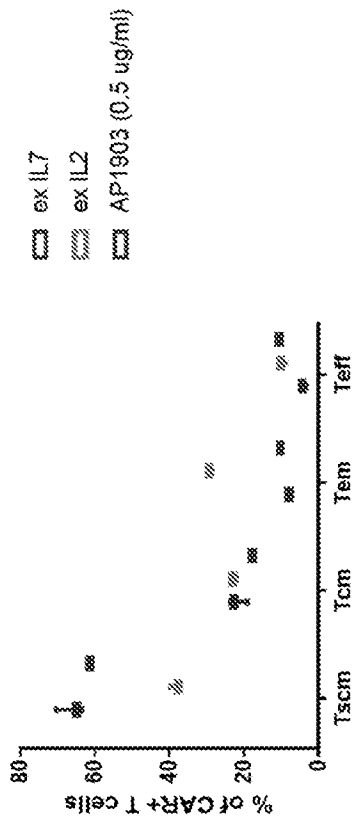


Figure label	Sequence
Y449	IL7R(424-459;Y456F)
IL7	IL7R(316-459)
IL12	IL12Rb2small(775-825)
EGFR	EGFR(1122-1165)
IL7-IL12	IL7R(316-459)-IL12Rb2small(775-825)
IL7-EGFR	IL7R(316-459)-EGFR(1122-1165)

FIG. 44G

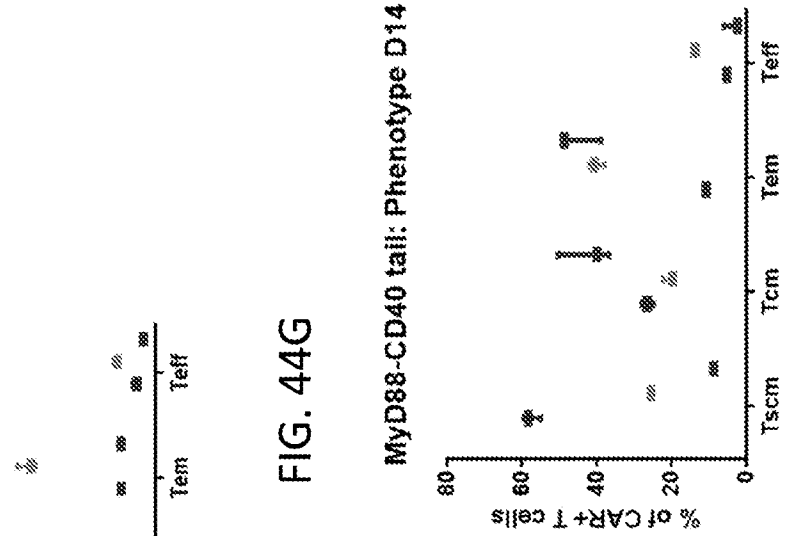


FIG. 45A

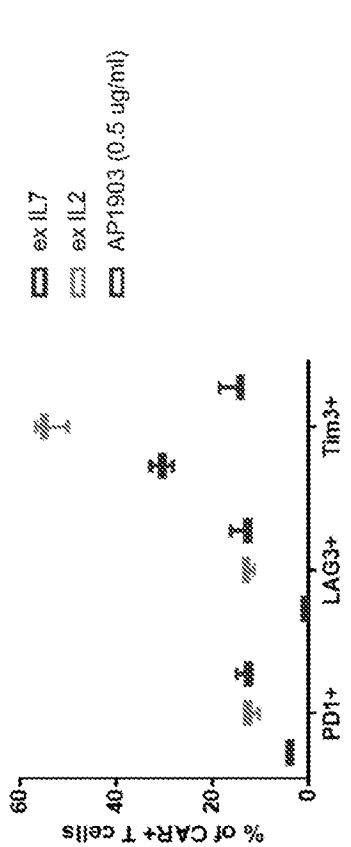


FIG. 45B

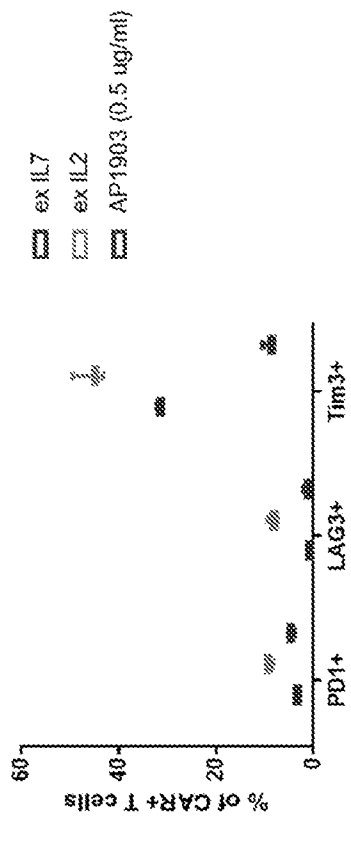


FIG. 45C

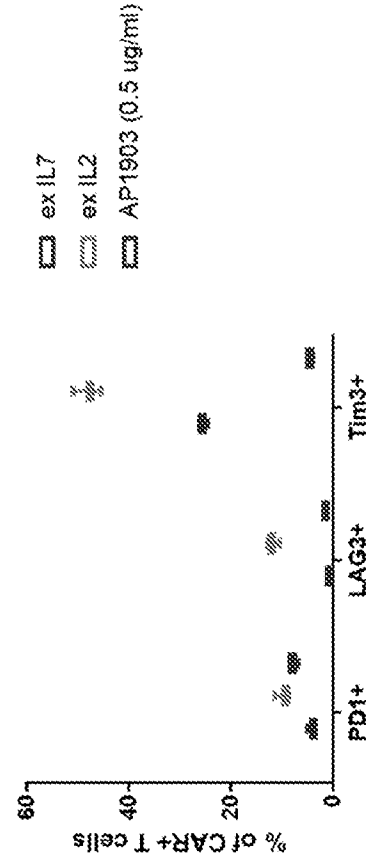


FIG. 45D

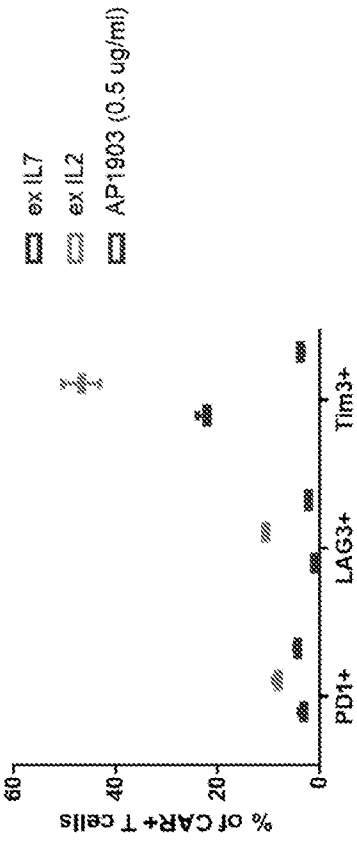


FIG. 45E

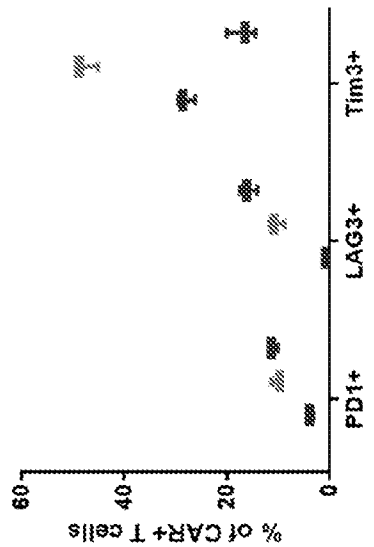


FIG. 45F

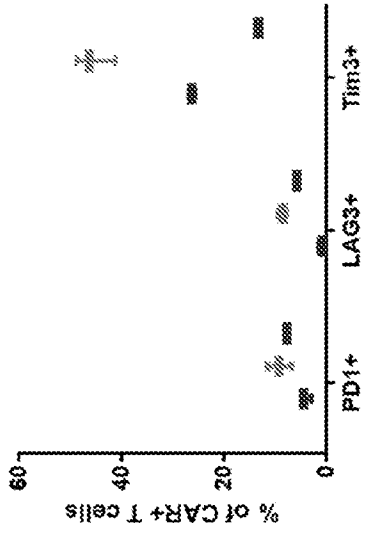
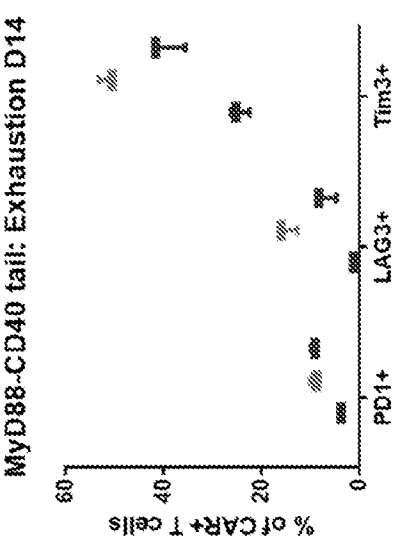


FIG. 45G



SEQUENCE LISTING

<110> ALLOGENE THERAPEUTICS, INC.

<120> INDUCIBLE CHIMERIC CYTOKINE RECEPTORS

<130> ALGN-016/01WO 333466-2243

<150> US 62/637,600
<151> 2018-03-02

<160> 311

<170> PatentIn version 3.5

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95
```

```
Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu Gly
                245                 250                 255

Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr Leu
            260                 265                 270

Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp Leu
        275                 280                 285
```

```
Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly Ser
    290                 295                 300

Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro Glu
305                 310                 315                 320

Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser Ser
                325                 330                 335

Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr Pro
            340                 345                 350

Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile Ser
        355                 360                 365

Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu Ser
    370                 375                 380

Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala Ala
385                 390                 395                 400

Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser Ile Pro Asn Pro Leu
                405                 410                 415

Leu Gly Leu Asp Ser Thr
            420
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<210> 2
<211> 461
<212> PRT
<213> Artificial Sequence

<220>
<223> V5-EpoR(273-508)-FKBP(F36V)-FKBP(F36V)

<400> 2

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Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr Ser His Arg Arg Ala
```

```
1               5                   10                  15

Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro Glu Ser Glu Phe
            20                  25                  30

Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln Leu Trp Leu Tyr
        35                  40                  45

Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr Pro Phe Thr Glu
    50                  55                  60

Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg Cys Trp Gly Thr
65                  70                  75                  80

Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu Gly Pro Leu Leu Glu
                85                  90                  95

Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr Leu Val Leu Asp Lys
            100                 105                 110

Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp Leu Pro Gly Pro Gly
        115                 120                 125

Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly Ser Glu Ala Ser Ser
    130                 135                 140

Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro Glu Gly Ala Ser Ala
145                 150                 155                 160

Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser Ser Gln Leu Leu Arg
                165                 170                 175

Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr Pro Pro His Leu Lys
            180                 185                 190

Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile Ser Thr Asp Tyr Ser
```

```
        195                 200                 205

Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu Ser Asp Gly Pro Tyr
    210                 215                 220

Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala Ala Glu Pro Leu Pro
225                 230                 235                 240

Pro Ser Tyr Val Ala Cys Ser Met Gly Val Gln Val Glu Thr Ile Ser
                245                 250                 255

Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val
            260                 265                 270

His Tyr Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg
        275                 280                 285

Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile
    290                 295                 300

Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala
305                 310                 315                 320

Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro
                325                 330                 335

Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu
            340                 345                 350

Lys Leu Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr
        355                 360                 365

Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu
    370                 375                 380

Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe
```

385 390 395 400

Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly
405 410 415

Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro
420 425 430

Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His
435 440 445

Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
450 455 460

<210> 3
<211> 461
<212> PRT
<213> Artificial Sequence

<220>
<223> V5-EpoR(273-508)-FKBP(E31G,36V,R71G,K105E)-FKBP(E31G,36V,R71G,K105E)

<400> 3

Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr Ser His Arg Arg Ala
1 5 10 15

Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro Glu Ser Glu Phe
20 25 30

Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln Leu Trp Leu Tyr
35 40 45

Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr Pro Phe Thr Glu
50 55 60

Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg Cys Trp Gly Thr
65 70 75 80

```
Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu Gly Pro Leu Leu Glu
                85                  90                  95

Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr Leu Val Leu Asp Lys
            100                 105                 110

Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp Leu Pro Gly Pro Gly
        115                 120                 125

Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly Ser Glu Ala Ser Ser
    130                 135                 140

Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro Glu Gly Ala Ser Ala
145                 150                 155                 160

Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser Ser Gln Leu Leu Arg
                165                 170                 175

Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr Pro Pro His Leu Lys
            180                 185                 190

Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile Ser Thr Asp Tyr Ser
        195                 200                 205

Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu Ser Asp Gly Pro Tyr
    210                 215                 220

Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala Ala Glu Pro Leu Pro
225                 230                 235                 240

Pro Ser Tyr Val Ala Cys Ser Met Gly Val Gln Val Glu Thr Ile Ser
                245                 250                 255

Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val
            260                 265                 270
```

```
His Tyr Thr Gly Met Leu Gly Asp Gly Lys Lys Val Asp Ser Ser Arg
        275                 280                 285

Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile
    290                 295                 300

Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Gly Ala
305                 310                 315                 320

Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro
                325                 330                 335

Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu
            340                 345                 350

Glu Leu Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr
        355                 360                 365

Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu
    370                 375                 380

Gly Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe
385                 390                 395                 400

Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly
                405                 410                 415

Val Ala Gln Met Ser Val Gly Gln Gly Ala Lys Leu Thr Ile Ser Pro
            420                 425                 430

Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His
        435                 440                 445

Ala Thr Leu Val Phe Asp Val Glu Leu Leu Glu Leu Glu
    450                 455                 460
```

<210> 4
<211> 527
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-GHR(353-638)

<400> 4

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140
```

```
Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175


His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190


Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Pro Asp Glu Lys Thr Glu Glu Ser Asp Thr Asp Arg Leu Leu Ser
                245                 250                 255


Ser Asp His Glu Lys Ser His Ser Asn Leu Gly Val Lys Asp Gly Asp
            260                 265                 270


Ser Gly Arg Thr Ser Cys Cys Glu Pro Asp Ile Leu Glu Thr Asp Phe
        275                 280                 285


Asn Ala Asn Asp Ile His Glu Gly Thr Ser Glu Val Ala Gln Pro Gln
    290                 295                 300


Arg Leu Lys Gly Glu Ala Asp Leu Leu Cys Leu Asp Gln Lys Asn Gln
305                 310                 315                 320


Asn Asn Ser Pro Tyr His Asp Ala Cys Pro Ala Thr Gln Gln Pro Ser
                325                 330                 335
```

```
Val Ile Gln Ala Glu Lys Asn Lys Pro Gln Pro Leu Pro Thr Glu Gly
            340                 345                 350


Ala Glu Ser Thr His Gln Ala Ala His Ile Gln Leu Ser Asn Pro Ser
        355                 360                 365


Ser Leu Ser Asn Ile Asp Phe Tyr Ala Gln Val Ser Asp Ile Thr Pro
    370                 375                 380


Ala Gly Ser Val Val Leu Ser Pro Gly Gln Lys Asn Lys Ala Gly Met
385                 390                 395                 400


Ser Gln Cys Asp Met His Pro Glu Met Val Ser Leu Cys Gln Glu Asn
                405                 410                 415


Phe Leu Met Asp Asn Ala Tyr Phe Cys Glu Ala Asp Ala Lys Lys Cys
            420                 425                 430


Ile Pro Val Ala Pro His Ile Lys Val Glu Ser His Ile Gln Pro Ser
        435                 440                 445


Leu Asn Gln Glu Asp Ile Tyr Ile Thr Thr Glu Ser Leu Thr Thr Ala
    450                 455                 460


Ala Gly Arg Pro Gly Thr Gly Glu His Val Pro Gly Ser Glu Met Pro
465                 470                 475                 480


Val Pro Asp Tyr Thr Ser Ile His Ile Val Gln Ser Pro Gln Gly Leu
                485                 490                 495


Ile Leu Asn Ala Thr Ala Leu Pro Leu Pro Asp Lys Glu Phe Leu Ser
            500                 505                 510


Ser Cys Gly Tyr Val Ser Thr Asp Gln Leu Asn Lys Ile Met Pro
        515                 520                 525
```

<210> 5
<211> 460
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)

<400> 5

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160
```

```
Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Val Thr Gln Leu Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala
                245                 250                 255

Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly
            260                 265                 270

Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln
        275                 280                 285

Val Tyr Phe Thr Tyr Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly
    290                 295                 300

Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu
305                 310                 315                 320

Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu
                325                 330                 335

Leu Leu Phe Ser Pro Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr
            340                 345                 350
```

```
Ala Pro Gly Gly Ser Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu
        355                 360                 365


Gln Glu Arg Val Pro Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro
    370                 375                 380


Thr Pro Gly Val Pro Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu
385                 390                 395                 400


Val Leu Arg Glu Ala Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu
                405                 410                 415


Gly Val Ser Phe Pro Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg
            420                 425                 430


Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu
        435                 440                 445


Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
    450                 455                 460


<210>  6
<211>  385
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)

<400>  6

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30
```

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220
```

```
Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln
                245                 250                 255


Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser
            260                 265                 270


Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly
        275                 280                 285


Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
    290                 295                 300


Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
305                 310                 315                 320


Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
                325                 330                 335


Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
            340                 345                 350


Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
        355                 360                 365


Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
    370                 375                 380


Gln
385


<210>  7
<211>  390
<212>  PRT
<213>  Artificial Sequence
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<220>
<223> CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862)

<400> 7

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Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175
```

```
His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Val Thr Pro Val Phe Arg His Pro Pro Cys Ser Asn Trp Pro Gln
                245                 250                 255

Arg Glu Lys Gly Ile Gln Gly His Gln Ala Ser Glu Lys Asp Met Met
            260                 265                 270

His Ser Ala Ser Ser Pro Pro Pro Pro Arg Ala Leu Gln Ala Glu Ser
        275                 280                 285

Arg Gln Leu Val Asp Leu Tyr Lys Val Leu Glu Ser Arg Gly Ser Asp
    290                 295                 300

Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
305                 310                 315                 320

Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
                325                 330                 335

Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
            340                 345                 350

Gln His Ile Ser Leu Ser Val Phe Pro Ser Ser Ser Leu His Pro Leu
        355                 360                 365
```

```
Thr Phe Ser Cys Gly Asp Lys Leu Thr Leu Asp Gln Leu Lys Met Arg
    370                 375                 380


Cys Asp Ser Leu Met Leu
385                 390


<210>  8
<211>  292
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(775-825)

<400>  8

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110
```

```
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175


His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190


Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
                245                 250                 255


Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
            260                 265                 270


Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
        275                 280                 285


Leu Glu Pro Gln
    290
```

<210> 9
<211> 458
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)

<400> 9

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160
```

```
Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr Glu Leu Gln Glu
                245                 250                 255

Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys Pro Ser Phe Trp
            260                 265                 270

Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser Glu Glu Arg Asp
        275                 280                 285

Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr Val Leu Asp Ala
    290                 295                 300

Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp Asp Gly Tyr Pro
305                 310                 315                 320

Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro Gly Leu Glu Asp
                325                 330                 335

Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys Gly Cys Val Ser
            340                 345                 350
```

```
Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser Leu Leu Asp Arg
        355                 360                 365


Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala Gly Gly Leu Pro
    370                 375                 380


Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser Glu Ala Gly Ser
385                 390                 395                 400


Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser Gly Phe Val Gly
                405                 410                 415


Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr Ser Pro Gly Asp
            420                 425                 430


Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Ile Pro Pro
        435                 440                 445


Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser
    450                 455


<210>  10
<211>  447
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)

<400>  10

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30
```

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220
```

```
Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp Ser
                245                 250                 255


Asp Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met His
            260                 265                 270


Gly Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Thr Ser Thr Glu
        275                 280                 285


Ser Gln Leu Ile Asp Pro Glu Ser Glu Glu Glu Pro Asp Leu Pro Glu
    290                 295                 300


Val Asp Val Glu Leu Pro Thr Met Pro Lys Asp Ser Pro Gln Gln Leu
305                 310                 315                 320


Glu Leu Leu Ser Gly Pro Cys Glu Arg Arg Lys Ser Pro Leu Gln Asp
                325                 330                 335


Pro Phe Pro Glu Glu Asp Tyr Ser Ser Thr Glu Gly Ser Gly Gly Arg
            340                 345                 350


Ile Thr Phe Asn Val Asp Leu Asn Ser Val Phe Leu Arg Val Leu Asp
        355                 360                 365


Asp Glu Asp Ser Asp Asp Leu Glu Ala Pro Leu Met Leu Ser Ser His
    370                 375                 380


Leu Glu Glu Met Val Asp Pro Glu Asp Pro Asp Asn Val Gln Ser Asn
385                 390                 395                 400


His Leu Leu Ala Ser Gly Glu Gly Thr Gln Pro Thr Phe Pro Ser Pro
                405                 410                 415
```

Ser Ser Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser Asp
420 425 430

Thr Ser Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
435 440 445

<210> 11
<211> 462
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR1(300-520)

<400> 11

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
115 120 125

```
Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Arg Gly Val Arg Pro Thr Pro Arg Val Arg Ala Pro Ala Thr Gln
                245                 250                 255

Gln Thr Arg Trp Lys Lys Asp Leu Ala Glu Asp Glu Glu Glu Glu Asp
            260                 265                 270

Glu Glu Asp Thr Glu Asp Gly Val Ser Phe Gln Pro Tyr Ile Glu Pro
        275                 280                 285

Pro Ser Phe Leu Gly Gln Glu His Gln Ala Pro Gly His Ser Glu Ala
    290                 295                 300

Gly Gly Val Asp Ser Gly Arg Pro Arg Ala Pro Leu Val Pro Ser Glu
305                 310                 315                 320
```

```
Gly Ser Ser Ala Trp Asp Ser Ser Asp Arg Ser Trp Ala Ser Thr Val
                325                 330                 335

Asp Ser Ser Trp Asp Arg Ala Gly Ser Ser Gly Tyr Leu Ala Glu Lys
            340                 345                 350

Gly Pro Gly Gln Gly Pro Gly Gly Asp Gly His Gln Glu Ser Leu Pro
        355                 360                 365

Pro Pro Glu Phe Ser Lys Asp Ser Gly Phe Leu Glu Glu Leu Pro Glu
    370                 375                 380

Asp Asn Leu Ser Ser Trp Ala Thr Trp Gly Thr Leu Pro Pro Glu Pro
385                 390                 395                 400

Asn Leu Val Pro Gly Gly Pro Pro Val Ser Leu Gln Thr Leu Thr Phe
                405                 410                 415

Cys Trp Glu Ser Ser Pro Glu Glu Glu Glu Glu Ala Arg Glu Ser Glu
            420                 425                 430

Ile Glu Asp Ser Asp Ala Gly Ser Trp Gly Ala Glu Ser Thr Gln Arg
        435                 440                 445

Thr Glu Asp Arg Gly Arg Thr Leu Gly His Tyr Met Ala Arg
    450                 455                 460
```

<210> 12
<211> 444
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8
SS-Myc-FKBP(F36V)-muEpoR(236-337;L264G,L265P)-muIL2Rb(337-539)

<400> 12

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Ala Ser
    130                 135                 140

Leu Leu Thr Ala Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Leu Ile Ser Leu Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Thr Leu Gln Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190
```

```
Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Leu Gln Arg Asp Gly Cys Leu Trp Trp Ser Pro Gly Ser
    210                 215                 220

Ser Phe Pro Glu Asp Pro Pro Ala His Leu Glu Val Leu Ser Glu Pro
225                 230                 235                 240

Arg Ala Val Gln Leu Leu Leu Leu Gln Lys Asp Ser Ala Pro Leu Pro
                245                 250                 255

Ser Pro Ser Gly His Ser Gln Ala Ser Cys Phe Thr Asn Gln Gly Tyr
            260                 265                 270

Phe Phe Phe His Leu Pro Asn Ala Leu Glu Ile Glu Ser Cys Gln Val
        275                 280                 285

Tyr Phe Thr Tyr Asp Pro Cys Val Glu Glu Glu Val Glu Glu Asp Gly
    290                 295                 300

Ser Arg Leu Pro Glu Gly Ser Pro His Pro Pro Leu Leu Pro Leu Ala
305                 310                 315                 320

Gly Glu Gln Asp Asp Tyr Cys Ala Phe Pro Pro Arg Asp Asp Leu Leu
                325                 330                 335

Leu Phe Ser Pro Ser Leu Ser Thr Pro Asn Thr Ala Tyr Gly Gly Ser
            340                 345                 350

Arg Ala Pro Glu Glu Arg Ser Pro Leu Ser Leu His Glu Gly Leu Pro
        355                 360                 365

Ser Leu Ala Ser Arg Asp Leu Met Gly Leu Gln Arg Pro Leu Glu Arg
    370                 375                 380
```

```
Met Pro Glu Gly Asp Gly Glu Gly Leu Ser Ala Asn Ser Ser Gly Glu
385                 390                 395                 400


Gln Ala Ser Val Pro Glu Gly Asn Leu His Gly Gln Asp Gln Asp Arg
                405                 410                 415


Gly Gln Gly Pro Ile Leu Thr Leu Asn Thr Asp Ala Tyr Leu Ser Leu
            420                 425                 430


Gln Glu Leu Gln Ala Gln Asp Ser Val His Leu Ile
        435                 440


<210>  13
<211>  385
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-muEpoR(236-337;L264G,L265P)-muIL7R(316-459)

<400>  13

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
```

```
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Ala Ser
    130                 135                 140

Leu Leu Thr Ala Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Leu Ile Ser Leu Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Thr Leu Gln Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Leu Gln Arg Asp Gly Cys Leu Trp Trp Ser Pro Gly Ser
    210                 215                 220

Ser Phe Pro Glu Asp Pro Pro Ala His Leu Glu Val Leu Ser Glu Pro
225                 230                 235                 240

Arg Ala Arg Asp Glu Val Glu Ser Phe Leu Pro Asn Asp Leu Pro Ala
                245                 250                 255

Gln Pro Glu Glu Leu Glu Thr Gln Gly His Arg Ala Ala Val His Ser
            260                 265                 270

Ala Asn Arg Ser Pro Glu Thr Ser Val Ser Pro Pro Glu Thr Val Arg
```

275 280 285

Arg Glu Ser Pro Leu Arg Cys Leu Ala Arg Asn Leu Ser Thr Cys Asn
290 295 300

Ala Pro Pro Leu Leu Ser Ser Arg Ser Pro Asp Tyr Arg Asp Gly Asp
305 310 315 320

Arg Asn Arg Pro Pro Val Tyr Gln Asp Leu Leu Pro Asn Ser Gly Asn
325 330 335

Thr Asn Val Pro Val Pro Val Pro Gln Pro Leu Pro Phe Gln Ser Gly
340 345 350

Ile Leu Ile Pro Val Ser Gln Arg Gln Pro Ile Ser Thr Ser Ser Val
355 360 365

Leu Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
370 375 380

Lys
385

<210> 14
<211> 436
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8
SS-Myc-FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)-IL12Rb2
(775-825)

<400> 14

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met

```
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
```

```
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln
                245                 250                 255

Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser
            260                 265                 270

Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly
        275                 280                 285

Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
    290                 295                 300

Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
305                 310                 315                 320

Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
                325                 330                 335

Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
            340                 345                 350

Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
        355                 360                 365

Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
    370                 375                 380

Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
385                 390                 395                 400

Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
```

405 410 415

Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
420 425 430

Leu Glu Pro Gln
435

<210> 15
<211> 426
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8
SS-Myc-FKBP(F36V)-GP130(609-700)-IL7R(316-459)-IL12Rb2(775-825)

<400> 15

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

```
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Thr Thr Pro Lys Phe
    130                 135                 140

Ala Gln Gly Glu Ile Glu Ala Ile Val Val Pro Val Cys Leu Ala Phe
145                 150                 155                 160

Leu Leu Thr Thr Leu Leu Gly Val Leu Phe Cys Phe Asn Lys Arg Asp
                165                 170                 175

Leu Ile Lys Lys His Ile Trp Pro Asn Val Pro Asp Pro Ser Lys Ser
            180                 185                 190

His Ile Ala Gln Trp Ser Pro His Thr Pro Pro Arg His Asn Phe Asn
        195                 200                 205

Ser Lys Asp Gln Met Tyr Ser Asp Gly Asn Phe Thr Asp Val Ser Val
    210                 215                 220

Val Glu Ile Glu Ala Asn Asp Ala Arg Asp Glu Val Glu Gly Phe Leu
225                 230                 235                 240

Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu
                245                 250                 255

Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile
            260                 265                 270

Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly
        275                 280                 285

Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu
    290                 295                 300
```

```
Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu
305                 310                 315                 320


Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser
                325                 330                 335


Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
            340                 345                 350


Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
        355                 360                 365


Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala
    370                 375                 380


Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
385                 390                 395                 400


Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
                405                 410                 415


Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425


<210>  16
<211>  433
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-PrlR(221-319)-IL7R(316-459)-IL12Rb2(775-825)

<400>  16

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ala Thr Phe Ile Gln
    130                 135                 140

Ile Pro Ser Asp Phe Thr Met Asn Asp Thr Thr Val Trp Ile Ser Val
145                 150                 155                 160

Ala Val Leu Ser Ala Val Ile Cys Leu Ile Ile Val Trp Ala Val Ala
                165                 170                 175

Leu Lys Gly Tyr Ser Met Val Thr Cys Ile Phe Pro Pro Val Pro Gly
            180                 185                 190

Pro Lys Ile Lys Gly Phe Asp Ala His Leu Leu Glu Lys Gly Lys Ser
        195                 200                 205
```

```
Glu Glu Leu Leu Ser Ala Leu Gly Cys Gln Asp Phe Pro Pro Thr Ser
    210                 215                 220

Asp Tyr Glu Asp Leu Leu Val Glu Tyr Leu Glu Val Asp Asp Ala Arg
225                 230                 235                 240

Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
                245                 250                 255

Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
            260                 265                 270

Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
        275                 280                 285

Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile
    290                 295                 300

Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
305                 310                 315                 320

Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
                325                 330                 335

Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
            340                 345                 350

Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
        355                 360                 365

Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp
    370                 375                 380

Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
385                 390                 395                 400
```

Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
405 410 415

Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
420 425 430

Gln

<210> 17
<211> 436
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)-GHR(251-352)-IL7R(316-459)-IL12Rb2(775-825)

<400> 17

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

```
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Leu Pro Gln Met Ser
    130                 135                 140

Gln Phe Thr Cys Glu Glu Asp Phe Tyr Phe Pro Trp Leu Leu Ile Ile
145                 150                 155                 160

Ile Phe Gly Ile Phe Gly Leu Thr Val Met Leu Phe Val Phe Leu Phe
                165                 170                 175

Ser Lys Gln Gln Arg Ile Lys Met Leu Ile Leu Pro Pro Val Pro Val
            180                 185                 190

Pro Lys Ile Lys Gly Ile Asp Pro Asp Leu Leu Lys Glu Gly Lys Leu
        195                 200                 205

Glu Glu Val Asn Thr Ile Leu Ala Ile His Asp Ser Tyr Lys Pro Glu
    210                 215                 220

Phe His Ser Asp Asp Ser Trp Val Glu Phe Ile Glu Leu Asp Ile Asp
225                 230                 235                 240

Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln
                245                 250                 255

Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser
            260                 265                 270

Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly
        275                 280                 285

Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
    290                 295                 300
```

```
Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
305                 310                 315                 320


Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
                325                 330                 335


Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
            340                 345                 350


Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
        355                 360                 365


Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
    370                 375                 380


Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
385                 390                 395                 400


Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
                405                 410                 415


Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
            420                 425                 430


Leu Glu Pro Gln
        435


<210>  18
<211>  431
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825)

<400>  18
```

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Leu Thr Leu Met Thr
    130                 135                 140

Leu Thr Pro Glu Gly Ser Glu Leu His Ile Ile Leu Gly Leu Phe Gly
145                 150                 155                 160

Leu Leu Leu Leu Leu Thr Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys
                165                 170                 175

Ser Pro Asn Arg Lys Asn Pro Leu Trp Pro Ser Val Pro Asp Pro Ala
            180                 185                 190
```

```
His Ser Ser Leu Gly Ser Trp Val Pro Thr Ile Met Glu Glu Asp Ala
        195                 200                 205

Phe Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile Thr Lys Leu Thr Val
    210                 215                 220

Leu Glu Glu Asp Glu Lys Lys Pro Val Pro Trp Glu Ala Arg Asp Glu
225                 230                 235                 240

Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
                245                 250                 255

Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
            260                 265                 270

Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
        275                 280                 285

Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser
    290                 295                 300

Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
305                 310                 315                 320

Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
                325                 330                 335

Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
            340                 345                 350

Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
        355                 360                 365

Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys
    370                 375                 380
```

```
Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
385                 390                 395                 400


Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
                405                 410                 415


His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425                 430


<210>  19
<211>  439
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)

<400>  19

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110
```

```
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr Arg
    130                 135                 140

Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala Leu
145                 150                 155                 160

His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
                165                 170                 175

Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
            180                 185                 190

Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
        195                 200                 205

Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
    210                 215                 220

Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
225                 230                 235                 240

Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
                245                 250                 255

Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
            260                 265                 270

Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
        275                 280                 285

Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
    290                 295                 300
```

```
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
305                 310                 315                 320


Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
                325                 330                 335


Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
            340                 345                 350


Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
        355                 360                 365


Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
    370                 375                 380


Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
385                 390                 395                 400


Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
                405                 410                 415


Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
            420                 425                 430


Leu Glu Glu Leu Glu Pro Gln
        435


<210>  20
<211>  282
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(376-416)

<400>  20
```

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175


His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190
```

```
Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
                245                 250                 255


Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
            260                 265                 270


Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
        275                 280


<210>  21
<211>  277
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(424-459)

<400>  21

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60
```

```
Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                245                 250                 255
```

```
Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            260                 265                 270


Phe Tyr Gln Asn Gln
        275


<210>  22
<211>  309
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459)

<400>  22

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110
```

```
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
                245                 250                 255

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
            260                 265                 270

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile Leu
        275                 280                 285

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
    290                 295                 300
```

Phe Tyr Gln Asn Gln
305

<210> 23
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(424-459;Y456F)

<400> 23

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
115 120 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
130 135 140

```
Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175


His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190


Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                245                 250                 255


Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            260                 265                 270


Phe Phe Gln Asn Gln
        275
```

<210> 24
<211> 309
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)-
EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459;Y456F)

<400> 24

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190
```

```
Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
                245                 250                 255


Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
            260                 265                 270


Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile Leu
        275                 280                 285


Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
    290                 295                 300


Phe Phe Gln Asn Gln
305


<210>  25
<211>  282
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(393-433)

<400>  25

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
```

```
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
```

210 215 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225 230 235 240

Cys Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro
245 250 255

Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser
260 265 270

Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser
275 280

<210> 26
<211> 275
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(518-551)

<400> 26

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

```
Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn
                245                 250                 255

Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr
            260                 265                 270
```

His Leu Val
275

<210> 27
<211> 323
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433)

<400> 27

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
115 120 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser

```
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His
                245                 250                 255

Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu
            260                 265                 270

Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly
        275                 280                 285

Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu
    290                 295                 300

Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe
305                 310                 315                 320

Ser Pro Ser
```

<210> 28
<211> 316
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(339-379,518-551)

<400> 28

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140
```

```
Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175


His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190


Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His
                245                 250                 255


Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu
            260                 265                 270


Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Gly Gln Gly Glu Phe Arg
        275                 280                 285


Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu
    290                 295                 300


Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
305                 310                 315


<210>  29
<211>  316
<212>  PRT
```

<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(393-433,518-551)

<400> 29

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
```

165 170 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
180 185 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
195 200 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
210 215 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225 230 235 240

Cys Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro
245 250 255

Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser
260 265 270

Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg
275 280 285

Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu
290 295 300

Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
305 310 315

<210> 30
<211> 357
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)-
EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433,518-551)

<400> 30

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190
```

```
Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His
                245                 250                 255

Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu
            260                 265                 270

Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly
        275                 280                 285

Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu
    290                 295                 300

Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe
305                 310                 315                 320

Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro
                325                 330                 335

Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp
            340                 345                 350

Pro Thr His Leu Val
        355
```

<210> 31
<211> 472

<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(955-1186)

<400> 31

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60


Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80


Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95


Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160
```

```
Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp
                245                 250                 255

Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val
            260                 265                 270

Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser Ser
        275                 280                 285

Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala Thr Ser
    290                 295                 300

Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser Cys
305                 310                 315                 320

Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Tyr Ser Ser Asp Pro Thr
                325                 330                 335

Gly Ala Leu Thr Glu Asp Ser Ile Asp Asp Thr Phe Leu Pro Val Pro
            340                 345                 350
```

```
Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser Val Gln
        355                 360                 365


Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser Arg Asp
    370                 375                 380


Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro Glu Tyr
385                 390                 395                 400


Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro
                405                 410                 415


Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro
            420                 425                 430


Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile
        435                 440                 445


Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro
    450                 455                 460


Gln Ser Ser Glu Phe Ile Gly Ala
465                 470


<210>  32
<211>  459
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-
EpoR(237-338;L241G,L242P)-EGFR(955-1044,1058-1186;Y974F)

<400>  32

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
```

```
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
```

```
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp
                245                 250                 255

Ser Asn Phe Phe Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val
            260                 265                 270

Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser Ser
        275                 280                 285

Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala Thr Ser
    290                 295                 300

Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser Cys
305                 310                 315                 320

Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu
                325                 330                 335

Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly
            340                 345                 350

Ser Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro
        355                 360                 365

Ser Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn
    370                 375                 380

Pro Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe
385                 390                 395                 400

Asp Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu
```

405 410 415

Asp Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro
420 425 430

Asn Gly Ile Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg
435 440 445

Val Ala Pro Gln Ser Ser Glu Phe Ile Gly Ala
450 455

<210> 33
<211> 295
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(955-1009;Y974F)

<400> 33

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

```
Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp
                245                 250                 255

Ser Asn Phe Phe Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val
            260                 265                 270

Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser Ser
        275                 280                 285
```

Pro Ser Thr Ser Arg Thr Pro
290 295

<210> 34
<211> 295
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1019-1085)

<400> 34

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
115 120 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser

```
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser
                245                 250                 255

Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe
            260                 265                 270

Leu Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala
        275                 280                 285

Gly Ser Val Gln Asn Pro Val
    290                 295


<210>  35
<211>  295
<212>  PRT
<213>  Artificial Sequence
```

<220>
<223> CD8 SS-Myc-FKBP(F36V)-
EpoR(237-338;L241G,L242P)-EGFR(1037-1044,1058-1103;Y1068/1101F)

<400> 35

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
115 120 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
130 135 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145 150 155 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
165 170 175

```
His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190


Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu Pro
                245                 250                 255


Val Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser
            260                 265                 270


Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser
        275                 280                 285


Arg Asp Pro His Phe Gln Asp
    290                 295


<210>  36
<211>  295
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)-
EpoR(237-338;L241G,L242P)-EGFR(1066-1118;Y1068/1086F)

<400>  36

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205
```

```
Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Val Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly
                245                 250                 255


Ser Val Gln Asn Pro Val Phe His Asn Gln Pro Leu Asn Pro Ala Pro
            260                 265                 270


Ser Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn
        275                 280                 285


Pro Glu Tyr Leu Asn Thr Val
    290                 295


<210>  37
<211>  295
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1122-1165)

<400>  37

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
            20                  25                  30


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


Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
```

```
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Pro Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr
```

245 250 255

Phe Asp Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser
260 265 270

Leu Asp Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys
275 280 285

Pro Asn Gly Ile Phe Lys Gly
290 295

<210> 38
<211> 295
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1133-1186;Y1148F)

<400> 38

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

```
Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110


Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125


Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140


Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160


Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175


His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190


Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205


Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220


Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240


Cys Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp
                245                 250                 255


Phe Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe
            260                 265                 270


Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln
        275                 280                 285
```

Ser Ser Glu Phe Ile Gly Ala
290 295

<210> 39
<211> 397
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-BLNK(53-208)

<400> 39

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
85 90 95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
100 105 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
115 120 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser

```
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp
                245                 250                 255

Phe Asp Ser Asp Tyr Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met
            260                 265                 270

Tyr Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro Pro
        275                 280                 285

Pro Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala
    290                 295                 300

Arg Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro
305                 310                 315                 320

Phe Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala
```

325 330 335

Arg Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln
340 345 350

Val Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val
355 360 365

Val Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser
370 375 380

Ser Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
385 390 395

<210> 40
<211> 397
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F)

<400> 40

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
20 25 30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
50 55 60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65 70 75 80

```
Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp
                245                 250                 255

Phe Asp Ser Asp Phe Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met
            260                 265                 270
```

```
Tyr Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro Pro
        275                 280                 285


Pro Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala
    290                 295                 300


Arg Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro
305                 310                 315                 320


Phe Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala
                325                 330                 335


Arg Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln
            340                 345                 350


Val Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val
        355                 360                 365


Val Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser
    370                 375                 380


Ser Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
385                 390                 395


<210>  41
<211>  397
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-Myc-FKBP(F36V)- EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F,Y96F)

<400>  41

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Met
```

```
            20                  25                  30

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

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
    50                  55                  60

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
65                  70                  75                  80

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
                85                  90                  95

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
            100                 105                 110

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
        115                 120                 125

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val Ser
    130                 135                 140

Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser Leu
145                 150                 155                 160

Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu Ser
                165                 170                 175

His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser Pro
            180                 185                 190

Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe Gln
        195                 200                 205

Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys Thr
```

```
    210                 215                 220

Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu Arg
225                 230                 235                 240

Cys Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp
                245                 250                 255

Phe Asp Ser Asp Phe Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met
            260                 265                 270

Tyr Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Phe Glu Pro Pro
        275                 280                 285

Pro Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala
    290                 295                 300

Arg Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro
305                 310                 315                 320

Phe Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala
                325                 330                 335

Arg Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln
            340                 345                 350

Val Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val
        355                 360                 365

Val Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser
    370                 375                 380

Ser Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
385                 390                 395
```

<210> 42

<211> 378
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)

<400> 42

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
130 135 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145 150 155 160

```
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
225                 230                 235                 240

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
                245                 250                 255

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
            260                 265                 270

Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
        275                 280                 285

Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
    290                 295                 300

Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
305                 310                 315                 320

Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
                325                 330                 335

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
            340                 345                 350
```

Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
355 360 365

Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
370 375

<210> 43
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rb(333-551)

<400> 43

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu

```
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Val Thr Gln Leu Leu Leu
225                 230                 235                 240

Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
                245                 250                 255

Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
            260                 265                 270

Asp Ala Leu Glu Ile Glu Ala Cys Gln Val Tyr Phe Thr Tyr Asp Pro
        275                 280                 285

Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val Ala Gly Ala Pro Thr Gly
    290                 295                 300

Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr
```

305 310 315 320

Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Leu
325 330 335

Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala Pro Gly Gly Ser Gly Ala
340 345 350

Gly Glu Glu Arg Met Pro Pro Ser Leu Gln Glu Arg Val Pro Arg Asp
355 360 365

Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr Pro Gly Val Pro Asp Leu
370 375 380

Val Asp Phe Gln Pro Pro Pro Glu Leu Val Leu Arg Glu Ala Gly Glu
385 390 395 400

Glu Val Pro Asp Ala Gly Pro Arg Glu Gly Val Ser Phe Pro Trp Ser
405 410 415

Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro
420 425 430

Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp
435 440 445

Pro Thr His Leu Val
450

<210> 44
<211> 309
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)

<400> 44

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190
```

```
Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205


Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220


Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Asp Glu Gly Val Ala Gly
225                 230                 235                 240


Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu
                245                 250                 255


Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe
            260                 265                 270


Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro
        275                 280                 285


Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp
    290                 295                 300


Pro Thr His Leu Val
305


<210>  45
<211>  350
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)

<400>  45

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
```

```
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
```

```
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Gln Gln Asp Lys Val Pro
225                 230                 235                 240

Glu Pro Ala Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr
                245                 250                 255

Asn Gln Gly Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu
            260                 265                 270

Ala Cys Gln Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro
        275                 280                 285

Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe
    290                 295                 300

Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu
305                 310                 315                 320

Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu
                325                 330                 335

Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
            340                 345                 350


<210>  46
<211>  429
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)

<400>  46

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205
```

```
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
225                 230                 235                 240

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
                245                 250                 255

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
            260                 265                 270

Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
        275                 280                 285

Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
    290                 295                 300

Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
305                 310                 315                 320

Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
                325                 330                 335

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
            340                 345                 350

Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
        355                 360                 365

Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu
    370                 375                 380

Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
385                 390                 395                 400
```

His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
405 410 415

Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
420 425

<210> 47
<211> 595
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-IL21R(322-538)

<400> 47

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu

```
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
225                 230                 235                 240

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
                245                 250                 255

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
            260                 265                 270

Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
        275                 280                 285

Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
    290                 295                 300

Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
```

```
305                 310                 315                 320

Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
                325                 330                 335

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
            340                 345                 350

Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
        355                 360                 365

Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Pro Arg Ser Pro Ala Lys
    370                 375                 380

Arg Leu Gln Leu Thr Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser
385                 390                 395                 400

Asp Gly Val Pro Lys Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly
                405                 410                 415

Gly Ser Ala Tyr Ser Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser
            420                 425                 430

Ile Asp Thr Val Thr Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro
        435                 440                 445

Cys Ser Cys Glu Asp Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly
    450                 455                 460

Leu Glu Pro Ser Pro Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr
465                 470                 475                 480

Thr Val Leu Ser Cys Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly
                485                 490                 495

Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp
```

500 505 510

Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly
515 520 525

Gly Val Ser Glu Ser Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met
530 535 540

Asp Thr Phe Asp Ser Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val
545 550 555 560

Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr
565 570 575

Leu Arg Gln Trp Val Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro
580 585 590

Gln Ala Ser
595

<210> 48
<211> 595
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)- IL21R(322-538)-IL7R(316-459)

<400> 48

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

```
Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Pro Arg Ser Pro Ala Lys
225                 230                 235                 240
```

```
Arg Leu Gln Leu Thr Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser
                245                 250                 255

Asp Gly Val Pro Lys Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly
            260                 265                 270

Gly Ser Ala Tyr Ser Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser
        275                 280                 285

Ile Asp Thr Val Thr Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro
    290                 295                 300

Cys Ser Cys Glu Asp Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly
305                 310                 315                 320

Leu Glu Pro Ser Pro Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr
                325                 330                 335

Thr Val Leu Ser Cys Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly
            340                 345                 350

Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp
        355                 360                 365

Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly
    370                 375                 380

Gly Val Ser Glu Ser Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met
385                 390                 395                 400

Asp Thr Phe Asp Ser Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val
                405                 410                 415

Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr
            420                 425                 430
```

```
Leu Arg Gln Trp Val Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro
        435                 440                 445


Gln Ala Ser Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
    450                 455                 460


Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val
465                 470                 475                 480


Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser
                485                 490                 495


Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala
            500                 505                 510


Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu
        515                 520                 525


Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu
    530                 535                 540


Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly
545                 550                 555                 560


Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser
                565                 570                 575


Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
            580                 585                 590


Gln Asn Gln
        595


<210>  49
<211>  526
<212>  PRT
```

<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-
TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)-IL21R(322-538)

<400> 49

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
130 135 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145 150 155 160

```
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Asp Glu Gly Val Ala Gly
225                 230                 235                 240

Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu
                245                 250                 255

Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe
            260                 265                 270

Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro
        275                 280                 285

Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp
    290                 295                 300

Pro Thr His Leu Val Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr
305                 310                 315                 320

Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys
                325                 330                 335

Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser
            340                 345                 350
```

```
Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr
        355                 360                 365

Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp
    370                 375                 380

Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro
385                 390                 395                 400

Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys
                405                 410                 415

Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser
            420                 425                 430

Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala
        435                 440                 445

Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser
    450                 455                 460

Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser
465                 470                 475                 480

Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr
                485                 490                 495

Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val
            500                 505                 510

Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser
        515                 520                 525
```

<210> 50
<211> 526
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-
IL21R(322-538)-IL2Rbsmall(393-433,518-551)

<400> 50

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140


Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160


Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
```

```
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Pro Arg Ser Pro Ala Lys
225                 230                 235                 240

Arg Leu Gln Leu Thr Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser
                245                 250                 255

Asp Gly Val Pro Lys Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly
            260                 265                 270

Gly Ser Ala Tyr Ser Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser
        275                 280                 285

Ile Asp Thr Val Thr Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro
    290                 295                 300

Cys Ser Cys Glu Asp Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly
305                 310                 315                 320

Leu Glu Pro Ser Pro Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr
                325                 330                 335

Thr Val Leu Ser Cys Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly
            340                 345                 350

Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp
```

```
        355                 360                 365

Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly
    370                 375                 380

Gly Val Ser Glu Ser Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met
385                 390                 395                 400

Asp Thr Phe Asp Ser Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val
                405                 410                 415

Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr
            420                 425                 430

Leu Arg Gln Trp Val Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro
        435                 440                 445

Gln Ala Ser Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro
    450                 455                 460

Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe
465                 470                 475                 480

Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu
                485                 490                 495

Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu
            500                 505                 510

Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
        515                 520                 525
```

<210> 51
<211> 567
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-
TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)-IL21R(322-538)

<400> 51

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140


Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160


Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175
```

```
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Gln Gln Asp Lys Val Pro
225                 230                 235                 240

Glu Pro Ala Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr
                245                 250                 255

Asn Gln Gly Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu
            260                 265                 270

Ala Cys Gln Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro
        275                 280                 285

Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe
    290                 295                 300

Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu
305                 310                 315                 320

Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu
                325                 330                 335

Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val Pro Arg
            340                 345                 350

Ser Pro Ala Lys Arg Leu Gln Leu Thr Glu Leu Gln Glu Pro Ala Glu
        355                 360                 365
```

```
Leu Val Glu Ser Asp Gly Val Pro Lys Pro Ser Phe Trp Pro Thr Ala
    370                 375                 380

Gln Asn Ser Gly Gly Ser Ala Tyr Ser Glu Glu Arg Asp Arg Pro Tyr
385                 390                 395                 400

Gly Leu Val Ser Ile Asp Thr Val Thr Val Leu Asp Ala Glu Gly Pro
                405                 410                 415

Cys Thr Trp Pro Cys Ser Cys Glu Asp Asp Gly Tyr Pro Ala Leu Asp
            420                 425                 430

Leu Asp Ala Gly Leu Glu Pro Ser Pro Gly Leu Glu Asp Pro Leu Leu
        435                 440                 445

Asp Ala Gly Thr Thr Val Leu Ser Cys Gly Cys Val Ser Ala Gly Ser
    450                 455                 460

Pro Gly Leu Gly Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu Lys Pro
465                 470                 475                 480

Pro Leu Ala Asp Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp Gly Gly
                485                 490                 495

Arg Ser Pro Gly Gly Val Ser Glu Ser Glu Ala Gly Ser Pro Leu Ala
            500                 505                 510

Gly Leu Asp Met Asp Thr Phe Asp Ser Gly Phe Val Gly Ser Asp Cys
        515                 520                 525

Ser Ser Pro Val Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu Gly Pro
    530                 535                 540

Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Ile Pro Pro Pro Leu Ser
545                 550                 555                 560
```

Ser Pro Gly Pro Gln Ala Ser
565

<210> 52
<211> 567
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-
IL21R(322-538)-IL2Rbsmall(339-379,393-433,518-551)

<400> 52

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

```
Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Pro Arg Ser Pro Ala Lys
225                 230                 235                 240

Arg Leu Gln Leu Thr Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser
                245                 250                 255

Asp Gly Val Pro Lys Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly
            260                 265                 270

Gly Ser Ala Tyr Ser Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser
        275                 280                 285

Ile Asp Thr Val Thr Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro
    290                 295                 300

Cys Ser Cys Glu Asp Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly
305                 310                 315                 320
```

```
Leu Glu Pro Ser Pro Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr
                325                 330                 335

Thr Val Leu Ser Cys Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly
            340                 345                 350

Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp
        355                 360                 365

Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly
    370                 375                 380

Gly Val Ser Glu Ser Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met
385                 390                 395                 400

Asp Thr Phe Asp Ser Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val
                405                 410                 415

Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr
            420                 425                 430

Leu Arg Gln Trp Val Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro
        435                 440                 445

Gln Ala Ser Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser
    450                 455                 460

Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe
465                 470                 475                 480

His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val
                485                 490                 495

Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser
            500                 505                 510
```

Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu
515 520 525

Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg
530 535 540

Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly
545 550 555 560

Gln Asp Pro Thr His Leu Val
565

<210> 53
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-
TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)-IL7R(316-459)

<400> 53

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

```
Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Asp Glu Gly Val Ala Gly
225                 230                 235                 240

Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu
                245                 250                 255

Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe
            260                 265                 270
```

```
Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro
        275                 280                 285

Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp
    290                 295                 300

Pro Thr His Leu Val Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
305                 310                 315                 320

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
                325                 330                 335

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
            340                 345                 350

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
        355                 360                 365

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
    370                 375                 380

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
385                 390                 395                 400

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
                405                 410                 415

Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
            420                 425                 430

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
        435                 440                 445

Phe Tyr Gln Asn Gln
    450
```

<210> 54
<211> 453
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-
TPOR/MPLR(478-582)-IL7R(316-459)-IL2Rbsmall(393-433,518-551)

<400> 54

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140


Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
```

```
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
225                 230                 235                 240

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
                245                 250                 255

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
            260                 265                 270

Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
        275                 280                 285

Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
    290                 295                 300

Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
305                 310                 315                 320

Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
                325                 330                 335

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
```

340 345 350

Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
355 360 365

Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Asp Glu Gly Val Ala Gly
370 375 380

Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu
385 390 395 400

Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe
405 410 415

Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro
420 425 430

Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp
435 440 445

Pro Thr His Leu Val
450

<210> 55
<211> 494
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-
IL2Rbsmall(339-379,393-433,518-551)-IL7R(316-459)

<400> 55

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

```
Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220
```

```
Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Gln Gln Asp Lys Val Pro
225                 230                 235                 240

Glu Pro Ala Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr
                245                 250                 255

Asn Gln Gly Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu
            260                 265                 270

Ala Cys Gln Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro
        275                 280                 285

Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe
    290                 295                 300

Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu
305                 310                 315                 320

Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu
                325                 330                 335

Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val Ala Arg
            340                 345                 350

Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
        355                 360                 365

Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
    370                 375                 380

Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
385                 390                 395                 400

Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile
                405                 410                 415
```

Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
420 425 430

Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
435 440 445

Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
450 455 460

Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
465 470 475 480

Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
485 490

<210> 56
<211> 494
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-IL2Rbsmall(339-379,393-433,518-551)

<400> 56

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

```
Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
225                 230                 235                 240

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
                245                 250                 255
```

```
Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
            260                 265                 270


Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
        275                 280                 285


Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
    290                 295                 300


Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
305                 310                 315                 320


Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
                325                 330                 335


Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
            340                 345                 350


Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
        355                 360                 365


Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Gln Gln Asp Lys Val Pro
    370                 375                 380


Glu Pro Ala Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr
385                 390                 395                 400


Asn Gln Gly Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu
                405                 410                 415


Ala Cys Gln Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro
            420                 425                 430


Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe
        435                 440                 445
```

Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu
450 455 460

Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu
465 470 475 480

Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
485 490

<210> 57
<211> 429
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-PD1(156-191)-TPOR/MPLR (514-582)-IL7R(316-459)-IL12Rb2(775-825)

<400> 57

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

```
Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Pro Ser Pro Ser Pro Arg Pro Ala Gly Gln Phe Gln Thr Leu Val
    130                 135                 140

Val Gly Val Val Gly Gly Leu Leu Gly Ser Leu Val Leu Leu Val Trp
145                 150                 155                 160

Val Leu Ala Val Ile Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
225                 230                 235                 240

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
                245                 250                 255

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
            260                 265                 270

Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
        275                 280                 285
```

```
Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
    290                 295                 300

Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
305                 310                 315                 320

Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
                325                 330                 335

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
            340                 345                 350

Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
        355                 360                 365

Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu
    370                 375                 380

Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
385                 390                 395                 400

His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
                405                 410                 415

Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425


<210>  58
<211>  288
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)- TPOR/MPLR(478-582)-EGFR(1122-1165)

<400>  58

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145                 150                 155                 160

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205
```

```
Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Pro Glu Tyr Leu Asn Thr
225                 230                 235                 240

Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro Ala His Trp
                245                 250                 255

Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp Tyr Gln
            260                 265                 270

Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe Lys Gly
        275                 280                 285


<210>  59
<211>  508
<212>  PRT
<213>  Homo sapiens

<400>  59

Met Asp His Leu Gly Ala Ser Leu Trp Pro Gln Val Gly Ser Leu Cys
1               5                   10                  15

Leu Leu Leu Ala Gly Ala Ala Trp Ala Pro Pro Pro Asn Leu Pro Asp
            20                  25                  30

Pro Lys Phe Glu Ser Lys Ala Ala Leu Leu Ala Ala Arg Gly Pro Glu
        35                  40                  45

Glu Leu Leu Cys Phe Thr Glu Arg Leu Glu Asp Leu Val Cys Phe Trp
    50                  55                  60

Glu Glu Ala Ala Ser Ala Gly Val Gly Pro Gly Asn Tyr Ser Phe Ser
65                  70                  75                  80
```

```
Tyr Gln Leu Glu Asp Glu Pro Trp Lys Leu Cys Arg Leu His Gln Ala
                85                  90                  95

Pro Thr Ala Arg Gly Ala Val Arg Phe Trp Cys Ser Leu Pro Thr Ala
            100                 105                 110

Asp Thr Ser Ser Phe Val Pro Leu Glu Leu Arg Val Thr Ala Ala Ser
        115                 120                 125

Gly Ala Pro Arg Tyr His Arg Val Ile His Ile Asn Glu Val Val Leu
    130                 135                 140

Leu Asp Ala Pro Val Gly Leu Val Ala Arg Leu Ala Asp Glu Ser Gly
145                 150                 155                 160

His Val Val Leu Arg Trp Leu Pro Pro Pro Glu Thr Pro Met Thr Ser
                165                 170                 175

His Ile Arg Tyr Glu Val Asp Val Ser Ala Gly Asn Gly Ala Gly Ser
            180                 185                 190

Val Gln Arg Val Glu Ile Leu Glu Gly Arg Thr Glu Cys Val Leu Ser
        195                 200                 205

Asn Leu Arg Gly Arg Thr Arg Tyr Thr Phe Ala Val Arg Ala Arg Met
    210                 215                 220

Ala Glu Pro Ser Phe Gly Gly Phe Trp Ser Ala Trp Ser Glu Pro Val
225                 230                 235                 240

Ser Leu Leu Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
                245                 250                 255

Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val Leu Ala Leu Leu
            260                 265                 270
```

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
        275                 280                 285

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
    290                 295                 300

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
305                 310                 315                 320

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
                325                 330                 335

Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
            340                 345                 350

Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
        355                 360                 365

Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
    370                 375                 380

Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
385                 390                 395                 400

Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
                405                 410                 415

Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
            420                 425                 430

Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
        435                 440                 445

Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
    450                 455                 460
```

```
Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
465                 470                 475                 480


Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala
                485                 490                 495


Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
            500                 505


<210>  60
<211>  918
<212>  PRT
<213>  Homo sapiens

<400>  60

Met Leu Thr Leu Gln Thr Trp Leu Val Gln Ala Leu Phe Ile Phe Leu
1               5                   10                  15


Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser
            20                  25                  30


Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
        35                  40                  45


Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
    50                  55                  60


Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr
65                  70                  75                  80


Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser
                85                  90                  95


Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu
            100                 105                 110
```

```
Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys
        115                 120                 125


Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys
    130                 135                 140


Glu Trp Asp Arg Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu
145                 150                 155                 160


Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg
                165                 170                 175


Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val
            180                 185                 190


Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr
        195                 200                 205


Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro
    210                 215                 220


Pro His Asn Leu Ser Val Ile Asn Ser Glu Glu Leu Ser Ser Ile Leu
225                 230                 235                 240


Lys Leu Thr Trp Thr Asn Pro Ser Ile Lys Ser Val Ile Ile Leu Lys
                245                 250                 255


Tyr Asn Ile Gln Tyr Arg Thr Lys Asp Ala Ser Thr Trp Ser Gln Ile
            260                 265                 270


Pro Pro Glu Asp Thr Ala Ser Thr Arg Ser Ser Phe Thr Val Gln Asp
        275                 280                 285


Leu Lys Pro Phe Thr Glu Tyr Val Phe Arg Ile Arg Cys Met Lys Glu
    290                 295                 300
```

```
Asp Gly Lys Gly Tyr Trp Ser Asp Trp Ser Glu Glu Ala Ser Gly Ile
305                 310                 315                 320


Thr Tyr Glu Asp Arg Pro Ser Lys Ala Pro Ser Phe Trp Tyr Lys Ile
                325                 330                 335


Asp Pro Ser His Thr Gln Gly Tyr Arg Thr Val Gln Leu Val Trp Lys
            340                 345                 350


Thr Leu Pro Pro Phe Glu Ala Asn Gly Lys Ile Leu Asp Tyr Glu Val
        355                 360                 365


Thr Leu Thr Arg Trp Lys Ser His Leu Gln Asn Tyr Thr Val Asn Ala
    370                 375                 380


Thr Lys Leu Thr Val Asn Leu Thr Asn Asp Arg Tyr Val Ala Thr Leu
385                 390                 395                 400


Thr Val Arg Asn Leu Val Gly Lys Ser Asp Ala Ala Val Leu Thr Ile
                405                 410                 415


Pro Ala Cys Asp Phe Gln Ala Thr His Pro Val Met Asp Leu Lys Ala
            420                 425                 430


Phe Pro Lys Asp Asn Met Leu Trp Val Glu Trp Thr Thr Pro Arg Glu
        435                 440                 445


Ser Val Lys Lys Tyr Ile Leu Glu Trp Cys Val Leu Ser Asp Lys Ala
    450                 455                 460


Pro Cys Ile Thr Asp Trp Gln Gln Glu Asp Gly Thr Val His Arg Thr
465                 470                 475                 480


Tyr Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu Ile Thr Val
                485                 490                 495
```

```
Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro Glu Ser Ile Lys Ala
            500                 505                 510

Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro Thr Val Arg Thr Lys
        515                 520                 525

Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp Asp Gln Leu Pro Val
    530                 535                 540

Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr Ile Phe Tyr Arg Thr
545                 550                 555                 560

Ile Ile Gly Asn Glu Thr Ala Val Asn Val Asp Ser Ser His Thr Glu
                565                 570                 575

Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu Tyr Met Val Arg Met
            580                 585                 590

Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly Pro Glu Phe Thr Phe
        595                 600                 605

Thr Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ala Ile Val Val Pro
    610                 615                 620

Val Cys Leu Ala Phe Leu Leu Thr Thr Leu Leu Gly Val Leu Phe Cys
625                 630                 635                 640

Phe Asn Lys Arg Asp Leu Ile Lys Lys His Ile Trp Pro Asn Val Pro
                645                 650                 655

Asp Pro Ser Lys Ser His Ile Ala Gln Trp Ser Pro His Thr Pro Pro
            660                 665                 670

Arg His Asn Phe Asn Ser Lys Asp Gln Met Tyr Ser Asp Gly Asn Phe
        675                 680                 685
```

```
Thr Asp Val Ser Val Val Glu Ile Glu Ala Asn Asp Lys Lys Pro Phe
    690                 695                 700

Pro Glu Asp Leu Lys Ser Leu Asp Leu Phe Lys Lys Glu Lys Ile Asn
705                 710                 715                 720

Thr Glu Gly His Ser Ser Gly Ile Gly Gly Ser Ser Cys Met Ser Ser
                725                 730                 735

Ser Arg Pro Ser Ile Ser Ser Ser Asp Glu Asn Glu Ser Ser Gln Asn
            740                 745                 750

Thr Ser Ser Thr Val Gln Tyr Ser Thr Val Val His Ser Gly Tyr Arg
        755                 760                 765

His Gln Val Pro Ser Val Gln Val Phe Ser Arg Ser Glu Ser Thr Gln
    770                 775                 780

Pro Leu Leu Asp Ser Glu Glu Arg Pro Glu Asp Leu Gln Leu Val Asp
785                 790                 795                 800

His Val Asp Gly Gly Asp Gly Ile Leu Pro Arg Gln Gln Tyr Phe Lys
                805                 810                 815

Gln Asn Cys Ser Gln His Glu Ser Ser Pro Asp Ile Ser His Phe Glu
            820                 825                 830

Arg Ser Lys Gln Val Ser Ser Val Asn Glu Glu Asp Phe Val Arg Leu
        835                 840                 845

Lys Gln Gln Ile Ser Asp His Ile Ser Gln Ser Cys Gly Ser Gly Gln
    850                 855                 860

Met Lys Met Phe Gln Glu Val Ser Ala Ala Asp Ala Phe Gly Pro Gly
865                 870                 875                 880
```

Thr Glu Gly Gln Val Glu Arg Phe Glu Thr Val Gly Met Glu Ala Ala
885 890 895

Thr Asp Glu Gly Met Pro Lys Ser Tyr Leu Pro Gln Thr Val Arg Gln
900 905 910

Gly Gly Tyr Met Pro Gln
915

<210> 61
<211> 622
<212> PRT
<213> Homo sapiens

<400> 61

Met Lys Glu Asn Val Ala Ser Ala Thr Val Phe Thr Leu Leu Leu Phe
1 5 10 15

Leu Asn Thr Cys Leu Leu Asn Gly Gln Leu Pro Pro Gly Lys Pro Glu
20 25 30

Ile Phe Lys Cys Arg Ser Pro Asn Lys Glu Thr Phe Thr Cys Trp Trp
35 40 45

Arg Pro Gly Thr Asp Gly Gly Leu Pro Thr Asn Tyr Ser Leu Thr Tyr
50 55 60

His Arg Glu Gly Glu Thr Leu Met His Glu Cys Pro Asp Tyr Ile Thr
65 70 75 80

Gly Gly Pro Asn Ser Cys His Phe Gly Lys Gln Tyr Thr Ser Met Trp
85 90 95

Arg Thr Tyr Ile Met Met Val Asn Ala Thr Asn Gln Met Gly Ser Ser
100 105 110

Phe Ser Asp Glu Leu Tyr Val Asp Val Thr Tyr Ile Val Gln Pro Asp

```
        115                 120                 125

Pro Pro Leu Glu Leu Ala Val Glu Val Lys Gln Pro Glu Asp Arg Lys
    130                 135                 140

Pro Tyr Leu Trp Ile Lys Trp Ser Pro Pro Thr Leu Ile Asp Leu Lys
145                 150                 155                 160

Thr Gly Trp Phe Thr Leu Leu Tyr Glu Ile Arg Leu Lys Pro Glu Lys
                165                 170                 175

Ala Ala Glu Trp Glu Ile His Phe Ala Gly Gln Gln Thr Glu Phe Lys
            180                 185                 190

Ile Leu Ser Leu His Pro Gly Gln Lys Tyr Leu Val Gln Val Arg Cys
        195                 200                 205

Lys Pro Asp His Gly Tyr Trp Ser Ala Trp Ser Pro Ala Thr Phe Ile
    210                 215                 220

Gln Ile Pro Ser Asp Phe Thr Met Asn Asp Thr Thr Val Trp Ile Ser
225                 230                 235                 240

Val Ala Val Leu Ser Ala Val Ile Cys Leu Ile Ile Val Trp Ala Val
                245                 250                 255

Ala Leu Lys Gly Tyr Ser Met Val Thr Cys Ile Phe Pro Pro Val Pro
            260                 265                 270

Gly Pro Lys Ile Lys Gly Phe Asp Ala His Leu Leu Glu Lys Gly Lys
        275                 280                 285

Ser Glu Glu Leu Leu Ser Ala Leu Gly Cys Gln Asp Phe Pro Pro Thr
    290                 295                 300

Ser Asp Tyr Glu Asp Leu Leu Val Glu Tyr Leu Glu Val Asp Asp Ser
```

```
305                 310                 315                 320

Glu Asp Gln His Leu Met Ser Val His Ser Lys Glu His Pro Ser Gln
                325                 330                 335

Gly Met Lys Pro Thr Tyr Leu Asp Pro Asp Thr Asp Ser Gly Arg Gly
            340                 345                 350

Ser Cys Asp Ser Pro Ser Leu Leu Ser Glu Lys Cys Glu Glu Pro Gln
        355                 360                 365

Ala Asn Pro Ser Thr Phe Tyr Asp Pro Glu Val Ile Glu Lys Pro Glu
    370                 375                 380

Asn Pro Glu Thr Thr His Thr Trp Asp Pro Gln Cys Ile Ser Met Glu
385                 390                 395                 400

Gly Lys Ile Pro Tyr Phe His Ala Gly Gly Ser Lys Cys Ser Thr Trp
                405                 410                 415

Pro Leu Pro Gln Pro Ser Gln His Asn Pro Arg Ser Ser Tyr His Asn
            420                 425                 430

Ile Thr Asp Val Cys Glu Leu Ala Val Gly Pro Ala Gly Ala Pro Ala
        435                 440                 445

Thr Leu Leu Asn Glu Ala Gly Lys Asp Ala Leu Lys Ser Ser Gln Thr
    450                 455                 460

Ile Lys Ser Arg Glu Glu Gly Lys Ala Thr Gln Gln Arg Glu Val Glu
465                 470                 475                 480

Ser Phe His Ser Glu Thr Asp Gln Asp Thr Pro Trp Leu Leu Pro Gln
                485                 490                 495

Glu Lys Thr Pro Phe Gly Ser Ala Lys Pro Leu Asp Tyr Val Glu Ile
```

```
            500                 505                 510

His Lys Val Asn Lys Asp Gly Ala Leu Ser Leu Leu Pro Lys Gln Arg
        515                 520                 525

Glu Asn Ser Gly Lys Pro Lys Lys Pro Gly Thr Pro Glu Asn Asn Lys
    530                 535                 540

Glu Tyr Ala Lys Val Ser Gly Val Met Asp Asn Asn Ile Leu Val Leu
545                 550                 555                 560

Val Pro Asp Pro His Ala Lys Asn Val Ala Cys Phe Glu Glu Ser Ala
                565                 570                 575

Lys Glu Ala Pro Pro Ser Leu Glu Gln Asn Gln Ala Glu Lys Ala Leu
            580                 585                 590

Ala Asn Phe Thr Ala Thr Ser Ser Lys Cys Arg Leu Gln Leu Gly Gly
        595                 600                 605

Leu Asp Tyr Leu Asp Pro Ala Cys Phe Thr His Ser Phe His
    610                 615                 620


<210>  62
<211>  638
<212>  PRT
<213>  Homo sapiens

<400>  62

Met Asp Leu Trp Gln Leu Leu Leu Thr Leu Ala Leu Ala Gly Ser Ser
1               5                   10                  15

Asp Ala Phe Ser Gly Ser Glu Ala Thr Ala Ala Ile Leu Ser Arg Ala
            20                  25                  30

Pro Trp Ser Leu Gln Ser Val Asn Pro Gly Leu Lys Thr Asn Ser Ser
        35                  40                  45
```

```
Lys Glu Pro Lys Phe Thr Lys Cys Arg Ser Pro Glu Arg Glu Thr Phe
    50                  55                  60

Ser Cys His Trp Thr Asp Glu Val His His Gly Thr Lys Asn Leu Gly
65                  70                  75                  80

Pro Ile Gln Leu Phe Tyr Thr Arg Arg Asn Thr Gln Glu Trp Thr Gln
                85                  90                  95

Glu Trp Lys Glu Cys Pro Asp Tyr Val Ser Ala Gly Glu Asn Ser Cys
            100                 105                 110

Tyr Phe Asn Ser Ser Phe Thr Ser Ile Trp Ile Pro Tyr Cys Ile Lys
        115                 120                 125

Leu Thr Ser Asn Gly Gly Thr Val Asp Glu Lys Cys Phe Ser Val Asp
    130                 135                 140

Glu Ile Val Gln Pro Asp Pro Pro Ile Ala Leu Asn Trp Thr Leu Leu
145                 150                 155                 160

Asn Val Ser Leu Thr Gly Ile His Ala Asp Ile Gln Val Arg Trp Glu
                165                 170                 175

Ala Pro Arg Asn Ala Asp Ile Gln Lys Gly Trp Met Val Leu Glu Tyr
            180                 185                 190

Glu Leu Gln Tyr Lys Glu Val Asn Glu Thr Lys Trp Lys Met Met Asp
        195                 200                 205

Pro Ile Leu Thr Thr Ser Val Pro Val Tyr Ser Leu Lys Val Asp Lys
    210                 215                 220

Glu Tyr Glu Val Arg Val Arg Ser Lys Gln Arg Asn Ser Gly Asn Tyr
225                 230                 235                 240
```

```
Gly Glu Phe Ser Glu Val Leu Tyr Val Thr Leu Pro Gln Met Ser Gln
                245                 250                 255

Phe Thr Cys Glu Glu Asp Phe Tyr Phe Pro Trp Leu Leu Ile Ile Ile
            260                 265                 270

Phe Gly Ile Phe Gly Leu Thr Val Met Leu Phe Val Phe Leu Phe Ser
        275                 280                 285

Lys Gln Gln Arg Ile Lys Met Leu Ile Leu Pro Pro Val Pro Val Pro
    290                 295                 300

Lys Ile Lys Gly Ile Asp Pro Asp Leu Leu Lys Glu Gly Lys Leu Glu
305                 310                 315                 320

Glu Val Asn Thr Ile Leu Ala Ile His Asp Ser Tyr Lys Pro Glu Phe
                325                 330                 335

His Ser Asp Asp Ser Trp Val Glu Phe Ile Glu Leu Asp Ile Asp Glu
            340                 345                 350

Pro Asp Glu Lys Thr Glu Glu Ser Asp Thr Asp Arg Leu Leu Ser Ser
        355                 360                 365

Asp His Glu Lys Ser His Ser Asn Leu Gly Val Lys Asp Gly Asp Ser
    370                 375                 380

Gly Arg Thr Ser Cys Cys Glu Pro Asp Ile Leu Glu Thr Asp Phe Asn
385                 390                 395                 400

Ala Asn Asp Ile His Glu Gly Thr Ser Glu Val Ala Gln Pro Gln Arg
                405                 410                 415

Leu Lys Gly Glu Ala Asp Leu Leu Cys Leu Asp Gln Lys Asn Gln Asn
            420                 425                 430
```

```
Asn Ser Pro Tyr His Asp Ala Cys Pro Ala Thr Gln Gln Pro Ser Val
        435                 440                 445

Ile Gln Ala Glu Lys Asn Lys Pro Gln Pro Leu Pro Thr Glu Gly Ala
    450                 455                 460

Glu Ser Thr His Gln Ala Ala His Ile Gln Leu Ser Asn Pro Ser Ser
465                 470                 475                 480

Leu Ser Asn Ile Asp Phe Tyr Ala Gln Val Ser Asp Ile Thr Pro Ala
                485                 490                 495

Gly Ser Val Val Leu Ser Pro Gly Gln Lys Asn Lys Ala Gly Met Ser
            500                 505                 510

Gln Cys Asp Met His Pro Glu Met Val Ser Leu Cys Gln Glu Asn Phe
        515                 520                 525

Leu Met Asp Asn Ala Tyr Phe Cys Glu Ala Asp Ala Lys Lys Cys Ile
    530                 535                 540

Pro Val Ala Pro His Ile Lys Val Glu Ser His Ile Gln Pro Ser Leu
545                 550                 555                 560

Asn Gln Glu Asp Ile Tyr Ile Thr Thr Glu Ser Leu Thr Thr Ala Ala
                565                 570                 575

Gly Arg Pro Gly Thr Gly Glu His Val Pro Gly Ser Glu Met Pro Val
            580                 585                 590

Pro Asp Tyr Thr Ser Ile His Ile Val Gln Ser Pro Gln Gly Leu Ile
        595                 600                 605

Leu Asn Ala Thr Ala Leu Pro Leu Pro Asp Lys Glu Phe Leu Ser Ser
    610                 615                 620
```

Cys Gly Tyr Val Ser Thr Asp Gln Leu Asn Lys Ile Met Pro
625 630 635

<210> 63
<211> 863
<212> PRT
<213> Homo sapiens

<400> 63

Met Ala Arg Leu Gly Asn Cys Ser Leu Thr Trp Ala Ala Leu Ile Ile
1 5 10 15

Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser
20 25 30

Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile
35 40 45

Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg
50 55 60

Leu Gly Ala Glu Leu Gln Pro Gly Gly Arg Gln Gln Arg Leu Ser Asp
65 70 75 80

Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln
85 90 95

Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu
100 105 110

Asp Gln Val Glu Leu Arg Ala Gly Tyr Pro Pro Ala Ile Pro His Asn
115 120 125

Leu Ser Cys Leu Met Asn Leu Thr Thr Ser Ser Leu Ile Cys Gln Trp
130 135 140

```
Glu Pro Gly Pro Glu Thr His Leu Pro Thr Ser Phe Thr Leu Lys Ser
145                 150                 155                 160

Phe Lys Ser Arg Gly Asn Cys Gln Thr Gln Gly Asp Ser Ile Leu Asp
                165                 170                 175

Cys Val Pro Lys Asp Gly Gln Ser His Cys Cys Ile Pro Arg Lys His
            180                 185                 190

Leu Leu Leu Tyr Gln Asn Met Gly Ile Trp Val Gln Ala Glu Asn Ala
        195                 200                 205

Leu Gly Thr Ser Met Ser Pro Gln Leu Cys Leu Asp Pro Met Asp Val
    210                 215                 220

Val Lys Leu Glu Pro Pro Met Leu Arg Thr Met Asp Pro Ser Pro Glu
225                 230                 235                 240

Ala Ala Pro Pro Gln Ala Gly Cys Leu Gln Leu Cys Trp Glu Pro Trp
                245                 250                 255

Gln Pro Gly Leu His Ile Asn Gln Lys Cys Glu Leu Arg His Lys Pro
            260                 265                 270

Gln Arg Gly Glu Ala Ser Trp Ala Leu Val Gly Pro Leu Pro Leu Glu
        275                 280                 285

Ala Leu Gln Tyr Glu Leu Cys Gly Leu Leu Pro Ala Thr Ala Tyr Thr
    290                 295                 300

Leu Gln Ile Arg Cys Ile Arg Trp Pro Leu Pro Gly His Trp Ser Asp
305                 310                 315                 320

Trp Ser Pro Ser Leu Glu Leu Arg Thr Thr Glu Arg Ala Pro Thr Val
                325                 330                 335
```

```
Arg Leu Asp Thr Trp Trp Arg Gln Arg Gln Leu Asp Pro Arg Thr Val
            340                 345                 350

Gln Leu Phe Trp Lys Pro Val Pro Leu Glu Glu Asp Ser Gly Arg Ile
        355                 360                 365

Gln Gly Tyr Val Val Ser Trp Arg Pro Ser Gly Gln Ala Gly Ala Ile
    370                 375                 380

Leu Pro Leu Cys Asn Thr Thr Glu Leu Ser Cys Thr Phe His Leu Pro
385                 390                 395                 400

Ser Glu Ala Gln Glu Val Ala Leu Val Ala Tyr Asn Ser Ala Gly Thr
                405                 410                 415

Ser Arg Pro Thr Pro Val Val Phe Ser Glu Ser Arg Gly Pro Ala Leu
            420                 425                 430

Thr Arg Leu His Ala Met Ala Arg Asp Pro His Ser Leu Trp Val Gly
        435                 440                 445

Trp Glu Pro Pro Asn Pro Trp Pro Gln Gly Tyr Val Ile Glu Trp Gly
    450                 455                 460

Leu Gly Pro Pro Ser Ala Ser Asn Ser Asn Lys Thr Trp Arg Met Glu
465                 470                 475                 480

Gln Asn Gly Arg Ala Thr Gly Phe Leu Leu Lys Glu Asn Ile Arg Pro
                485                 490                 495

Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln Asp Thr Met
            500                 505                 510

Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met Ala Pro Ser
        515                 520                 525
```

```
His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr Trp Ala Gln
    530                 535                 540

Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser Pro Leu Thr
545                 550                 555                 560

His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser Phe Ser Ala
                565                 570                 575

Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu His Gly Leu Glu Pro
            580                 585                 590

Ala Ser Leu Tyr His Ile His Leu Met Ala Ala Ser Gln Ala Gly Ala
        595                 600                 605

Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser
    610                 615                 620

Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu Leu Leu Leu Leu Thr
625                 630                 635                 640

Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn
                645                 650                 655

Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser
            660                 665                 670

Trp Val Pro Thr Ile Met Glu Glu Leu Pro Gly Pro Arg Gln Gly Gln
        675                 680                 685

Trp Leu Gly Gln Thr Ser Glu Met Ser Arg Ala Leu Thr Pro His Pro
    690                 695                 700

Cys Val Gln Asp Ala Phe Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile
705                 710                 715                 720
```

```
Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys Lys Pro Val Pro Trp
                725                 730                 735


Glu Ser His Asn Ser Ser Glu Thr Cys Gly Leu Pro Thr Leu Val Gln
            740                 745                 750


Thr Tyr Val Leu Gln Gly Asp Pro Arg Ala Val Ser Thr Gln Pro Gln
        755                 760                 765


Ser Gln Ser Gly Thr Ser Asp Gln Val Leu Tyr Gly Gln Leu Leu Gly
    770                 775                 780


Ser Pro Thr Ser Pro Gly Pro Gly His Tyr Leu Arg Cys Asp Ser Thr
785                 790                 795                 800


Gln Pro Leu Leu Ala Gly Leu Thr Pro Ser Pro Lys Ser Tyr Glu Asn
                805                 810                 815


Leu Trp Phe Gln Ala Ser Pro Leu Gly Thr Leu Val Thr Pro Ala Pro
            820                 825                 830


Ser Gln Glu Asp Asp Cys Val Phe Gly Pro Leu Leu Asn Phe Pro Leu
        835                 840                 845


Leu Gln Gly Ile Arg Val His Gly Met Glu Ala Leu Gly Ser Phe
    850                 855                 860


<210>  64
<211>  635
<212>  PRT
<213>  Homo sapiens

<400>  64

Met Pro Ser Trp Ala Leu Phe Met Val Thr Ser Cys Leu Leu Leu Ala
1               5                   10                  15
```

```
Pro Gln Asn Leu Ala Gln Val Ser Ser Gln Asp Val Ser Leu Leu Ala
            20                  25                  30

Ser Asp Ser Glu Pro Leu Lys Cys Phe Ser Arg Thr Phe Glu Asp Leu
        35                  40                  45

Thr Cys Phe Trp Asp Glu Glu Glu Ala Ala Pro Ser Gly Thr Tyr Gln
    50                  55                  60

Leu Leu Tyr Ala Tyr Pro Arg Glu Lys Pro Arg Ala Cys Pro Leu Ser
65                  70                  75                  80

Ser Gln Ser Met Pro His Phe Gly Thr Arg Tyr Val Cys Gln Phe Pro
                85                  90                  95

Asp Gln Glu Glu Val Arg Leu Phe Phe Pro Leu His Leu Trp Val Lys
            100                 105                 110

Asn Val Phe Leu Asn Gln Thr Arg Thr Gln Arg Val Leu Phe Val Asp
        115                 120                 125

Ser Val Gly Leu Pro Ala Pro Pro Ser Ile Ile Lys Ala Met Gly Gly
    130                 135                 140

Ser Gln Pro Gly Glu Leu Gln Ile Ser Trp Glu Glu Pro Ala Pro Glu
145                 150                 155                 160

Ile Ser Asp Phe Leu Arg Tyr Glu Leu Arg Tyr Gly Pro Arg Asp Pro
                165                 170                 175

Lys Asn Ser Thr Gly Pro Thr Val Ile Gln Leu Ile Ala Thr Glu Thr
            180                 185                 190

Cys Cys Pro Ala Leu Gln Arg Pro His Ser Ala Ser Ala Leu Asp Gln
        195                 200                 205
```

```
Ser Pro Cys Ala Gln Pro Thr Met Pro Trp Gln Asp Gly Pro Lys Gln
    210                 215                 220

Thr Ser Pro Ser Arg Glu Ala Ser Ala Leu Thr Ala Glu Gly Gly Ser
225                 230                 235                 240

Cys Leu Ile Ser Gly Leu Gln Pro Gly Asn Ser Tyr Trp Leu Gln Leu
                245                 250                 255

Arg Ser Glu Pro Asp Gly Ile Ser Leu Gly Gly Ser Trp Gly Ser Trp
            260                 265                 270

Ser Leu Pro Val Thr Val Asp Leu Pro Gly Asp Ala Val Ala Leu Gly
        275                 280                 285

Leu Gln Cys Phe Thr Leu Asp Leu Lys Asn Val Thr Cys Gln Trp Gln
    290                 295                 300

Gln Gln Asp His Ala Ser Ser Gln Gly Phe Phe Tyr His Ser Arg Ala
305                 310                 315                 320

Arg Cys Cys Pro Arg Asp Arg Tyr Pro Ile Trp Glu Asn Cys Glu Glu
                325                 330                 335

Glu Glu Lys Thr Asn Pro Gly Leu Gln Thr Pro Gln Phe Ser Arg Cys
            340                 345                 350

His Phe Lys Ser Arg Asn Asp Ser Ile Ile His Ile Leu Val Glu Val
        355                 360                 365

Thr Thr Ala Pro Gly Thr Val His Ser Tyr Leu Gly Ser Pro Phe Trp
    370                 375                 380

Ile His Gln Ala Val Arg Leu Pro Thr Pro Asn Leu His Trp Arg Glu
385                 390                 395                 400
```

```
Ile Ser Ser Gly His Leu Glu Leu Glu Trp Gln His Pro Ser Ser Trp
                405                 410                 415

Ala Ala Gln Glu Thr Cys Tyr Gln Leu Arg Tyr Thr Gly Glu Gly His
            420                 425                 430

Gln Asp Trp Lys Val Leu Glu Pro Pro Leu Gly Ala Arg Gly Gly Thr
        435                 440                 445

Leu Glu Leu Arg Pro Arg Ser Arg Tyr Arg Leu Gln Leu Arg Ala Arg
    450                 455                 460

Leu Asn Gly Pro Thr Tyr Gln Gly Pro Trp Ser Ser Trp Ser Asp Pro
465                 470                 475                 480

Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr
                485                 490                 495

Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
            500                 505                 510

Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
        515                 520                 525

Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
    530                 535                 540

Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
545                 550                 555                 560

Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
                565                 570                 575

Arg Thr Pro Leu Pro Leu Cys Ser Ser Gln Ala Gln Met Asp Tyr Arg
            580                 585                 590
```

```
Arg Leu Gln Pro Ser Cys Leu Gly Thr Met Pro Leu Ser Val Cys Pro
        595                 600                 605


Pro Met Ala Glu Ser Gly Ser Cys Cys Thr Thr His Ile Ala Asn His
    610                 615                 620


Ser Tyr Leu Pro Leu Ser Tyr Trp Gln Gln Pro
625                 630                 635


<210>  65
<211>  21
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 signal peptide

<400>  65

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro
            20


<210>  66
<211>  14
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Myristoylation Motif

<400>  66

Met Gly Ser Ser Lys Ser Lys Pro Lys Asp Pro Ser Gln Arg
1               5                   10


<210>  67
<211>  10
<212>  PRT
<213>  Artificial Sequence
```

<220>
<223> Myc epitope tag

<400> 67

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
1   5   10

<210> 68
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> V5 epitope tag

<400> 68

Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr
1   5   10

<210> 69
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V) dimerization domain

<400> 69

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1   5   10   15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20   25   30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35   40   45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50   55   60

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
            100                 105


<210>  70
<211>  214
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V)-FKBP(F36V) dimerization domain

<400>  70

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95
```

```
Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Gly Val Gln Val Glu
            100                 105                 110


Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr
        115                 120                 125


Cys Val Val His Tyr Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp
    130                 135                 140


Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln
145                 150                 155                 160


Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly
                165                 170                 175


Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr
            180                 185                 190


Gly His Pro Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val
        195                 200                 205


Glu Leu Leu Lys Leu Glu
    210


<210>  71
<211>  107
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V,L106P) dimerization domain

<400>  71

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30
```

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35   40   45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50   55   60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65   70   75   80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85   90   95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Pro
            100   105

<210> 72
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V,L106P)-FKBP(F36V,L106P) dimerization domain

<400> 72

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1   5   10   15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20   25   30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35   40   45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50   55   60

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Pro Gly Val Gln Val Glu
            100                 105                 110


Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr
        115                 120                 125


Cys Val Val His Tyr Thr Gly Met Leu Glu Asp Lys Lys Val Asp Ser
    130                 135                 140


Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu
145                 150                 155                 160


Val Ile Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln
                165                 170                 175


Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly
            180                 185                 190


His Pro Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu
        195                 200                 205


Leu Leu Lys Pro Glu
    210
```

<210> 73
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(E31G,36V,R71G,K105E)-FKBP(E31G,36V,R71G,K105E) dimerization domain

<400> 73

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Gly
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Gly Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Glu Leu Gly Val Gln Val Glu
            100                 105                 110

Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr
        115                 120                 125

Cys Val Val His Tyr Thr Gly Met Leu Gly Asp Gly Lys Lys Val Asp
    130                 135                 140

Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln
145                 150                 155                 160

Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly
                165                 170                 175

Gln Gly Ala Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr
            180                 185                 190
```

```
Gly His Pro Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val
        195                 200                 205


Glu Leu Leu Glu Leu Glu
    210


<210>  74
<211>  126
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  ALK5/TGFBR1(1-126) dimerization domain

<400>  74

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 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
115 120 125

<210> 75
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> TGFBR2(1-166) dimerization domain

<400> 75

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
                165


<210>  76
<211>  236
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EpoR(1-236) dimerization domain

<400>  76

Met Asp His Leu Gly Ala Ser Leu Trp Pro Gln Val Gly Ser Leu Cys
1               5                   10                  15


Leu Leu Leu Ala Gly Ala Ala Trp Ala Pro Pro Pro Asn Leu Pro Asp
            20                  25                  30


Pro Lys Phe Glu Ser Lys Ala Ala Leu Leu Ala Ala Arg Gly Pro Glu
        35                  40                  45


Glu Leu Leu Cys Phe Thr Glu Arg Leu Glu Asp Leu Val Cys Phe Trp
    50                  55                  60


Glu Glu Ala Ala Ser Ala Gly Val Gly Pro Gly Asn Tyr Ser Phe Ser
65                  70                  75                  80


Tyr Gln Leu Glu Asp Glu Pro Trp Lys Leu Cys Arg Leu His Gln Ala
                85                  90                  95


Pro Thr Ala Arg Gly Ala Val Arg Phe Trp Cys Ser Leu Pro Thr Ala
            100                 105                 110
```

```
Asp Thr Ser Ser Phe Val Pro Leu Glu Leu Arg Val Thr Ala Ala Ser
        115                 120                 125


Gly Ala Pro Arg Tyr His Arg Val Ile His Ile Asn Glu Val Val Leu
    130                 135                 140


Leu Asp Ala Pro Val Gly Leu Val Ala Arg Leu Ala Asp Glu Ser Gly
145                 150                 155                 160


His Val Val Leu Arg Trp Leu Pro Pro Pro Glu Thr Pro Met Thr Ser
                165                 170                 175


His Ile Arg Tyr Glu Val Asp Val Ser Ala Gly Asn Gly Ala Gly Ser
            180                 185                 190


Val Gln Arg Val Glu Ile Leu Glu Gly Arg Thr Glu Cys Val Leu Ser
        195                 200                 205


Asn Leu Arg Gly Arg Thr Arg Tyr Thr Phe Ala Val Arg Ala Arg Met
    210                 215                 220


Ala Glu Pro Ser Phe Gly Gly Phe Trp Ser Ala Trp
225                 230                 235


<210>  77
<211>  220
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  PrlR(1-220) dimerization domain

<400>  77

Met Lys Glu Asn Val Ala Ser Ala Thr Val Phe Thr Leu Leu Leu Phe
1               5                   10                  15


Leu Asn Thr Cys Leu Leu Asn Gly Gln Leu Pro Pro Gly Lys Pro Glu
            20                  25                  30
```

```
Ile Phe Lys Cys Arg Ser Pro Asn Lys Glu Thr Phe Thr Cys Trp Trp
        35                  40                  45

Arg Pro Gly Thr Asp Gly Gly Leu Pro Thr Asn Tyr Ser Leu Thr Tyr
    50                  55                  60

His Arg Glu Gly Glu Thr Leu Met His Glu Cys Pro Asp Tyr Ile Thr
65                  70                  75                  80

Gly Gly Pro Asn Ser Cys His Phe Gly Lys Gln Tyr Thr Ser Met Trp
                85                  90                  95

Arg Thr Tyr Ile Met Met Val Asn Ala Thr Asn Gln Met Gly Ser Ser
            100                 105                 110

Phe Ser Asp Glu Leu Tyr Val Asp Val Thr Tyr Ile Val Gln Pro Asp
        115                 120                 125

Pro Pro Leu Glu Leu Ala Val Glu Val Lys Gln Pro Glu Asp Arg Lys
    130                 135                 140

Pro Tyr Leu Trp Ile Lys Trp Ser Pro Pro Thr Leu Ile Asp Leu Lys
145                 150                 155                 160

Thr Gly Trp Phe Thr Leu Leu Tyr Glu Ile Arg Leu Lys Pro Glu Lys
                165                 170                 175

Ala Ala Glu Trp Glu Ile His Phe Ala Gly Gln Gln Thr Glu Phe Lys
            180                 185                 190

Ile Leu Ser Leu His Pro Gly Gln Lys Tyr Leu Val Gln Val Arg Cys
        195                 200                 205

Lys Pro Asp His Gly Tyr Trp Ser Ala Trp Ser Pro
    210                 215                 220
```

<210> 78
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> GHR(1-250) dimerization domain

<400> 78

```
Met Asp Leu Trp Gln Leu Leu Leu Thr Leu Ala Leu Ala Gly Ser Ser
1               5                  10                  15


Asp Ala Phe Ser Gly Ser Glu Ala Thr Ala Ala Ile Leu Ser Arg Ala
            20                  25                  30


Pro Trp Ser Leu Gln Ser Val Asn Pro Gly Leu Lys Thr Asn Ser Ser
        35                  40                  45


Lys Glu Pro Lys Phe Thr Lys Cys Arg Ser Pro Glu Arg Glu Thr Phe
    50                  55                  60


Ser Cys His Trp Thr Asp Glu Val His His Gly Thr Lys Asn Leu Gly
65                  70                  75                  80


Pro Ile Gln Leu Phe Tyr Thr Arg Arg Asn Thr Gln Glu Trp Thr Gln
                85                  90                  95


Glu Trp Lys Glu Cys Pro Asp Tyr Val Ser Ala Gly Glu Asn Ser Cys
            100                 105                 110


Tyr Phe Asn Ser Ser Phe Thr Ser Ile Trp Ile Pro Tyr Cys Ile Lys
        115                 120                 125


Leu Thr Ser Asn Gly Gly Thr Val Asp Glu Lys Cys Phe Ser Val Asp
    130                 135                 140
```

```
Glu Ile Val Gln Pro Asp Pro Pro Ile Ala Leu Asn Trp Thr Leu Leu
145                 150                 155                 160


Asn Val Ser Leu Thr Gly Ile His Ala Asp Ile Gln Val Arg Trp Glu
                165                 170                 175


Ala Pro Arg Asn Ala Asp Ile Gln Lys Gly Trp Met Val Leu Glu Tyr
            180                 185                 190


Glu Leu Gln Tyr Lys Glu Val Asn Glu Thr Lys Trp Lys Met Met Asp
        195                 200                 205


Pro Ile Leu Thr Thr Ser Val Pro Val Tyr Ser Leu Lys Val Asp Lys
    210                 215                 220


Glu Tyr Glu Val Arg Val Arg Ser Lys Gln Arg Asn Ser Gly Asn Tyr
225                 230                 235                 240


Gly Glu Phe Ser Glu Val Leu Tyr Val Thr
                245                 250


<210>  79
<211>  477
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(1-478) dimerization domain

<400>  79

Met Pro Ser Trp Ala Leu Phe Met Val Thr Ser Cys Leu Leu Leu Ala
1               5                   10                  15


Pro Gln Asn Leu Ala Gln Val Ser Ser Gln Asp Val Ser Leu Leu Ala
            20                  25                  30


Ser Asp Ser Glu Pro Leu Lys Cys Phe Ser Arg Thr Phe Glu Asp Leu
        35                  40                  45
```

```
Thr Cys Phe Trp Asp Glu Glu Glu Ala Ala Pro Ser Gly Thr Tyr Gln
    50                  55                  60

Leu Leu Tyr Ala Tyr Pro Arg Glu Lys Pro Arg Ala Cys Pro Leu Ser
65                  70                  75                  80

Ser Gln Ser Met Pro His Phe Gly Thr Arg Tyr Val Cys Gln Phe Pro
                85                  90                  95

Asp Gln Glu Glu Val Arg Leu Phe Phe Pro Leu His Leu Trp Val Lys
            100                 105                 110

Asn Val Phe Leu Asn Gln Thr Arg Thr Gln Arg Val Leu Phe Val Asp
        115                 120                 125

Ser Val Gly Leu Pro Ala Pro Pro Ser Ile Ile Lys Ala Met Gly Gly
    130                 135                 140

Ser Gln Pro Gly Glu Leu Gln Ile Ser Trp Glu Glu Pro Ala Pro Glu
145                 150                 155                 160

Ile Ser Asp Phe Leu Arg Tyr Glu Leu Arg Tyr Gly Pro Arg Asp Pro
                165                 170                 175

Lys Asn Ser Thr Gly Pro Thr Val Ile Gln Leu Ile Ala Thr Glu Thr
            180                 185                 190

Cys Cys Pro Ala Leu Gln Arg Pro His Ser Ala Ser Ala Leu Asp Gln
        195                 200                 205

Ser Pro Cys Ala Gln Pro Thr Met Pro Trp Gln Asp Gly Pro Lys Gln
    210                 215                 220

Thr Ser Pro Ser Arg Glu Ala Ser Ala Leu Thr Ala Glu Gly Gly Ser
225                 230                 235                 240
```

```
Cys Leu Ile Ser Gly Leu Gln Pro Gly Asn Ser Tyr Trp Leu Gln Leu
                245                 250                 255

Arg Ser Glu Pro Asp Gly Ile Ser Leu Gly Gly Ser Trp Gly Ser Trp
            260                 265                 270

Ser Leu Pro Val Thr Val Asp Leu Pro Gly Asp Ala Val Ala Leu Gly
        275                 280                 285

Leu Gln Cys Phe Thr Leu Asp Leu Lys Asn Val Thr Cys Gln Trp Gln
    290                 295                 300

Gln Gln Asp His Ala Ser Ser Gln Gly Phe Phe Tyr His Ser Arg Ala
305                 310                 315                 320

Arg Cys Cys Pro Arg Asp Arg Tyr Pro Ile Trp Glu Asn Cys Glu Glu
                325                 330                 335

Glu Glu Lys Thr Asn Pro Gly Leu Gln Thr Pro Gln Phe Ser Arg Cys
            340                 345                 350

His Phe Lys Ser Arg Asn Asp Ser Ile Ile His Ile Leu Val Glu Val
        355                 360                 365

Thr Thr Ala Pro Gly Thr Val His Ser Tyr Leu Gly Ser Pro Phe Trp
    370                 375                 380

Ile His Gln Ala Val Arg Leu Pro Thr Pro Asn Leu His Trp Arg Glu
385                 390                 395                 400

Ile Ser Ser Gly His Leu Glu Leu Glu Trp Gln His Pro Ser Ser Trp
                405                 410                 415

Ala Ala Gln Glu Thr Cys Tyr Gln Leu Arg Tyr Thr Gly Glu Gly His
            420                 425                 430
```

```
Gln Asp Trp Lys Val Leu Glu Pro Pro Leu Gly Ala Arg Gly Gly Thr
        435                 440                 445


Leu Glu Leu Arg Pro Arg Ser Arg Tyr Arg Leu Gln Leu Arg Ala Arg
    450                 455                 460


Leu Asn Gly Pro Thr Tyr Gln Gly Pro Trp Ser Ser Trp
465                 470                 475


<210>  80
<211>  631
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EGFR(1-631) dimerization domain

<400>  80

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


Ala Leu Cys Pro Ala Ser Arg Ala Leu Glu Glu Lys Lys Val Cys Gln
            20                  25                  30


Gly Thr Ser Asn Lys Leu Thr Gln Leu Gly Thr Phe Glu Asp His Phe
        35                  40                  45


Leu Ser Leu Gln Arg Met Phe Asn Asn Cys Glu Val Val Leu Gly Asn
    50                  55                  60


Leu Glu Ile Thr Tyr Val Gln Arg Asn Tyr Asp Leu Ser Phe Leu Lys
65                  70                  75                  80


Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
                85                  90                  95
```

```
Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Met Tyr
            100                 105                 110

Tyr Glu Asn Ser Tyr Ala Leu Ala Val Leu Ser Asn Tyr Asp Ala Asn
        115                 120                 125

Lys Thr Gly Leu Lys Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu
    130                 135                 140

His Gly Ala Val Arg Phe Ser Asn Asn Pro Ala Leu Cys Asn Val Glu
145                 150                 155                 160

Ser Ile Gln Trp Arg Asp Ile Val Ser Ser Asp Phe Leu Ser Asn Met
                165                 170                 175

Ser Met Asp Phe Gln Asn His Leu Gly Ser Cys Gln Lys Cys Asp Pro
            180                 185                 190

Ser Cys Pro Asn Gly Ser Cys Trp Gly Ala Gly Glu Glu Asn Cys Gln
        195                 200                 205

Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser Gly Arg Cys Arg
    210                 215                 220

Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys
225                 230                 235                 240

Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg Lys Phe Arg Asp
                245                 250                 255

Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met Leu Tyr Asn Pro
            260                 265                 270

Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys Tyr Ser Phe Gly
        275                 280                 285
```

```
Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His
    290                 295                 300

Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr Glu Met Glu Glu
305                 310                 315                 320

Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro Cys Arg Lys Val
                325                 330                 335

Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Ser Leu Ser Ile Asn
            340                 345                 350

Ala Thr Asn Ile Lys His Phe Lys Asn Cys Thr Ser Ile Ser Gly Asp
        355                 360                 365

Leu His Ile Leu Pro Val Ala Phe Arg Gly Asp Ser Phe Thr His Thr
    370                 375                 380

Pro Pro Leu Asp Pro Gln Glu Leu Asp Ile Leu Lys Thr Val Lys Glu
385                 390                 395                 400

Ile Thr Gly Phe Leu Leu Ile Gln Ala Trp Pro Glu Asn Arg Thr Asp
                405                 410                 415

Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
            420                 425                 430

His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr Ser Leu
        435                 440                 445

Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile Ile Ser
    450                 455                 460

Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys Lys Leu
465                 470                 475                 480
```

```
Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg Gly Glu
                485                 490                 495


Asn Ser Cys Lys Ala Thr Gly Gln Val Cys His Ala Leu Cys Ser Pro
            500                 505                 510


Glu Gly Cys Trp Gly Pro Glu Pro Arg Asp Cys Val Ser Cys Arg Asn
        515                 520                 525


Val Ser Arg Gly Arg Glu Cys Val Asp Lys Cys Asn Leu Leu Glu Gly
    530                 535                 540


Glu Pro Arg Glu Phe Val Glu Asn Ser Glu Cys Ile Gln Cys His Pro
545                 550                 555                 560


Glu Cys Leu Pro Gln Ala Met Asn Ile Thr Cys Thr Gly Arg Gly Pro
                565                 570                 575


Asp Asn Cys Ile Gln Cys Ala His Tyr Ile Asp Gly Pro His Cys Val
            580                 585                 590


Lys Thr Cys Pro Ala Gly Val Met Gly Glu Asn Asn Thr Leu Val Trp
        595                 600                 605


Lys Tyr Ala Asp Ala Gly His Val Cys His Leu Cys His Pro Asn Cys
    610                 615                 620


Thr Tyr Gly Cys Thr Gly Pro
625                 630


<210>  81
<211>  362
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FGFR1(1-362) dimerization domain
```

<400> 81

```
Met Trp Ser Trp Lys Cys Leu Leu Phe Trp Ala Val Leu Val Thr Ala
1               5                  10                  15

Thr Leu Cys Thr Ala Arg Pro Ser Pro Thr Leu Pro Glu Gln Ala Gln
            20                  25                  30

Pro Trp Gly Ala Pro Val Glu Val Glu Ser Phe Leu Val His Pro Gly
        35                  40                  45

Asp Leu Leu Gln Leu Arg Cys Arg Leu Arg Asp Asp Val Gln Ser Ile
    50                  55                  60

Asn Trp Leu Arg Asp Gly Val Gln Leu Ala Glu Ser Asn Arg Thr Arg
65                  70                  75                  80

Ile Thr Gly Glu Glu Val Glu Val Gln Asp Ser Val Pro Ala Asp Ser
                85                  90                  95

Gly Leu Tyr Ala Cys Val Thr Ser Ser Pro Ser Gly Ser Asp Thr Thr
            100                 105                 110

Tyr Phe Ser Val Asn Val Ser Asp Ala Leu Pro Ser Ser Glu Asp Asp
        115                 120                 125

Asp Asp Asp Asp Asp Ser Ser Ser Glu Glu Lys Glu Thr Asp Asn Thr
    130                 135                 140

Lys Pro Asn Arg Met Pro Val Ala Pro Tyr Trp Thr Ser Pro Glu Lys
145                 150                 155                 160

Met Glu Lys Lys Leu His Ala Val Pro Ala Ala Lys Thr Val Lys Phe
                165                 170                 175

Lys Cys Pro Ser Ser Gly Thr Pro Asn Pro Thr Leu Arg Trp Leu Lys
            180                 185                 190
```

```
Asn Gly Lys Glu Phe Lys Pro Asp His Arg Ile Gly Gly Tyr Lys Val
        195                 200                 205

Arg Tyr Ala Thr Trp Ser Ile Ile Met Asp Ser Val Val Pro Ser Asp
    210                 215                 220

Lys Gly Asn Tyr Thr Cys Ile Val Glu Asn Glu Tyr Gly Ser Ile Asn
225                 230                 235                 240

His Thr Tyr Gln Leu Asp Val Val Glu Arg Ser Pro His Arg Pro Ile
                245                 250                 255

Leu Gln Ala Gly Leu Pro Ala Asn Lys Thr Val Ala Leu Gly Ser Asn
            260                 265                 270

Val Glu Phe Met Cys Lys Val Tyr Ser Asp Pro Gln Pro His Ile Gln
        275                 280                 285

Trp Leu Lys His Ile Glu Val Asn Gly Ser Lys Ile Gly Pro Asp Asn
    290                 295                 300

Leu Pro Tyr Val Gln Ile Leu Lys Thr Ala Gly Val Asn Thr Thr Asp
305                 310                 315                 320

Lys Glu Met Glu Val Leu His Leu Arg Asn Val Ser Phe Glu Asp Ala
                325                 330                 335

Gly Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Leu Ser His His
            340                 345                 350

Ser Ala Trp Leu Thr Val Leu Glu Ala Leu
        355                 360
```

<210> 82
<211> 514

<212> PRT
<213> Artificial Sequence

<220>
<223> PDGFRA(1-514) dimerization domain

<400> 82

```
Met Gly Thr Ser His Pro Ala Phe Leu Val Leu Gly Cys Leu Leu Thr
1               5                  10                  15


Gly Leu Ser Leu Ile Leu Cys Gln Leu Ser Leu Pro Ser Ile Leu Pro
            20                  25                  30


Asn Glu Asn Glu Lys Val Val Gln Leu Asn Ser Ser Phe Ser Leu Arg
        35                  40                  45


Cys Phe Gly Glu Ser Glu Val Ser Trp Gln Tyr Pro Met Ser Glu Glu
    50                  55                  60


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


Phe Val Thr Val Leu Glu Val Ser Ser Ala Ser Ala Ala His Thr Gly
                85                  90                  95


Leu Tyr Thr Cys Tyr Tyr Asn His Thr Gln Thr Glu Glu Asn Glu Leu
            100                 105                 110


Glu Gly Arg His Ile Tyr Ile Tyr Val Pro Asp Pro Asp Val Ala Phe
        115                 120                 125


Val Pro Leu Gly Met Thr Asp Tyr Leu Val Ile Val Glu Asp Asp Asp
    130                 135                 140


Ser Ala Ile Ile Pro Cys Arg Thr Thr Asp Pro Glu Thr Pro Val Thr
145                 150                 155                 160
```

```
Leu His Asn Ser Glu Gly Val Val Pro Ala Ser Tyr Asp Ser Arg Gln
                165                 170                 175

Gly Phe Asn Gly Thr Phe Thr Val Gly Pro Tyr Ile Cys Glu Ala Thr
            180                 185                 190

Val Lys Gly Lys Lys Phe Gln Thr Ile Pro Phe Asn Val Tyr Ala Leu
        195                 200                 205

Lys Ala Thr Ser Glu Leu Asp Leu Glu Met Glu Ala Leu Lys Thr Val
    210                 215                 220

Tyr Lys Ser Gly Glu Thr Ile Val Val Thr Cys Ala Val Phe Asn Asn
225                 230                 235                 240

Glu Val Val Asp Leu Gln Trp Thr Tyr Pro Gly Glu Val Lys Gly Lys
                245                 250                 255

Gly Ile Thr Met Leu Glu Glu Ile Lys Val Pro Ser Ile Lys Leu Val
            260                 265                 270

Tyr Thr Leu Thr Val Pro Glu Ala Thr Val Lys Asp Ser Gly Asp Tyr
        275                 280                 285

Glu Cys Ala Ala Arg Gln Ala Thr Arg Glu Val Lys Glu Met Lys Lys
    290                 295                 300

Val Thr Ile Ser Val His Glu Lys Gly Phe Ile Glu Ile Lys Pro Thr
305                 310                 315                 320

Phe Ser Gln Leu Glu Ala Val Asn Leu His Glu Val Lys His Phe Val
                325                 330                 335

Val Glu Val Arg Ala Tyr Pro Pro Pro Arg Ile Ser Trp Leu Lys Asn
            340                 345                 350
```

```
Asn Leu Thr Leu Ile Glu Asn Leu Thr Glu Ile Thr Thr Asp Val Glu
        355                 360                 365


Lys Ile Gln Glu Ile Arg Tyr Arg Ser Lys Leu Lys Leu Ile Arg Ala
    370                 375                 380


Lys Glu Glu Asp Ser Gly His Tyr Thr Ile Val Ala Gln Asn Glu Asp
385                 390                 395                 400


Ala Val Lys Ser Tyr Thr Phe Glu Leu Leu Thr Gln Val Pro Ser Ser
                405                 410                 415


Ile Leu Asp Leu Val Asp Asp His His Gly Ser Thr Gly Gly Gln Thr
            420                 425                 430


Val Arg Cys Thr Ala Glu Gly Thr Pro Leu Pro Asp Ile Glu Trp Met
        435                 440                 445


Ile Cys Lys Asp Ile Lys Lys Cys Asn Asn Glu Thr Ser Trp Thr Ile
    450                 455                 460


Leu Ala Asn Asn Val Ser Asn Ile Ile Thr Glu Ile His Ser Arg Asp
465                 470                 475                 480


Arg Ser Thr Val Glu Gly Arg Val Thr Phe Ala Lys Val Glu Glu Thr
                485                 490                 495


Ile Ala Val Arg Cys Leu Ala Lys Asn Leu Leu Gly Ala Glu Asn Arg
            500                 505                 510


Glu Leu
```

<210> 83
<211> 518
<212> PRT
<213> Artificial Sequence

<220>
<223> PDGFRB(1-518) dimerization domain

<400> 83

```
Met Arg Leu Pro Gly Ala Met Pro Ala Leu Ala Leu Lys Gly Glu Leu
1               5                  10                  15


Leu Leu Leu Ser Leu Leu Leu Leu Leu Glu Pro Gln Ile Ser Gln Gly
            20                  25                  30


Leu Val Val Thr Pro Pro Gly Pro Glu Leu Val Leu Asn Val Ser Ser
        35                  40                  45


Thr Phe Val Leu Thr Cys Ser Gly Ser Ala Pro Val Val Trp Glu Arg
    50                  55                  60


Met Ser Gln Glu Pro Pro Gln Glu Met Ala Lys Ala Gln Asp Gly Thr
65                  70                  75                  80


Phe Ser Ser Val Leu Thr Leu Thr Asn Leu Thr Gly Leu Asp Thr Gly
                85                  90                  95


Glu Tyr Phe Cys Thr His Asn Asp Ser Arg Gly Leu Glu Thr Asp Glu
            100                 105                 110


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


Pro Asn Asp Ala Glu Glu Leu Phe Ile Phe Leu Thr Glu Ile Thr Glu
    130                 135                 140


Ile Thr Ile Pro Cys Arg Val Thr Asp Pro Gln Leu Val Val Thr Leu
145                 150                 155                 160


His Glu Lys Lys Gly Asp Val Ala Leu Pro Val Pro Tyr Asp His Gln
                165                 170                 175
```

```
Arg Gly Phe Ser Gly Ile Phe Glu Asp Arg Ser Tyr Ile Cys Lys Thr
            180                 185                 190

Thr Ile Gly Asp Arg Glu Val Asp Ser Asp Ala Tyr Tyr Val Tyr Arg
        195                 200                 205

Leu Gln Val Ser Ser Ile Asn Val Ser Val Asn Ala Val Gln Thr Val
    210                 215                 220

Val Arg Gln Gly Glu Asn Ile Thr Leu Met Cys Ile Val Ile Gly Asn
225                 230                 235                 240

Glu Val Val Asn Phe Glu Trp Thr Tyr Pro Arg Lys Glu Ser Gly Arg
                245                 250                 255

Leu Val Glu Pro Val Thr Asp Phe Leu Leu Asp Met Pro Tyr His Ile
            260                 265                 270

Arg Ser Ile Leu His Ile Pro Ser Ala Glu Leu Glu Asp Ser Gly Thr
        275                 280                 285

Tyr Thr Cys Asn Val Thr Glu Ser Val Asn Asp His Gln Asp Glu Lys
    290                 295                 300

Ala Ile Asn Ile Thr Val Val Glu Ser Gly Tyr Val Arg Leu Leu Gly
305                 310                 315                 320

Glu Val Gly Thr Leu Gln Phe Ala Glu Leu His Arg Ser Arg Thr Leu
                325                 330                 335

Gln Val Val Phe Glu Ala Tyr Pro Pro Pro Thr Val Leu Trp Phe Lys
            340                 345                 350

Asp Asn Arg Thr Leu Gly Asp Ser Ser Ala Gly Glu Ile Ala Leu Ser
        355                 360                 365
```

```
Thr Arg Asn Val Ser Glu Thr Arg Tyr Val Ser Glu Leu Thr Leu Val
    370                 375                 380

Arg Val Lys Val Ala Glu Ala Gly His Tyr Thr Met Arg Ala Phe His
385                 390                 395                 400

Glu Asp Ala Glu Val Gln Leu Ser Phe Gln Leu Gln Ile Asn Val Pro
                405                 410                 415

Val Arg Val Leu Glu Leu Ser Glu Ser His Pro Asp Ser Gly Glu Gln
            420                 425                 430

Thr Val Arg Cys Arg Gly Arg Gly Met Pro Gln Pro Asn Ile Ile Trp
        435                 440                 445

Ser Ala Cys Arg Asp Leu Lys Arg Cys Pro Arg Glu Leu Pro Pro Thr
    450                 455                 460

Leu Leu Gly Asn Ser Ser Glu Glu Glu Ser Gln Leu Glu Thr Asn Val
465                 470                 475                 480

Thr Tyr Trp Glu Glu Glu Gln Glu Phe Glu Val Val Ser Thr Leu Arg
                485                 490                 495

Leu Gln His Val Asp Arg Pro Leu Ser Val Arg Cys Thr Leu Arg Asn
            500                 505                 510

Ala Val Gly Gln Asp Thr
        515
```

<210> 84
<211> 54
<212> PRT
<213> Artificial Sequence

<220>

<223> BCMA (1-54) dimerization domain

<400> 84

Met Leu Gln Met Ala Gly Gln Cys Ser Gln Asn Glu Tyr Phe Asp Ser
1 5 10 15

Leu Leu His Ala Cys Ile Pro Cys Gln Leu Arg Cys Ser Ser Asn Thr
20 25 30

Pro Pro Leu Thr Cys Gln Arg Tyr Cys Asn Ala Ser Val Thr Asn Ser
35 40 45

Val Lys Gly Thr Asn Ala
50

<210> 85
<211> 78
<212> PRT
<213> Artificial Sequence

<220>
<223> BAFF-R (1-78) dimerization domain

<400> 85

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

Thr Pro Cys Val Pro Ala Glu Cys Phe Asp Leu Leu Val Arg His Cys
20 25 30

Val Ala Cys Gly Leu Leu Arg Thr Pro Arg Pro Lys Pro Ala Gly Ala
35 40 45

Ser Ser Pro Ala Pro Arg Thr Ala Leu Gln Pro Gln Glu Ser Val Gly
50 55 60

Ala Gly Ala Gly Glu Ala Ala Leu Pro Leu Pro Gly Leu Leu
65 70 75

<210> 86
<211> 165
<212> PRT
<213> Artificial Sequence

<220>
<223> TACI (1-165) dimerization domain

<400> 86

```
Met Ser Gly Leu Gly Arg Ser Arg Arg Gly Gly Arg Ser Arg Val Asp
1               5                  10                  15


Gln Glu Glu Arg Phe Pro Gln Gly Leu Trp Thr Gly Val Ala Met Arg
            20                  25                  30


Ser Cys Pro Glu Glu Gln Tyr Trp Asp Pro Leu Leu Gly Thr Cys Met
        35                  40                  45


Ser Cys Lys Thr Ile Cys Asn His Gln Ser Gln Arg Thr Cys Ala Ala
    50                  55                  60


Phe Cys Arg Ser Leu Ser Cys Arg Lys Glu Gln Gly Lys Phe Tyr Asp
65                  70                  75                  80


His Leu Leu Arg Asp Cys Ile Ser Cys Ala Ser Ile Cys Gly Gln His
                85                  90                  95


Pro Lys Gln Cys Ala Tyr Phe Cys Glu Asn Lys Leu Arg Ser Pro Val
            100                 105                 110


Asn Leu Pro Pro Glu Leu Arg Arg Gln Arg Ser Gly Glu Val Glu Asn
        115                 120                 125


Asn Ser Asp Asn Ser Gly Arg Tyr Gln Gly Leu Glu His Arg Gly Ser
    130                 135                 140
```

Glu Ala Ser Pro Ala Leu Pro Gly Leu Lys Leu Ser Ala Asp Gln Val
145 150 155 160

Ala Leu Val Tyr Ser
165

<210> 87
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> OX40 (1-214) dimerization domain

<400> 87

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

Leu Leu Leu Gly Leu Gly Leu Ser Thr Val Thr Gly Leu His Cys Val
20 25 30

Gly Asp Thr Tyr Pro Ser Asn Asp Arg Cys Cys His Glu Cys Arg Pro
35 40 45

Gly Asn Gly Met Val Ser Arg Cys Ser Arg Ser Gln Asn Thr Val Cys
50 55 60

Arg Pro Cys Gly Pro Gly Phe Tyr Asn Asp Val Val Ser Ser Lys Pro
65 70 75 80

Cys Lys Pro Cys Thr Trp Cys Asn Leu Arg Ser Gly Ser Glu Arg Lys
85 90 95

Gln Leu Cys Thr Ala Thr Gln Asp Thr Val Cys Arg Cys Arg Ala Gly
100 105 110

Thr Gln Pro Leu Asp Ser Tyr Lys Pro Gly Val Asp Cys Ala Pro Cys
115 120 125

```
Pro Pro Gly His Phe Ser Pro Gly Asp Asn Gln Ala Cys Lys Pro Trp
    130                 135                 140

Thr Asn Cys Thr Leu Ala Gly Lys His Thr Leu Gln Pro Ala Ser Asn
145                 150                 155                 160

Ser Ser Asp Ala Ile Cys Glu Asp Arg Asp Pro Pro Ala Thr Gln Pro
                165                 170                 175

Gln Glu Thr Gln Gly Pro Pro Ala Arg Pro Ile Thr Val Gln Pro Thr
            180                 185                 190

Glu Ala Trp Pro Arg Thr Ser Gln Gly Pro Ser Thr Arg Pro Val Glu
        195                 200                 205

Val Pro Gly Gly Arg Ala
    210
```

<210> 88
<211> 69
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8(138-206) tyrosine kinase activating domain

<400> 88

```
Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1               5                   10                  15

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
            20                  25                  30

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile
        35                  40                  45
```

Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val
50 55 60

Ile Thr Leu Tyr Cys
65

<210> 89
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> EpoR(237-338;L241G,L242P) tyrosine kinase activating domain

<400> 89

Ser Glu Pro Val Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile
1 5 10 15

Leu Thr Leu Ser Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val
20 25 30

Leu Ala Leu Leu Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro
35 40 45

Gly Ile Pro Ser Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His
50 55 60

Lys Gly Asn Phe Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp
65 70 75 80

Trp Ser Pro Cys Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu
85 90 95

Val Leu Ser Glu Arg Cys
100

<210> 90
<211> 102

<212> PRT
<213> Artificial Sequence

<220>
<223> EpoR(237-338) tyrosine kinase activating domain

<400> 90

Ser Glu Pro Val Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile
1   5   10   15

Leu Thr Leu Ser Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val
            20   25   30

Leu Ala Leu Leu Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro
        35   40   45

Gly Ile Pro Ser Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His
    50   55   60

Lys Gly Asn Phe Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp
65   70   75   80

Trp Ser Pro Cys Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu
                85   90   95

Val Leu Ser Glu Arg Cys
            100

<210> 91
<211> 46
<212> PRT
<213> Artificial Sequence

<220>
<223> EpoR(237-282;L241G,L242P) tyrosine kinase activating domain

<400> 91

Ser Glu Pro Val Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile
1   5   10   15

Leu Thr Leu Ser Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val
            20   25   30

Leu Ala Leu Leu Ser His Arg Arg Ala Leu Lys Gln Lys Ile
        35   40   45

<210> 92
<211> 92
<212> PRT
<213> Artificial Sequence

<220>
<223> GP130(609-700) tyrosine kinase activating domain

<400> 92

Thr Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ala Ile Val Val Pro
1   5   10   15

Val Cys Leu Ala Phe Leu Leu Thr Thr Leu Leu Gly Val Leu Phe Cys
            20   25   30

Phe Asn Lys Arg Asp Leu Ile Lys Lys His Ile Trp Pro Asn Val Pro
        35   40   45

Asp Pro Ser Lys Ser His Ile Ala Gln Trp Ser Pro His Thr Pro Pro
    50   55   60

Arg His Asn Phe Asn Ser Lys Asp Gln Met Tyr Ser Asp Gly Asn Phe
65   70   75   80

Thr Asp Val Ser Val Val Glu Ile Glu Ala Asn Asp
                85   90

<210> 93
<211> 99
<212> PRT
<213> Artificial Sequence

<220>
<223> PrlR(221-319) tyrosine kinase activating domain

<400> 93

Ala Thr Phe Ile Gln Ile Pro Ser Asp Phe Thr Met Asn Asp Thr Thr
1   5   10   15

Val Trp Ile Ser Val Ala Val Leu Ser Ala Val Ile Cys Leu Ile Ile
            20   25   30

Val Trp Ala Val Ala Leu Lys Gly Tyr Ser Met Val Thr Cys Ile Phe
        35   40   45

Pro Pro Val Pro Gly Pro Lys Ile Lys Gly Phe Asp Ala His Leu Leu
    50   55   60

Glu Lys Gly Lys Ser Glu Glu Leu Leu Ser Ala Leu Gly Cys Gln Asp
65   70   75   80

Phe Pro Pro Thr Ser Asp Tyr Glu Asp Leu Leu Val Glu Tyr Leu Glu
                85   90   95

Val Asp Asp

<210> 94
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> GHR(251-352) tyrosine kinase activating domain

<400> 94

Leu Pro Gln Met Ser Gln Phe Thr Cys Glu Glu Asp Phe Tyr Phe Pro
1   5   10   15

Trp Leu Leu Ile Ile Ile Phe Gly Ile Phe Gly Leu Thr Val Met Leu
            20   25   30

Phe Val Phe Leu Phe Ser Lys Gln Gln Arg Ile Lys Met Leu Ile Leu
        35   40   45

Pro Pro Val Pro Val Pro Lys Ile Lys Gly Ile Asp Pro Asp Leu Leu
    50   55   60

Lys Glu Gly Lys Leu Glu Glu Val Asn Thr Ile Leu Ala Ile His Asp
65   70   75   80

Ser Tyr Lys Pro Glu Phe His Ser Asp Asp Ser Trp Val Glu Phe Ile
                85   90   95

Glu Leu Asp Ile Asp Glu
            100

<210> 95
<211> 97
<212> PRT
<213> Artificial Sequence

<220>
<223> GCSFR(614-710) tyrosine kinase activating domain

<400> 95

Leu Thr Leu Met Thr Leu Thr Pro Glu Gly Ser Glu Leu His Ile Ile
1   5   10   15

Leu Gly Leu Phe Gly Leu Leu Leu Leu Leu Thr Cys Leu Cys Gly Thr
            20   25   30

Ala Trp Leu Cys Cys Ser Pro Asn Arg Lys Asn Pro Leu Trp Pro Ser
        35   40   45

Val Pro Asp Pro Ala His Ser Ser Leu Gly Ser Trp Val Pro Thr Ile
    50   55   60

```
Met Glu Glu Asp Ala Phe Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile
65                  70                  75                  80


Thr Lys Leu Thr Val Leu Glu Glu Asp Glu Lys Lys Pro Val Pro Trp
                85                  90                  95


Glu
```

<210> 96
<211> 105
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(478-582) tyrosine kinase activating domain

<400> 96

```
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1               5                   10                  15


Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
            20                  25                  30


Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
        35                  40                  45


His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
    50                  55                  60


Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
65                  70                  75                  80


Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
                85                  90                  95
```

Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 97
<211> 51
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(478-528) tyrosine kinase activating domain

<400> 97

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15

Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
20 25 30

Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
35 40 45

His Ala Leu
50

<210> 98
<211> 348
<212> PRT
<213> Artificial Sequence

<220>
<223> EGFR(632-979) tyrosine kinase activating domain

<400> 98

Gly Leu Glu Gly Cys Pro Thr Asn Gly Pro Lys Ile Pro Ser Ile Ala
1 5 10 15

Thr Gly Met Val Gly Ala Leu Leu Leu Leu Leu Val Val Ala Leu Gly
20 25 30

```
Ile Gly Leu Phe Met Arg Arg Arg His Ile Val Arg Lys Arg Thr Leu
        35                  40                  45

Arg Arg Leu Leu Gln Glu Arg Glu Leu Val Glu Pro Leu Thr Pro Ser
    50                  55                  60

Gly Glu Ala Pro Asn Gln Ala Leu Leu Arg Ile Leu Lys Glu Thr Glu
65                  70                  75                  80

Phe Lys Lys Ile Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr
                85                  90                  95

Lys Gly Leu Trp Ile Pro Glu Gly Glu Lys Val Lys Ile Pro Val Ala
            100                 105                 110

Ile Lys Glu Leu Arg Glu Ala Thr Ser Pro Lys Ala Asn Lys Glu Ile
        115                 120                 125

Leu Asp Glu Ala Tyr Val Met Ala Ser Val Asp Asn Pro His Val Cys
    130                 135                 140

Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Ile Thr Gln
145                 150                 155                 160

Leu Met Pro Phe Gly Cys Leu Leu Asp Tyr Val Arg Glu His Lys Asp
                165                 170                 175

Asn Ile Gly Ser Gln Tyr Leu Leu Asn Trp Cys Val Gln Ile Ala Lys
            180                 185                 190

Gly Met Asn Tyr Leu Glu Asp Arg Arg Leu Val His Arg Asp Leu Ala
        195                 200                 205

Ala Arg Asn Val Leu Val Lys Thr Pro Gln His Val Lys Ile Thr Asp
    210                 215                 220
```

```
Phe Gly Leu Ala Lys Leu Leu Gly Ala Glu Glu Lys Glu Tyr His Ala
225                 230                 235                 240


Glu Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu
                245                 250                 255


His Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr
            260                 265                 270


Val Trp Glu Leu Met Thr Phe Gly Ser Lys Pro Tyr Asp Gly Ile Pro
        275                 280                 285


Ala Ser Glu Ile Ser Ser Ile Leu Glu Lys Gly Glu Arg Leu Pro Gln
    290                 295                 300


Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp
305                 310                 315                 320


Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Arg Glu Leu Ile Ile Glu
                325                 330                 335


Phe Ser Lys Met Ala Arg Asp Pro Gln Arg Tyr Leu
            340                 345


<210>  99
<211>  405
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FGFR1(363-767) tyrosine kinase activating domain

<400>  99

Glu Glu Arg Pro Ala Val Met Thr Ser Pro Leu Tyr Leu Glu Ile Ile
1               5                   10                  15


Ile Tyr Cys Thr Gly Ala Phe Leu Ile Ser Cys Met Val Gly Ser Val
            20                  25                  30
```

```
Ile Val Tyr Lys Met Lys Ser Gly Thr Lys Lys Ser Asp Phe His Ser
        35                  40                  45

Gln Met Ala Val His Lys Leu Ala Lys Ser Ile Pro Leu Arg Arg Gln
    50                  55                  60

Val Thr Val Ser Ala Asp Ser Ser Ala Ser Met Asn Ser Gly Val Leu
65                  70                  75                  80

Leu Val Arg Pro Ser Arg Leu Ser Ser Ser Gly Thr Pro Met Leu Ala
                85                  90                  95

Gly Val Ser Glu Tyr Glu Leu Pro Glu Asp Pro Arg Trp Glu Leu Pro
            100                 105                 110

Arg Asp Arg Leu Val Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly
        115                 120                 125

Gln Val Val Leu Ala Glu Ala Ile Gly Leu Asp Lys Asp Lys Pro Asn
    130                 135                 140

Arg Val Thr Lys Val Ala Val Lys Met Leu Lys Ser Asp Ala Thr Glu
145                 150                 155                 160

Lys Asp Leu Ser Asp Leu Ile Ser Glu Met Glu Met Met Lys Met Ile
                165                 170                 175

Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp
            180                 185                 190

Gly Pro Leu Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg
        195                 200                 205

Glu Tyr Leu Gln Ala Arg Arg Pro Pro Gly Leu Glu Tyr Cys Tyr Asn
    210                 215                 220
```

```
Pro Ser His Asn Pro Glu Glu Gln Leu Ser Ser Lys Asp Leu Val Ser
225                 230                 235                 240

Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu Ala Ser Lys Lys
                245                 250                 255

Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asp
            260                 265                 270

Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp Ile His His
        275                 280                 285

Ile Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp
    290                 295                 300

Met Ala Pro Glu Ala Leu Phe Asp Arg Ile Tyr Thr His Gln Ser Asp
305                 310                 315                 320

Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Thr Leu Gly Gly
                325                 330                 335

Ser Pro Tyr Pro Gly Val Pro Val Glu Glu Leu Phe Lys Leu Leu Lys
            340                 345                 350

Glu Gly His Arg Met Asp Lys Pro Ser Asn Cys Thr Asn Glu Leu Tyr
        355                 360                 365

Met Met Met Arg Asp Cys Trp His Ala Val Pro Ser Gln Arg Pro Thr
    370                 375                 380

Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Ile Val Ala Leu Thr Ser
385                 390                 395                 400

Asn Gln Glu Tyr Leu
                405
```

<210> 100
<211> 440
<212> PRT
<213> Artificial Sequence

<220>
<223> PDGFRA(515-954) tyrosine kinase activating domain

<400> 100

```
Lys Leu Val Ala Pro Thr Leu Arg Ser Glu Leu Thr Val Ala Ala Ala
1               5                   10                  15


Val Leu Val Leu Leu Val Ile Val Ile Ile Ser Leu Ile Val Leu Val
            20                  25                  30


Val Ile Trp Lys Gln Lys Pro Arg Tyr Glu Ile Arg Trp Arg Val Ile
        35                  40                  45


Glu Ser Ile Ser Pro Asp Gly His Glu Tyr Ile Tyr Val Asp Pro Met
    50                  55                  60


Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp Gly Leu Val
65                  70                  75                  80


Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val Val Glu Gly
                85                  90                  95


Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys Val Ala Val
            100                 105                 110


Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln Ala Leu Met
        115                 120                 125


Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu Asn Ile Val
    130                 135                 140
```

```
Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr Ile Ile Thr
145                 150                 155                 160


Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His Lys Asn Arg
                165                 170                 175


Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys Glu Leu Asp
            180                 185                 190


Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser Tyr Val Ile
        195                 200                 205


Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys Gln Ala Asp
    210                 215                 220


Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val Ser Lys Tyr
225                 230                 235                 240


Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser Tyr Lys Lys
                245                 250                 255


Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser Asp Asp Asn
            260                 265                 270


Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr Tyr Gln Val
        275                 280                 285


Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val His Arg Asp
    290                 295                 300


Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile Val Lys Ile
305                 310                 315                 320


Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser Asn Tyr Val
                325                 330                 335
```

```
Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala Pro Glu Ser
            340                 345                 350


Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp Ser Tyr Gly
        355                 360                 365


Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro Tyr Pro Gly
    370                 375                 380


Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser Gly Tyr Arg
385                 390                 395                 400


Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu Ile Met Val
                405                 410                 415


Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe Tyr His Leu
            420                 425                 430


Ser Glu Ile Val Glu Asn Leu Leu
        435                 440


<210>  101
<211>  444
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  PDGFRB(519-962) tyrosine kinase activating domain

<400>  101

Gln Glu Val Ile Val Val Pro His Ser Leu Pro Phe Lys Val Val Val
1               5                   10                  15


Ile Ser Ala Ile Leu Ala Leu Val Val Leu Thr Ile Ile Ser Leu Ile
            20                  25                  30


Ile Leu Ile Met Leu Trp Gln Lys Lys Pro Arg Tyr Glu Ile Arg Trp
        35                  40                  45
```

```
Lys Val Ile Glu Ser Val Ser Ser Asp Gly His Glu Tyr Ile Tyr Val
    50                  55                  60

Asp Pro Met Gln Leu Pro Tyr Asp Ser Thr Trp Glu Leu Pro Arg Asp
65                  70                  75                  80

Gln Leu Val Leu Gly Arg Thr Leu Gly Ser Gly Ala Phe Gly Gln Val
                85                  90                  95

Val Glu Ala Thr Ala His Gly Leu Ser His Ser Gln Ala Thr Met Lys
            100                 105                 110

Val Ala Val Lys Met Leu Lys Ser Thr Ala Arg Ser Ser Glu Lys Gln
        115                 120                 125

Ala Leu Met Ser Glu Leu Lys Ile Met Ser His Leu Gly Pro His Leu
    130                 135                 140

Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Gly Gly Pro Ile Tyr
145                 150                 155                 160

Ile Ile Thr Glu Tyr Cys Arg Tyr Gly Asp Leu Val Asp Tyr Leu His
                165                 170                 175

Arg Asn Lys His Thr Phe Leu Gln His His Ser Asp Lys Arg Arg Pro
            180                 185                 190

Pro Ser Ala Glu Leu Tyr Ser Asn Ala Leu Pro Val Gly Leu Pro Leu
        195                 200                 205

Pro Ser His Val Ser Leu Thr Gly Glu Ser Asp Gly Gly Tyr Met Asp
    210                 215                 220

Met Ser Lys Asp Glu Ser Val Asp Tyr Val Pro Met Leu Asp Met Lys
225                 230                 235                 240
```

```
Gly Asp Val Lys Tyr Ala Asp Ile Glu Ser Ser Asn Tyr Met Ala Pro
                245                 250                 255

Tyr Asp Asn Tyr Val Pro Ser Ala Pro Glu Arg Thr Cys Arg Ala Thr
            260                 265                 270

Leu Ile Asn Glu Ser Pro Val Leu Ser Tyr Met Asp Leu Val Gly Phe
        275                 280                 285

Ser Tyr Gln Val Ala Asn Gly Met Glu Phe Leu Ala Ser Lys Asn Cys
    290                 295                 300

Val His Arg Asp Leu Ala Ala Arg Asn Val Leu Ile Cys Glu Gly Lys
305                 310                 315                 320

Leu Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met Arg Asp
                325                 330                 335

Ser Asn Tyr Ile Ser Lys Gly Ser Thr Phe Leu Pro Leu Lys Trp Met
            340                 345                 350

Ala Pro Glu Ser Ile Phe Asn Ser Leu Tyr Thr Thr Leu Ser Asp Val
        355                 360                 365

Trp Ser Phe Gly Ile Leu Leu Trp Glu Ile Phe Thr Leu Gly Gly Thr
    370                 375                 380

Pro Tyr Pro Glu Leu Pro Met Asn Glu Gln Phe Tyr Asn Ala Ile Lys
385                 390                 395                 400

Arg Gly Tyr Arg Met Ala Gln Pro Ala His Ala Ser Asp Glu Ile Tyr
                405                 410                 415

Glu Ile Met Gln Lys Cys Trp Glu Glu Lys Phe Glu Ile Arg Pro Pro
            420                 425                 430
```

Phe Ser Gln Leu Val Leu Leu Leu Glu Arg Leu Leu
        435   440

<210> 102
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> murine EpoR(236-337;L264G,L265P) tyrosine kinase activating domain

<400> 102

Ser Glu Pro Ala Ser Leu Leu Thr Ala Ser Asp Leu Asp Pro Leu Ile
1   5   10   15

Leu Thr Leu Ser Leu Ile Leu Val Leu Ile Ser Leu Gly Pro Thr Val
            20   25   30

Leu Ala Leu Leu Ser His Arg Arg Thr Leu Gln Gln Lys Ile Trp Pro
        35   40   45

Gly Ile Pro Ser Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His
    50   55   60

Lys Gly Asn Phe Gln Leu Trp Leu Leu Gln Arg Asp Gly Cys Leu Trp
65   70   75   80

Trp Ser Pro Gly Ser Ser Phe Pro Glu Asp Pro Pro Ala His Leu Glu
                85   90   95

Val Leu Ser Glu Pro Arg
            100

<210> 103
<211> 236
<212> PRT
<213> Artificial Sequence

<220>
<223> EpoR(273-508) tyrosine kinase activating domain

<400> 103

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
1               5                  10                  15


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
            20                  25                  30


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
        35                  40                  45


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
    50                  55                  60


Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
65                  70                  75                  80


Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
                85                  90                  95


Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
            100                 105                 110


Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
        115                 120                 125


Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
    130                 135                 140


Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
145                 150                 155                 160


Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
                165                 170                 175
```

```
Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
            180                 185                 190


Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
        195                 200                 205


Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala
    210                 215                 220


Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
225                 230                 235


<210>  104
<211>  105
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  PD1(156-191)-TPOR/MPLR (514-582) TpoR tyrosine kinase activating domain
       with transmembrane domain variant

<400>  104

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


Gly Val Val Gly Gly Leu Leu Gly Ser Leu Val Leu Leu Val Trp Val
            20                  25                  30


Leu Ala Val Ile Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
        35                  40                  45


His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
    50                  55                  60


Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
65                  70                  75                  80
```

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
85 90 95

Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 105
<211> 105
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(478-582) (wildtype sequence) TpoR tyrosine kinase activating domain
with transmembrane domain variant

<400> 105

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser
1 5 10 15

Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
20 25 30

Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
35 40 45

His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
50 55 60

Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
65 70 75 80

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
85 90 95

Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 106
<211> 104
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-1) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 106

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Trp Ile Ser Leu
1 5 10 15

Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
20 25 30

Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
35 40 45

Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
50 55 60

Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
65 70 75 80

Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
85 90 95

Ser Glu Arg Thr Pro Leu Pro Leu
100

<210> 107
<211> 103
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-2) TpoR tyrosine kinase activating domain with transmembrane

domain
variant

<400> 107

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ile Ser Leu Val
1 5 10 15

Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
20 25 30

Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
35 40 45

Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
50 55 60

Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
65 70 75 80

Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
85 90 95

Glu Arg Thr Pro Leu Pro Leu
100

<210> 108
<211> 104
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-2+1) TpoR tyrosine kinase activating domain with transmembrane
domain
variant

<400> 108

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Ile Ser Leu
1 5 10 15

```
Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
            20                  25                  30


Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
        35                  40                  45


Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
    50                  55                  60


Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
65                  70                  75                  80


Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
                85                  90                  95


Ser Glu Arg Thr Pro Leu Pro Leu
            100


<210>  109
<211>  102
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N-3) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  109

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ser Leu Val Thr
1               5                   10                  15


Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
            20                  25                  30


Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
        35                  40                  45
```

```
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
    50                  55                  60


Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
65                  70                  75                  80


Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
                85                  90                  95


Arg Thr Pro Leu Pro Leu
            100


<210>  110
<211>  101
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N-4) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  110

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Val Thr Ala
1               5                   10                  15


Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
            20                  25                  30


Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
        35                  40                  45


Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
    50                  55                  60


Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
65                  70                  75                  80
```

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
85 90 95

Thr Pro Leu Pro Leu
100

<210> 111
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-4+1) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 111

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ile Leu Val Thr
1 5 10 15

Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
20 25 30

Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
35 40 45

Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
50 55 60

Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
65 70 75 80

Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
85 90 95

Arg Thr Pro Leu Pro Leu
100

<210> 112
<211> 100
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-5) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 112

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Thr Ala Leu
1 5 10 15

His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
20 25 30

Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
35 40 45

Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
50 55 60

Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
65 70 75 80

Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
85 90 95

Pro Leu Pro Leu
100

<210> 113
<211> 99
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-6) TpoR tyrosine kinase activating domain with transmembrane

domain
variant

<400> 113

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Thr Ala Leu His
1 5 10 15

Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
20 25 30

Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
35 40 45

Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
50 55 60

Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
65 70 75 80

Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
85 90 95

Leu Pro Leu

<210> 114
<211> 98
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-7) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 114

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu
1 5 10 15

```
Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
            20                  25                  30


Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
        35                  40                  45


Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
    50                  55                  60


Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
65                  70                  75                  80


Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
                85                  90                  95


Pro Leu



<210>  115
<211>  97
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N-8) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  115

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu His Leu Val
1               5                   10                  15


Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
            20                  25                  30


Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
        35                  40                  45
```

```
Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
    50                  55                  60


Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
65                  70                  75                  80


Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
                85                  90                  95


Leu
```

<210> 116
<211> 96
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-9) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 116

```
Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr His Leu Val Leu
1               5                   10                  15


Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
            20                  25                  30


Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
        35                  40                  45


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


Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
65                  70                  75                  80
```

Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90 95

<210> 117
<211> 95
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-10) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 117

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

Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
20 25 30

His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
35 40 45

His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
50 55 60

Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
65 70 75 80

Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90 95

<210> 118
<211> 94
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-11) TpoR tyrosine kinase activating domain with transmembrane

domain
variant

<400> 118

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

Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
20 25 30

Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
35 40 45

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

Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
65 70 75 80

Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 119
<211> 93
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-12) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 119

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

Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
20 25 30

```
Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
        35                  40                  45


Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
    50                  55                  60


Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
65                  70                  75                  80


Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
                85                  90


<210>  120
<211>  92
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N-13) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  120

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


Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
            20                  25                  30


Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
        35                  40                  45


Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
    50                  55                  60


Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
65                  70                  75                  80
```

Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 121
<211> 91
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-14) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 121

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Ser Ala Val
1 5 10 15

Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
20 25 30

Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
35 40 45

Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
50 55 60

Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
65 70 75 80

Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 122
<211> 90
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-15) TpoR tyrosine kinase activating domain with transmembrane

domain
variant

<400> 122

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ser Ala Val Leu
1 5 10 15

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
20 25 30

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
35 40 45

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
50 55 60

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
65 70 75 80

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
85 90

<210> 123
<211> 89
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-16) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 123

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

Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
20 25 30

```
His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
        35                  40                  45


Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
    50                  55                  60


Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
65                  70                  75                  80


Ser Ser Glu Arg Thr Pro Leu Pro Leu
                85


<210>  124
<211>  88
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N-17) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  124

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


Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
            20                  25                  30


Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
        35                  40                  45


Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
    50                  55                  60


Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
65                  70                  75                  80
```

Ser Glu Arg Thr Pro Leu Pro Leu
85

<210> 125
<211> 87
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N-18) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 125

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

Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
20 25 30

Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
35 40 45

Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
50 55 60

Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
65 70 75 80

Glu Arg Thr Pro Leu Pro Leu
85

<210> 126
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N+1) TpoR tyrosine kinase activating domain with transmembrane

domain
variant

<400> 126

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile
1 5 10 15

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
20 25 30

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
35 40 45

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
50 55 60

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
65 70 75 80

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
85 90 95

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105

<210> 127
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N+2) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 127

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu
1 5 10 15

```
Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val
            20                  25                  30


Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
        35                  40                  45


Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
    50                  55                  60


Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
65                  70                  75                  80


Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
                85                  90                  95


Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
            100                 105


<210>  128
<211>  108
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N+3) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  128

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val
1               5                   10                  15


Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala
            20                  25                  30


Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
        35                  40                  45
```

```
Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
    50                  55                  60


Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
65                  70                  75                  80


Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
                85                  90                  95


Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
            100                 105


<210>  129
<211>  109
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N+4) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  129

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu
1               5                   10                  15


Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser
            20                  25                  30


Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
        35                  40                  45


Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
    50                  55                  60


Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
65                  70                  75                  80
```

```
Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
                85                  90                  95


Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
            100                 105


<210>  130
<211>  110
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TPOR/MPLR(N+5) TpoR tyrosine kinase activating domain with transmembrane
domain
       variant

<400>  130

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile
1               5                   10                  15


Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu
            20                  25                  30


Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
        35                  40                  45


Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
    50                  55                  60


Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
65                  70                  75                  80


Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
                85                  90                  95


Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
            100                 105                 110
```

<210> 131
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N+6) TpoR tyrosine kinase activating domain with transmembrane domain
variant

<400> 131

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Leu
1 5 10 15

Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly
20 25 30

Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
35 40 45

His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
50 55 60

His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
65 70 75 80

Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
85 90 95

Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105 110

<210> 132
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N+7) TpoR tyrosine kinase activating domain with transmembrane

domain
variant

<400> 132

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu
1 5 10 15

Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu
20 25 30

Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
35 40 45

Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
50 55 60

Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
65 70 75 80

Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
85 90 95

Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
100 105 110

<210> 133
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> TPOR/MPLR(N+8) TpoR tyrosine kinase activating domain with transmembrane
domain
variant

<400> 133

Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val
1 5 10 15

Leu Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val
            20   25   30

Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
        35   40   45

Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
    50   55   60

Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
65   70   75   80

Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
                85   90   95

Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
            100   105   110

Leu

<210> 134
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> IL7R(316-459) tyrosine kinase effector domains

<400> 134

Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
1   5   10   15

Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
            20   25   30

Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg

35 40 45

Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
50 55 60

Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
65 70 75 80

Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
85 90 95

Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
100 105 110

Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
115 120 125

Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
130 135 140

<210> 135
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> IL2Rb(333-551) tyrosine kinase effector domains

<400> 135

Val Thr Gln Leu Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser
1 5 10 15

Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr
20 25 30

Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Val
35 40 45

```
Tyr Phe Thr Tyr Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val
    50                  55                  60

Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser
65                  70                  75                  80

Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu
                85                  90                  95

Leu Phe Ser Pro Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala
            100                 105                 110

Pro Gly Gly Ser Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu Gln
        115                 120                 125

Glu Arg Val Pro Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr
    130                 135                 140

Pro Gly Val Pro Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu Val
145                 150                 155                 160

Leu Arg Glu Ala Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly
                165                 170                 175

Val Ser Phe Pro Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala
            180                 185                 190

Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
        195                 200                 205

Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
    210                 215
```

<210> 136
<211> 50
<212> PRT

<213> Artificial Sequence

<220>
<223> IFNAR1(508-557) tyrosine kinase effector domains

<400> 136

Ile Ser Thr Ile Ala Thr Val Glu Glu Thr Asn Gln Thr Asp Glu Asp
1 5 10 15

His Lys Lys Tyr Ser Ser Gln Thr Ser Gln Asp Ser Gly Asn Tyr Ser
20 25 30

Asn Glu Asp Glu Ser Glu Ser Lys Thr Ser Glu Glu Leu Gln Gln Asp
35 40 45

Phe Val
50

<210> 137
<211> 206
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNAR2(310-515) tyrosine kinase effector domains

<400> 137

Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp Ser Asp
1 5 10 15

Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met His Gly
20 25 30

Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Thr Ser Thr Glu Ser
35 40 45

Gln Leu Ile Asp Pro Glu Ser Glu Glu Glu Pro Asp Leu Pro Glu Val
50 55 60

```
Asp Val Glu Leu Pro Thr Met Pro Lys Asp Ser Pro Gln Gln Leu Glu
65                  70                  75                  80


Leu Leu Ser Gly Pro Cys Glu Arg Arg Lys Ser Pro Leu Gln Asp Pro
                85                  90                  95


Phe Pro Glu Glu Asp Tyr Ser Ser Thr Glu Gly Ser Gly Gly Arg Ile
            100                 105                 110


Thr Phe Asn Val Asp Leu Asn Ser Val Phe Leu Arg Val Leu Asp Asp
        115                 120                 125


Glu Asp Ser Asp Asp Leu Glu Ala Pro Leu Met Leu Ser Ser His Leu
    130                 135                 140


Glu Glu Met Val Asp Pro Glu Asp Pro Asp Asn Val Gln Ser Asn His
145                 150                 155                 160


Leu Leu Ala Ser Gly Glu Gly Thr Gln Pro Thr Phe Pro Ser Pro Ser
                165                 170                 175


Ser Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser Asp Thr
            180                 185                 190


Ser Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
        195                 200                 205


<210>  138
<211>  256
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  IFNAR1/2(IFNAR1 residues 508-557-IFNAR2 residues 310-515) tyrosine
       kinase effector domains

<400>  138
```

```
Ile Ser Thr Ile Ala Thr Val Glu Glu Thr Asn Gln Thr Asp Glu Asp
1               5                  10                  15

His Lys Lys Tyr Ser Ser Gln Thr Ser Gln Asp Ser Gly Asn Tyr Ser
            20                  25                  30

Asn Glu Asp Glu Ser Glu Ser Lys Thr Ser Glu Glu Leu Gln Gln Asp
        35                  40                  45

Phe Val Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp
    50                  55                  60

Ser Asp Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met
65                  70                  75                  80

His Gly Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Thr Ser Thr
                85                  90                  95

Glu Ser Gln Leu Ile Asp Pro Glu Ser Glu Glu Glu Pro Asp Leu Pro
            100                 105                 110

Glu Val Asp Val Glu Leu Pro Thr Met Pro Lys Asp Ser Pro Gln Gln
        115                 120                 125

Leu Glu Leu Leu Ser Gly Pro Cys Glu Arg Arg Lys Ser Pro Leu Gln
    130                 135                 140

Asp Pro Phe Pro Glu Glu Asp Tyr Ser Ser Thr Glu Gly Ser Gly Gly
145                 150                 155                 160

Arg Ile Thr Phe Asn Val Asp Leu Asn Ser Val Phe Leu Arg Val Leu
                165                 170                 175

Asp Asp Glu Asp Ser Asp Asp Leu Glu Ala Pro Leu Met Leu Ser Ser
            180                 185                 190
```

His Leu Glu Glu Met Val Asp Pro Glu Asp Pro Asp Asn Val Gln Ser
195 200 205

Asn His Leu Leu Ala Ser Gly Glu Gly Thr Gln Pro Thr Phe Pro Ser
210 215 220

Pro Ser Ser Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser
225 230 235 240

Asp Thr Ser Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
245 250 255

<210> 139
<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNLR1(300-520) tyrosine kinase effector domains

<400> 139

Arg Gly Val Arg Pro Thr Pro Arg Val Arg Ala Pro Ala Thr Gln Gln
1 5 10 15

Thr Arg Trp Lys Lys Asp Leu Ala Glu Asp Glu Glu Glu Glu Asp Glu
20 25 30

Glu Asp Thr Glu Asp Gly Val Ser Phe Gln Pro Tyr Ile Glu Pro Pro
35 40 45

Ser Phe Leu Gly Gln Glu His Gln Ala Pro Gly His Ser Glu Ala Gly
50 55 60

Gly Val Asp Ser Gly Arg Pro Arg Ala Pro Leu Val Pro Ser Glu Gly
65 70 75 80

Ser Ser Ala Trp Asp Ser Ser Asp Arg Ser Trp Ala Ser Thr Val Asp
85 90 95

```
Ser Ser Trp Asp Arg Ala Gly Ser Ser Gly Tyr Leu Ala Glu Lys Gly
            100                 105                 110

Pro Gly Gln Gly Pro Gly Gly Asp Gly His Gln Glu Ser Leu Pro Pro
        115                 120                 125

Pro Glu Phe Ser Lys Asp Ser Gly Phe Leu Glu Glu Leu Pro Glu Asp
    130                 135                 140

Asn Leu Ser Ser Trp Ala Thr Trp Gly Thr Leu Pro Pro Glu Pro Asn
145                 150                 155                 160

Leu Val Pro Gly Gly Pro Pro Val Ser Leu Gln Thr Leu Thr Phe Cys
                165                 170                 175

Trp Glu Ser Ser Pro Glu Glu Glu Glu Glu Ala Arg Glu Ser Glu Ile
            180                 185                 190

Glu Asp Ser Asp Ala Gly Ser Trp Gly Ala Glu Ser Thr Gln Arg Thr
        195                 200                 205

Glu Asp Arg Gly Arg Thr Leu Gly His Tyr Met Ala Arg
    210                 215                 220


<210>  140
<211>  35
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  Common Gamma Chain(335-369) tyrosine kinase effector domains

<400>  140

Ile Pro Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly Ala Ser Pro
1               5                   10                  15
```

Cys Asn Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr Thr Leu Lys
            20   25   30

Pro Glu Thr
        35

<210> 141
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> IL9R(356-521) tyrosine kinase effector domains

<400> 141

Thr Ala Leu Leu Thr Cys Gly Pro Ala Arg Pro Trp Lys Ser Val Ala
1   5   10   15

Leu Glu Glu Glu Gln Glu Gly Pro Gly Thr Arg Leu Pro Gly Asn Leu
            20   25   30

Ser Ser Glu Asp Val Leu Pro Ala Gly Cys Thr Glu Trp Arg Val Gln
        35   40   45

Thr Leu Ala Tyr Leu Pro Gln Glu Asp Trp Ala Pro Thr Ser Leu Thr
    50   55   60

Arg Pro Ala Pro Pro Asp Ser Glu Gly Ser Arg Ser Ser Ser Ser Ser
65   70   75   80

Ser Ser Ser Asn Asn Asn Asn Tyr Cys Ala Leu Gly Cys Tyr Gly Gly
                85   90   95

Trp His Leu Ser Ala Leu Pro Gly Asn Thr Gln Ser Ser Gly Pro Ile
            100   105   110

Pro Ala Leu Ala Cys Gly Leu Ser Cys Asp His Gln Gly Leu Glu Thr
        115   120   125

```
Gln Gln Gly Val Ala Trp Val Leu Ala Gly His Cys Gln Arg Pro Gly
    130                 135                 140


Leu His Glu Asp Leu Gln Gly Met Leu Leu Pro Ser Val Leu Ser Lys
145                 150                 155                 160


Ala Arg Ser Trp Thr Phe
                165


<210>  142
<211>  217
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  IL21R(322-538) tyrosine kinase effector domains

<400>  142

Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr Glu Leu Gln Glu Pro
1               5                   10                  15


Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys Pro Ser Phe Trp Pro
            20                  25                  30


Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser Glu Glu Arg Asp Arg
        35                  40                  45


Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr Val Leu Asp Ala Glu
    50                  55                  60


Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp Asp Gly Tyr Pro Ala
65                  70                  75                  80


Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro Gly Leu Glu Asp Pro
                85                  90                  95
```

Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys Gly Cys Val Ser Ala
100 105 110

Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu
115 120 125

Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp
130 135 140

Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser Glu Ala Gly Ser Pro
145 150 155 160

Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser Gly Phe Val Gly Ser
165 170 175

Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu
180 185 190

Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Ile Pro Pro Pro
195 200 205

Leu Ser Ser Pro Gly Pro Gln Ala Ser
210 215

<210> 143
<211> 286
<212> PRT
<213> Artificial Sequence

<220>
<223> GHR(353-638) tyrosine kinase effector domains

<400> 143

Pro Asp Glu Lys Thr Glu Glu Ser Asp Thr Asp Arg Leu Leu Ser Ser
1 5 10 15

Asp His Glu Lys Ser His Ser Asn Leu Gly Val Lys Asp Gly Asp Ser
20 25 30

```
Gly Arg Thr Ser Cys Cys Glu Pro Asp Ile Leu Glu Thr Asp Phe Asn
        35                  40                  45

Ala Asn Asp Ile His Glu Gly Thr Ser Glu Val Ala Gln Pro Gln Arg
    50                  55                  60

Leu Lys Gly Glu Ala Asp Leu Leu Cys Leu Asp Gln Lys Asn Gln Asn
65                  70                  75                  80

Asn Ser Pro Tyr His Asp Ala Cys Pro Ala Thr Gln Gln Pro Ser Val
                85                  90                  95

Ile Gln Ala Glu Lys Asn Lys Pro Gln Pro Leu Pro Thr Glu Gly Ala
            100                 105                 110

Glu Ser Thr His Gln Ala Ala His Ile Gln Leu Ser Asn Pro Ser Ser
        115                 120                 125

Leu Ser Asn Ile Asp Phe Tyr Ala Gln Val Ser Asp Ile Thr Pro Ala
    130                 135                 140

Gly Ser Val Val Leu Ser Pro Gly Gln Lys Asn Lys Ala Gly Met Ser
145                 150                 155                 160

Gln Cys Asp Met His Pro Glu Met Val Ser Leu Cys Gln Glu Asn Phe
                165                 170                 175

Leu Met Asp Asn Ala Tyr Phe Cys Glu Ala Asp Ala Lys Lys Cys Ile
            180                 185                 190

Pro Val Ala Pro His Ile Lys Val Glu Ser His Ile Gln Pro Ser Leu
        195                 200                 205

Asn Gln Glu Asp Ile Tyr Ile Thr Thr Glu Ser Leu Thr Thr Ala Ala
    210                 215                 220
```

```
Gly Arg Pro Gly Thr Gly Glu His Val Pro Gly Ser Glu Met Pro Val
225                 230                 235                 240


Pro Asp Tyr Thr Ser Ile His Ile Val Gln Ser Pro Gln Gly Leu Ile
                245                 250                 255


Leu Asn Ala Thr Ala Leu Pro Leu Pro Asp Lys Glu Phe Leu Ser Ser
            260                 265                 270


Cys Gly Tyr Val Ser Thr Asp Gln Leu Asn Lys Ile Met Pro
        275                 280                 285


<210>  144
<211>  170
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EpoR(339-508) tyrosine kinase effector domains

<400>  144

Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu Gly Pro
1               5                   10                  15


Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr Leu Val
            20                  25                  30


Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp Leu Pro
        35                  40                  45


Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly Ser Glu
    50                  55                  60


Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro Glu Gly
65                  70                  75                  80
```

```
Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser Ser Gln
                85                  90                  95

Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr Pro Pro
            100                 105                 110

His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile Ser Thr
        115                 120                 125

Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu Ser Asp
    130                 135                 140

Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala Ala Glu
145                 150                 155                 160

Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
                165                 170
```

<210> 145
<211> 203
<212> PRT
<213> Artificial Sequence

<220>
<223> murine IL2Rb(337-539) tyrosine kinase effector domains

<400> 145

```
Ala Val Gln Leu Leu Leu Leu Gln Lys Asp Ser Ala Pro Leu Pro Ser
1               5                   10                  15

Pro Ser Gly His Ser Gln Ala Ser Cys Phe Thr Asn Gln Gly Tyr Phe
            20                  25                  30

Phe Phe His Leu Pro Asn Ala Leu Glu Ile Glu Ser Cys Gln Val Tyr
        35                  40                  45

Phe Thr Tyr Asp Pro Cys Val Glu Glu Glu Val Glu Glu Asp Gly Ser
    50                  55                  60
```

```
Arg Leu Pro Glu Gly Ser Pro His Pro Pro Leu Leu Pro Leu Ala Gly
65                  70                  75                  80

Glu Gln Asp Asp Tyr Cys Ala Phe Pro Pro Arg Asp Asp Leu Leu Leu
                85                  90                  95

Phe Ser Pro Ser Leu Ser Thr Pro Asn Thr Ala Tyr Gly Gly Ser Arg
            100                 105                 110

Ala Pro Glu Glu Arg Ser Pro Leu Ser Leu His Glu Gly Leu Pro Ser
        115                 120                 125

Leu Ala Ser Arg Asp Leu Met Gly Leu Gln Arg Pro Leu Glu Arg Met
    130                 135                 140

Pro Glu Gly Asp Gly Glu Gly Leu Ser Ala Asn Ser Ser Gly Glu Gln
145                 150                 155                 160

Ala Ser Val Pro Glu Gly Asn Leu His Gly Gln Asp Gln Asp Arg Gly
                165                 170                 175

Gln Gly Pro Ile Leu Thr Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
            180                 185                 190

Glu Leu Gln Ala Gln Asp Ser Val His Leu Ile
        195                 200
```

<210> 146
<211> 144
<212> PRT
<213> Artificial Sequence

<220>
<223> murine IL7Ra(316-459) tyrosine kinase effector domains

<400> 146

```
Ala Arg Asp Glu Val Glu Ser Phe Leu Pro Asn Asp Leu Pro Ala Gln
1               5                   10                  15


Pro Glu Glu Leu Glu Thr Gln Gly His Arg Ala Ala Val His Ser Ala
            20                  25                  30


Asn Arg Ser Pro Glu Thr Ser Val Ser Pro Pro Glu Thr Val Arg Arg
        35                  40                  45


Glu Ser Pro Leu Arg Cys Leu Ala Arg Asn Leu Ser Thr Cys Asn Ala
    50                  55                  60


Pro Pro Leu Leu Ser Ser Arg Ser Pro Asp Tyr Arg Asp Gly Asp Arg
65                  70                  75                  80


Asn Arg Pro Pro Val Tyr Gln Asp Leu Leu Pro Asn Ser Gly Asn Thr
                85                  90                  95


Asn Val Pro Val Pro Val Pro Gln Pro Leu Pro Phe Gln Ser Gly Ile
            100                 105                 110


Leu Ile Pro Val Ser Gln Arg Gln Pro Ile Ser Thr Ser Ser Val Leu
        115                 120                 125


Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Lys
    130                 135                 140


<210>  147
<211>  231
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EGFR(955-1186) tyrosine kinase effector domains

<400>  147

Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp Ser
1               5                   10                  15
```

```
Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val Val
            20                  25                  30

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

Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala Thr Ser Asn
    50                  55                  60

Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser Cys Pro
65                  70                  75                  80

Ile Lys Glu Asp Ser Phe Leu Gln Arg Tyr Ser Ser Asp Pro Thr Gly
                85                  90                  95

Ala Leu Thr Glu Asp Ser Ile Asp Asp Thr Phe Leu Pro Val Pro Glu
            100                 105                 110

Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser Val Gln Asn
        115                 120                 125

Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser Arg Asp Pro
    130                 135                 140

His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro Glu Tyr Leu
145                 150                 155                 160

Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro Ala
                165                 170                 175

His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp
            180                 185                 190

Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe
        195                 200                 205
```

Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln
210 215 220

Ser Ser Glu Phe Ile Gly Ala
225 230

<210> 148
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<223> EGFR(955-1186;Y974F,d1045-1057) tyrosine kinase effector domains

<400> 148

Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp Ser
1 5 10 15

Asn Phe Phe Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val Val
20 25 30

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

Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala Thr Ser Asn
50 55 60

Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser Cys Pro
65 70 75 80

Ile Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu Pro
85 90 95

Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser
100 105 110

Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser
115 120 125

Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro
130 135 140

Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp
145 150 155 160

Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp
165 170 175

Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn
180 185 190

Gly Ile Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val
195 200 205

Ala Pro Gln Ser Ser Glu Phe Ile Gly Ala
210 215

<210> 149
<211> 54
<212> PRT
<213> Artificial Sequence

<220>
<223> EGFR(955-1009;Y974F) tyrosine kinase effector domains

<400> 149

Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp Ser
1 5 10 15

Asn Phe Phe Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val Val
20 25 30

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

Ser Thr Ser Arg Thr Pro
    50

<210> 150
<211> 54
<212> PRT
<213> Artificial Sequence

<220>
<223> EGFR(1019-1085) tyrosine kinase effector domains

<400> 150

Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser Cys
1   5   10   15

Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu
            20   25   30

Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly
        35   40   45

Ser Val Gln Asn Pro Val
    50

<210> 151
<211> 54
<212> PRT
<213> Artificial Sequence

<220>
<223> EGFR(1037-1103;Y1068/1101F,d1045-1057) tyrosine kinase effector domains

<400> 151

Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu Pro Val
1   5   10   15

Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser Val
            20   25   30

```
Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser Arg
        35                  40                  45


Asp Pro His Phe Gln Asp
    50


<210>  152
<211>  54
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EGFR(1066-1118;Y1068/1086F) tyrosine kinase effector domains

<400>  152

Val Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser
1               5                   10                  15


Val Gln Asn Pro Val Phe His Asn Gln Pro Leu Asn Pro Ala Pro Ser
            20                  25                  30


Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro
        35                  40                  45


Glu Tyr Leu Asn Thr Val
    50


<210>  153
<211>  54
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EGFR(1122-1165) tyrosine kinase effector domains

<400>  153

Pro Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe
1               5                   10                  15
```

```
Asp Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu
            20                  25                  30


Asp Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro
        35                  40                  45


Asn Gly Ile Phe Lys Gly
    50


<210>  154
<211>  54
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EGFR(1133-1186;Y1148F) tyrosine kinase effector domains

<400>  154

Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp Phe
1               5                   10                  15


Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe Lys
            20                  25                  30


Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln Ser
        35                  40                  45


Ser Glu Phe Ile Gly Ala
    50


<210>  155
<211>  51
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  IL12Rb2(775-825) tyrosine kinase effector domains
```

<400> 155

Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
1 5 10 15

Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
20 25 30

Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
35 40 45

Glu Pro Gln
50

<210> 156
<211> 41
<212> PRT
<213> Artificial Sequence

<220>
<223> IL7R(376-416) tyrosine kinase effector domains

<400> 156

Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
1 5 10 15

Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
20 25 30

Leu Gly Thr Thr Asn Ser Thr Leu Pro
35 40

<210> 157
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> IL7R(424-459) tyrosine kinase effector domains

<400> 157

Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
1 5 10 15

Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
20 25 30

Tyr Gln Asn Gln
35

<210> 158
<211> 68
<212> PRT
<213> Artificial Sequence

<220>
<223> IL7R(376-416,424-459) tyrosine kinase effector domains

<400> 158

Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
1 5 10 15

Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
20 25 30

Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile Leu Thr
35 40 45

Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
50 55 60

Tyr Gln Asn Gln
65

<210> 159
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> IL7R(424-459;Y456F) tyrosine kinase effector domains

<400> 159

Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
1   5   10   15

Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
            20   25   30

Phe Gln Asn Gln
        35

<210> 160
<211> 68
<212> PRT
<213> Artificial Sequence

<220>
<223> IL7R(376-416,424-459,Y456F) tyrosine kinase effector domains

<400> 160

Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
1   5   10   15

Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
            20   25   30

Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile Leu Thr
        35   40   45

Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
    50   55   60

Phe Gln Asn Gln
65

<210> 161
<211> 75
<212> PRT
<213> Artificial Sequence

<220>
<223> IL2small(393-433) tyrosine kinase effector domains

<400> 161

```
Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu
1               5                   10                  15


Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg
            20                  25                  30


Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala
        35                  40                  45


Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
    50                  55                  60


Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
65                  70                  75
```

<210> 162
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> IL2small(518-551) tyrosine kinase effector domains

<400> 162

```
Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr
1               5                   10                  15


Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His
            20                  25                  30
```

Leu Val

<210> 163
<211> 82
<212> PRT
<213> Artificial Sequence

<220>
<223> IL2small(339-379,393-433) tyrosine kinase effector domains

<400> 163

Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
1 5 10 15

Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
20 25 30

Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly Ala
35 40 45

Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp
50 55 60

Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser
65 70 75 80

Pro Ser

<210> 164
<211> 75
<212> PRT
<213> Artificial Sequence

<220>
<223> IL2small(339-379,518-551) tyrosine kinase effector domains

<400> 164

Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
1 5 10 15

Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
20 25 30

Asp Ala Leu Glu Ile Glu Ala Cys Gln Gly Gln Gly Glu Phe Arg Ala
35 40 45

Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
50 55 60

Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
65 70 75

<210> 165
<211> 75
<212> PRT
<213> Artificial Sequence

<220>
<223> IL2small(393-433,518-551) tyrosine kinase effector domains

<400> 165

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

Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg
20 25 30

Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala
35 40 45

Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
50 55 60

Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
65 70 75

<210> 166
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> IL2small(339-379,393-433,518-551) tyrosine kinase effector domains

<400> 166

Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser
1 5 10 15

Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro
20 25 30

Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly Ala
35 40 45

Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp
50 55 60

Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser
65 70 75 80

Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu
85 90 95

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

Thr His Leu Val
115

<210> 167
<211> 43
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNAR2small(310-352) tyrosine kinase effector domains

<400> 167

Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp Ser Asp
1   5   10   15

Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met His Gly
            20   25   30

Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala
        35   40

<210> 168
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNAR2small(486-515) tyrosine kinase effector domains

<400> 168

Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser Asp Thr Ser
1   5   10   15

Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
            20   25

<210> 169
<211> 72
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNAR2small(310-352,486-515) tyrosine kinase effector domains

<400> 169

Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp Ser Asp
1   5   10   15

```
Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met His Gly
            20                  25                  30


Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Glu Gly Leu Trp Ser
        35                  40                  45


Glu Asp Ala Pro Ser Asp Gln Ser Asp Thr Ser Glu Ser Asp Val Asp
    50                  55                  60


Leu Gly Asp Gly Tyr Ile Met Arg
65                  70


<210>  170
<211>  156
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  BLNK(53-208) tyrosine kinase effector domains

<400>  170

Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp Phe
1               5                   10                  15


Asp Ser Asp Tyr Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met Tyr
            20                  25                  30


Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro Pro Pro
        35                  40                  45


Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala Arg
    50                  55                  60


Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro Phe
65                  70                  75                  80
```

```
Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala Arg
                85                  90                  95


Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln Val
            100                 105                 110


Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val Val
        115                 120                 125


Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser Ser
    130                 135                 140


Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
145                 150                 155


<210>  171
<211>  156
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  BLNK(53-208;Y72F) tyrosine kinase effector domains

<400>  171

Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp Phe
1               5                   10                  15


Asp Ser Asp Phe Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met Tyr
            20                  25                  30


Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro Pro Pro
        35                  40                  45


Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala Arg
    50                  55                  60


Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro Phe
65                  70                  75                  80
```

```
Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala Arg
                85                  90                  95


Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln Val
            100                 105                 110


Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val Val
        115                 120                 125


Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser Ser
    130                 135                 140


Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
145                 150                 155


<210>  172
<211>  156
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  BLNK(53-208;Y72F,Y96F) tyrosine kinase effector domains

<400>  172

Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp Phe
1               5                   10                  15


Asp Ser Asp Phe Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met Tyr
            20                  25                  30


Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Phe Glu Pro Pro Pro
        35                  40                  45


Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala Arg
    50                  55                  60
```

```
Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro Phe
65                  70                  75                  80


Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala Arg
                85                  90                  95


Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln Val
            100                 105                 110


Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val Val
        115                 120                 125


Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser Ser
    130                 135                 140


Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
145                 150                 155


<210>  173
<211>  170
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  EpoR(339-508) tyrosine kinase effector domains

<400>  173

Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu Gly Pro
1               5                   10                  15


Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr Leu Val
            20                  25                  30


Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp Leu Pro
        35                  40                  45


Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly Ser Glu
    50                  55                  60
```

```
Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro Glu Gly
65                  70                  75                  80

Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser Ser Gln
                85                  90                  95

Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr Pro Pro
            100                 105                 110

His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile Ser Thr
        115                 120                 125

Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu Ser Asp
    130                 135                 140

Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala Ala Glu
145                 150                 155                 160

Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
                165                 170
```

<210> 174
<211> 149
<212> PRT
<213> Artificial Sequence

<220>
<223> IL12Rb2(714-862) tyrosine kinase effector domains

<400> 174

```
Val Thr Pro Val Phe Arg His Pro Pro Cys Ser Asn Trp Pro Gln Arg
1               5                   10                  15

Glu Lys Gly Ile Gln Gly His Gln Ala Ser Glu Lys Asp Met Met His
            20                  25                  30
```

Ser Ala Ser Ser Pro Pro Pro Pro Arg Ala Leu Gln Ala Glu Ser Arg
35 40 45

Gln Leu Val Asp Leu Tyr Lys Val Leu Glu Ser Arg Gly Ser Asp Pro
50 55 60

Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
65 70 75 80

Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
85 90 95

Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
100 105 110

His Ile Ser Leu Ser Val Phe Pro Ser Ser Ser Leu His Pro Leu Thr
115 120 125

Phe Ser Cys Gly Asp Lys Leu Thr Leu Asp Gln Leu Lys Met Arg Cys
130 135 140

Asp Ser Leu Met Leu
145

<210> 175
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<223> IL12Rb1(622-662) tyrosine kinase effector domains

<400> 175

Trp Asp Lys Gly Glu Arg Thr Glu Pro Leu Glu Lys Thr Glu Leu Pro
1 5 10 15

Glu Gly Ala Pro Glu Leu Ala Leu Asp Thr Glu Leu Ser Leu Glu Asp
20 25 30

Gly Asp Arg Cys Lys Ala Lys Met
        35   40

<210> 176
<211> 275
<212> PRT
<213> Artificial Sequence

<220>
<223> IL10R1(304-578) tyrosine kinase effector domains

<400> 176

Val Ser Pro Glu Leu Lys Asn Leu Asp Leu His Gly Ser Thr Asp Ser
1   5   10   15

Gly Phe Gly Ser Thr Lys Pro Ser Leu Gln Thr Glu Glu Pro Gln Phe
            20   25   30

Leu Leu Pro Asp Pro His Pro Gln Ala Asp Arg Thr Leu Gly Asn Arg
        35   40   45

Glu Pro Pro Val Leu Gly Asp Ser Cys Ser Ser Gly Ser Ser Asn Ser
    50   55   60

Thr Asp Ser Gly Ile Cys Leu Gln Glu Pro Ser Leu Ser Pro Ser Thr
65   70   75   80

Gly Pro Thr Trp Glu Gln Gln Val Gly Ser Asn Ser Arg Gly Gln Asp
                85   90   95

Asp Ser Gly Ile Asp Leu Val Gln Asn Ser Glu Gly Arg Ala Gly Asp
            100   105   110

Thr Gln Gly Gly Ser Ala Leu Gly His His Ser Pro Pro Glu Pro Glu
        115   120   125

```
Val Pro Gly Glu Glu Asp Pro Ala Ala Val Ala Phe Gln Gly Tyr Leu
    130                 135                 140

Arg Gln Thr Arg Cys Ala Glu Glu Lys Ala Thr Lys Thr Gly Cys Leu
145                 150                 155                 160

Glu Glu Glu Ser Pro Leu Thr Asp Gly Leu Gly Pro Lys Phe Gly Arg
                165                 170                 175

Cys Leu Val Asp Glu Ala Gly Leu His Pro Pro Ala Leu Ala Lys Gly
            180                 185                 190

Tyr Leu Lys Gln Asp Pro Leu Glu Met Thr Leu Ala Ser Ser Gly Ala
        195                 200                 205

Pro Thr Gly Gln Trp Asn Gln Pro Thr Glu Glu Trp Ser Leu Leu Ala
    210                 215                 220

Leu Ser Ser Cys Ser Asp Leu Gly Ile Ser Asp Trp Ser Phe Ala His
225                 230                 235                 240

Asp Leu Ala Pro Leu Gly Cys Val Ala Ala Pro Gly Gly Leu Leu Gly
                245                 250                 255

Ser Phe Asn Ser Asp Leu Val Thr Leu Pro Leu Ile Ser Ser Leu Gln
            260                 265                 270

Ser Ser Glu
        275
```

<210> 177
<211> 461
<212> PRT
<213> Artificial Sequence

<220>
<223> Myristoyl-Myd88-CD40-FKBP(F36V)x2 (GoCART) construct

<400> 177

```
Met Gly Ser Ser Lys Ser Lys Pro Lys Asp Pro Ser Gln Arg Met Ala
1               5                  10                  15

Ala Gly Gly Pro Gly Ala Gly Ser Ala Ala Pro Val Ser Ser Thr Ser
            20                  25                  30

Ser Leu Pro Leu Ala Ala Leu Asn Met Arg Val Arg Arg Arg Leu Ser
        35                  40                  45

Leu Phe Leu Asn Val Arg Thr Gln Val Ala Ala Asp Trp Thr Ala Leu
    50                  55                  60

Ala Glu Glu Met Asp Phe Glu Tyr Leu Glu Ile Arg Gln Leu Glu Thr
65                  70                  75                  80

Gln Ala Asp Pro Thr Gly Arg Leu Leu Asp Ala Trp Gln Gly Arg Pro
                85                  90                  95

Gly Ala Ser Val Gly Arg Leu Leu Glu Leu Leu Thr Lys Leu Gly Arg
            100                 105                 110

Asp Asp Val Leu Leu Glu Leu Gly Pro Ser Ile Glu Glu Asp Cys Gln
        115                 120                 125

Lys Tyr Ile Leu Lys Gln Gln Gln Glu Glu Ala Glu Lys Pro Leu Gln
    130                 135                 140

Val Ala Ala Val Asp Ser Ser Val Pro Arg Thr Ala Glu Leu Ala Gly
145                 150                 155                 160

Ile Thr Thr Leu Asp Asp Pro Leu Gly His Met Pro Glu Arg Phe Asp
                165                 170                 175

Ala Phe Ile Cys Tyr Cys Pro Ser Asp Ile Lys Lys Val Ala Lys Lys
            180                 185                 190
```

```
Pro Thr Asn Lys Ala Pro His Pro Lys Gln Glu Pro Gln Glu Ile Asn
        195                 200                 205

Phe Pro Asp Asp Leu Pro Gly Ser Asn Thr Ala Ala Pro Val Gln Glu
    210                 215                 220

Thr Leu His Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser
225                 230                 235                 240

Arg Ile Ser Val Gln Glu Arg Gln Gly Val Gln Val Glu Thr Ile Ser
                245                 250                 255

Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val
            260                 265                 270

His Tyr Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg
        275                 280                 285

Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile
    290                 295                 300

Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala
305                 310                 315                 320

Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro
                325                 330                 335

Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu
            340                 345                 350

Lys Leu Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr
        355                 360                 365

Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu
    370                 375                 380
```

```
Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe
385                 390                 395                 400


Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly
                405                 410                 415


Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro
            420                 425                 430


Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His
        435                 440                 445


Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
    450                 455                 460


<210>  178
<211>  233
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  TagBFP construct

<400>  178

Met Ser Glu Leu Ile Lys Glu Asn Met His Met Lys Leu Tyr Met Glu
1               5                   10                  15


Gly Thr Val Asp Asn His His Phe Lys Cys Thr Ser Glu Gly Glu Gly
            20                  25                  30


Lys Pro Tyr Glu Gly Thr Gln Thr Met Arg Ile Lys Val Val Glu Gly
        35                  40                  45


Gly Pro Leu Pro Phe Ala Phe Asp Ile Leu Ala Thr Ser Phe Leu Tyr
    50                  55                  60
```

```
Gly Ser Lys Thr Phe Ile Asn His Thr Gln Gly Ile Pro Asp Phe Phe
65                  70                  75                  80

Lys Gln Ser Phe Pro Glu Gly Phe Thr Trp Glu Arg Val Thr Thr Tyr
                85                  90                  95

Glu Asp Gly Gly Val Leu Thr Ala Thr Gln Asp Thr Ser Leu Gln Asp
            100                 105                 110

Gly Cys Leu Ile Tyr Asn Val Lys Ile Arg Gly Val Asn Phe Thr Ser
        115                 120                 125

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

Glu Thr Leu Tyr Pro Ala Asp Gly Gly Leu Glu Gly Arg Asn Asp Met
145                 150                 155                 160

Ala Leu Lys Leu Val Gly Gly Ser His Leu Ile Ala Asn Ile Lys Thr
                165                 170                 175

Thr Tyr Arg Ser Lys Lys Pro Ala Lys Asn Leu Lys Met Pro Gly Val
            180                 185                 190

Tyr Tyr Val Asp Tyr Arg Leu Glu Arg Ile Lys Glu Ala Asn Asn Glu
        195                 200                 205

Thr Tyr Val Glu Gln His Glu Val Ala Val Ala Arg Tyr Cys Asp Leu
    210                 215                 220

Pro Ser Lys Leu Gly His Lys Leu Asn
225                 230
```

<210> 179
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> V5 epitope tag

<400> 179

Lys Pro Ile Pro Asn Pro Leu Leu Gly Leu Asp Ser Thr
1   5   10

<210> 180
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> 2173 scFv domain

<400> 180

Glu Ile Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1   5   10   15

Ser Leu Arg Ile Ser Cys Lys Gly Ser Gly Phe Asn Ile Glu Asp Tyr
            20   25   30

Tyr Ile His Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35   40   45

Gly Arg Ile Asp Pro Glu Asn Asp Glu Thr Lys Tyr Gly Pro Ile Phe
    50   55   60

Gln Gly His Val Thr Ile Ser Ala Asp Thr Ser Ile Asn Thr Val Tyr
65   70   75   80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85   90   95

Ala Phe Arg Gly Gly Val Tyr Trp Gly Gln Gly Thr Thr Val Thr Val
            100   105   110

```
Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser Pro Asp Ser
    130                 135                 140


Leu Ala Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser
145                 150                 155                 160


Gln Ser Leu Leu Asp Ser Asp Gly Lys Thr Tyr Leu Asn Trp Leu Gln
                165                 170                 175


Gln Lys Pro Gly Gln Pro Pro Lys Arg Leu Ile Ser Leu Val Ser Lys
            180                 185                 190


Leu Asp Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
        195                 200                 205


Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val
    210                 215                 220


Tyr Tyr Cys Trp Gln Gly Thr His Phe Pro Gly Thr Phe Gly Gly Gly
225                 230                 235                 240


Thr Lys Val Glu Ile Lys
                245


<210>  181
<211>  241
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  26C8 scFv domain

<400>  181

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1               5                   10                  15
```

```
Thr Leu Ser Leu Thr Cys Thr Val Ser Asp Asn Ser Ile Ser Asn Tyr
            20                  25                  30

Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45

Ala Tyr Ile Tyr Tyr Ser Gly Thr Thr Asn Tyr Asn Pro Ser Leu Lys
    50                  55                  60

Ser Arg Val Thr Ile Ser Leu Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Gln Leu Ser Ser Val Thr Ala Ala Asp Ala Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Val Phe His Trp Gly Phe Ala Phe Asp Ile Trp Gly Gln Gly Thr
            100                 105                 110

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
    130                 135                 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145                 150                 155                 160

Arg Val Ser Asn Thr Tyr Leu Ala Trp Tyr Gln Gln Asn Pro Gly Gln
                165                 170                 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
            180                 185                 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
        195                 200                 205
```

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln
210 215 220

Tyr Gly Thr Ser Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

<210> 182
<211> 69
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 hinge and transmembrane domain

<400> 182

Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1 5 10 15

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
20 25 30

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile
35 40 45

Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val
50 55 60

Ile Thr Leu Tyr Cys
65

<210> 183
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> 4-1BB intracellular signaling domain

<400> 183

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1   5   10   15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
            20   25   30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
        35   40

<210> 184
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> CD3z intracellular signaling domain

<400> 184

Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1   5   10   15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
            20   25   30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
        35   40   45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
    50   55   60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65   70   75   80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 185
<211> 233
<212> PRT
<213> Artificial Sequence

<220>
<223> BFP domain

<400> 185

Met Ser Glu Leu Ile Lys Glu Asn Met His Met Lys Leu Tyr Met Glu
1 5 10 15

Gly Thr Val Asp Asn His His Phe Lys Cys Thr Ser Glu Gly Glu Gly
20 25 30

Lys Pro Tyr Glu Gly Thr Gln Thr Met Arg Ile Lys Val Val Glu Gly
35 40 45

Gly Pro Leu Pro Phe Ala Phe Asp Ile Leu Ala Thr Ser Phe Leu Tyr
50 55 60

Gly Ser Lys Thr Phe Ile Asn His Thr Gln Gly Ile Pro Asp Phe Phe
65 70 75 80

Lys Gln Ser Phe Pro Glu Gly Phe Thr Trp Glu Arg Val Thr Thr Tyr
85 90 95

Glu Asp Gly Gly Val Leu Thr Ala Thr Gln Asp Thr Ser Leu Gln Asp
100 105 110

Gly Cys Leu Ile Tyr Asn Val Lys Ile Arg Gly Val Asn Phe Thr Ser
115 120 125

```
Asn Gly Pro Val Met Gln Lys Lys Thr Leu Gly Trp Glu Ala Phe Thr
    130                 135                 140

Glu Thr Leu Tyr Pro Ala Asp Gly Gly Leu Glu Gly Arg Asn Asp Met
145                 150                 155                 160

Ala Leu Lys Leu Val Gly Gly Ser His Leu Ile Ala Asn Ile Lys Thr
                165                 170                 175

Thr Tyr Arg Ser Lys Lys Pro Ala Lys Asn Leu Lys Met Pro Gly Val
            180                 185                 190

Tyr Tyr Val Asp Tyr Arg Leu Glu Arg Ile Lys Glu Ala Asn Asn Glu
        195                 200                 205

Thr Tyr Val Glu Gln His Glu Val Ala Val Ala Arg Tyr Cys Asp Leu
    210                 215                 220

Pro Ser Lys Leu Gly His Lys Leu Asn
225                 230


<210>  186
<211>  22
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  P2A domain

<400>  186

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1               5                   10                  15

Glu Glu Asn Pro Gly Pro
            20
```

<210> 187
<211> 429
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)

<400> 187

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
130 135 140

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
145 150 155 160

```
Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
                165                 170                 175

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
            180                 185                 190

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
        195                 200                 205

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
    210                 215                 220

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
225                 230                 235                 240

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
                245                 250                 255

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
            260                 265                 270

Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
        275                 280                 285

Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
    290                 295                 300

Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
305                 310                 315                 320

Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
                325                 330                 335

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
            340                 345                 350
```

```
Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
        355                 360                 365

Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu
    370                 375                 380

Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
385                 390                 395                 400

His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
                405                 410                 415

Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425


<210>  188
<211>  428
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-1)-IL7R(316-459)-IL12Rb2(775-825)

<400>  188

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60
```

```
Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Trp Ile Ser
    130                 135                 140

Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
145                 150                 155                 160

Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
                165                 170                 175

His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
            180                 185                 190

Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
        195                 200                 205

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
    210                 215                 220

Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly
225                 230                 235                 240

Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
                245                 250                 255
```

```
Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
            260                 265                 270


Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
        275                 280                 285


Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
    290                 295                 300


Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
305                 310                 315                 320


Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
                325                 330                 335


Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
            340                 345                 350


Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
        355                 360                 365


Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn
    370                 375                 380


Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
385                 390                 395                 400


Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
                405                 410                 415


Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425


<210>  189
<211>  427
<212>  PRT
<213>  Artificial Sequence
```

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-2)-IL7R(316-459)-IL12Rb2(775-825)

<400> 189

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


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


Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
145                 150                 155                 160


Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
                165                 170                 175
```

```
Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
            180                 185                 190

Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
        195                 200                 205

Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
    210                 215                 220

Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe
225                 230                 235                 240

Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
                245                 250                 255

Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
            260                 265                 270

Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala
        275                 280                 285

Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
    290                 295                 300

Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
305                 310                 315                 320

Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
                325                 330                 335

Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
            340                 345                 350

Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
        355                 360                 365
```

```
Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro
    370                 375                 380


Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
385                 390                 395                 400


Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
                405                 410                 415


Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425


<210>  190
<211>  428
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-2+1)-IL7R(316-459)-IL12Rb2(775-825)

<400>  190

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80
```

```
Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

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

Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly
145                 150                 155                 160

Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
                165                 170                 175

His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
            180                 185                 190

Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
        195                 200                 205

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
    210                 215                 220

Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly
225                 230                 235                 240

Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
                245                 250                 255

Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
            260                 265                 270
```

```
Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
        275                 280                 285


Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
    290                 295                 300


Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
305                 310                 315                 320


Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
                325                 330                 335


Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
            340                 345                 350


Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
        355                 360                 365


Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn
    370                 375                 380


Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
385                 390                 395                 400


Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
                405                 410                 415


Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425


<210>  191
<211>  426
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-3)-IL7R(316-459)-IL12Rb2(775-825)
```

<400> 191

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ser Leu Val
    130                 135                 140

Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
145                 150                 155                 160

Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
                165                 170                 175

Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
            180                 185                 190
```

```
Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
        195                 200                 205

Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
    210                 215                 220

Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu
225                 230                 235                 240

Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu
                245                 250                 255

Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile
            260                 265                 270

Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly
        275                 280                 285

Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu
    290                 295                 300

Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu
305                 310                 315                 320

Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser
                325                 330                 335

Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
            340                 345                 350

Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
        355                 360                 365

Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala
    370                 375                 380
```

```
Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
385                 390                 395                 400


Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
                405                 410                 415


Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425


<210>  192
<211>  425
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-4)-IL7R(316-459)-IL12Rb2(775-825)

<400>  192

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95
```

```
Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Val Thr
    130                 135                 140

Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
145                 150                 155                 160

Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
                165                 170                 175

Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
            180                 185                 190

Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
        195                 200                 205

Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
    210                 215                 220

Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
225                 230                 235                 240

Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
                245                 250                 255

Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
            260                 265                 270

Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
        275                 280                 285
```

```
Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
    290                 295                 300

Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
305                 310                 315                 320

Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
                325                 330                 335

Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
            340                 345                 350

Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
        355                 360                 365

Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
    370                 375                 380

Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
385                 390                 395                 400

Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
                405                 410                 415

Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425
```

<210> 193
<211> 426
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-4+1)-IL7R(316-459)-IL12Rb2(775-825)

<400> 193

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

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

Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
145                 150                 155                 160

Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
                165                 170                 175

Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
            180                 185                 190

Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
        195                 200                 205
```

```
Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
    210                 215                 220

Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu
225                 230                 235                 240

Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu
                245                 250                 255

Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile
            260                 265                 270

Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly
        275                 280                 285

Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu
    290                 295                 300

Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu
305                 310                 315                 320

Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser
                325                 330                 335

Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
            340                 345                 350

Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
        355                 360                 365

Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala
    370                 375                 380

Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
385                 390                 395                 400
```

Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
405 410 415

Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
420 425

<210> 194
<211> 424
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-5)-IL7R(316-459)-IL12Rb2(775-825)

<400> 194

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

```
Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Thr Ala
    130                 135                 140


Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
145                 150                 155                 160


Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
                165                 170                 175


Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
            180                 185                 190


Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
        195                 200                 205


Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
    210                 215                 220


Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
225                 230                 235                 240


Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
                245                 250                 255


Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
            260                 265                 270


Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
        275                 280                 285


Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
    290                 295                 300
```

```
Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
305                 310                 315                 320


Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
                325                 330                 335


Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
            340                 345                 350


Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
        355                 360                 365


Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
    370                 375                 380


Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
385                 390                 395                 400


Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
                405                 410                 415


Ser Leu Glu Glu Leu Glu Pro Gln
            420


<210>  195
<211>  423
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-6)-IL7R(316-459)-IL12Rb2(775-825)

<400>  195

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30
```

```
Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Thr Ala Leu
    130                 135                 140

His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
145                 150                 155                 160

Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
                165                 170                 175

Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
            180                 185                 190

Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
        195                 200                 205

Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
    210                 215                 220
```

```
Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
225                 230                 235                 240

Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
                245                 250                 255

Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
            260                 265                 270

Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
        275                 280                 285

Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
    290                 295                 300

Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
305                 310                 315                 320

Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
                325                 330                 335

Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
            340                 345                 350

Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
        355                 360                 365

Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
    370                 375                 380

Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
385                 390                 395                 400

Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
                405                 410                 415
```

Leu Glu Glu Leu Glu Pro Gln
420

<210> 196
<211> 422
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-7)-IL7R(316-459)-IL12Rb2(775-825)

<400> 196

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

```
Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Leu His
    130                 135                 140

Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
145                 150                 155                 160

Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
                165                 170                 175

Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
            180                 185                 190

Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
        195                 200                 205

Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
    210                 215                 220

Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
225                 230                 235                 240

Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val
                245                 250                 255

Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser
            260                 265                 270

Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala
        275                 280                 285

Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu
    290                 295                 300

Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu
305                 310                 315                 320
```

Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly
325 330 335

Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser
340 345 350

Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
355 360 365

Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr
370 375 380

Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser
385 390 395 400

Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu
405 410 415

Glu Glu Leu Glu Pro Gln
420

<210> 197
<211> 421
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-8)-IL7R(316-459)-IL12Rb2(775-825)

<400> 197

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

```
Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

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

Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
145                 150                 155                 160

Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
                165                 170                 175

Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
            180                 185                 190

Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
        195                 200                 205

Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
    210                 215                 220

Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
225                 230                 235                 240
```

```
Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
                245                 250                 255

Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
            260                 265                 270

Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
        275                 280                 285

Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
    290                 295                 300

Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
305                 310                 315                 320

Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
                325                 330                 335

Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
            340                 345                 350

Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
        355                 360                 365

Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
    370                 375                 380

Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
385                 390                 395                 400

Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
                405                 410                 415

Glu Leu Glu Pro Gln
            420
```

<210> 198
<211> 420
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-9)-IL7R(316-459)-IL12Rb2(775-825)

<400> 198

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

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

```
Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
145                 150                 155                 160


Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
                165                 170                 175


Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
            180                 185                 190


Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
        195                 200                 205


Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
    210                 215                 220


Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln
225                 230                 235                 240


Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser
                245                 250                 255


Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly
            260                 265                 270


Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
        275                 280                 285


Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
    290                 295                 300


Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
305                 310                 315                 320


Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
                325                 330                 335
```

Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
340 345 350

Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
355 360 365

Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
370 375 380

Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
385 390 395 400

Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
405 410 415

Leu Glu Pro Gln
420

<210> 199
<211> 419
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-10)-IL7R(316-459)-IL12Rb2(775-825)

<400> 199

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

```
Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Val Leu
    130                 135                 140

Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
145                 150                 155                 160

Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
                165                 170                 175

Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
            180                 185                 190

Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
        195                 200                 205

Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
    210                 215                 220

Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
225                 230                 235                 240

Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
                245                 250                 255
```

```
Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
            260                 265                 270

Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
        275                 280                 285

Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
    290                 295                 300

Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
305                 310                 315                 320

Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
                325                 330                 335

Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
            340                 345                 350

Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
        355                 360                 365

Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
    370                 375                 380

Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
385                 390                 395                 400

Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
                405                 410                 415

Glu Pro Gln
```

<210> 200
<211> 418

<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-11)-IL7R(316-459)-IL12Rb2(775-825)

<400> 200

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Leu Gly
    130                 135                 140


Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
145                 150                 155                 160
```

```
His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
                165                 170                 175

His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
            180                 185                 190

Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
        195                 200                 205

Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala
    210                 215                 220

Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu
225                 230                 235                 240

Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn
                245                 250                 255

Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp
            260                 265                 270

Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro
        275                 280                 285

Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn
    290                 295                 300

Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn
305                 310                 315                 320

Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu
                325                 330                 335

Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn
            340                 345                 350
```

Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser
355 360 365

Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
370 375 380

Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
385 390 395 400

Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu
405 410 415

Pro Gln

<210> 201
<211> 417
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-12)-IL7R(316-459)-IL12Rb2(775-825)

<400> 201

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

```
Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Gly Leu
    130                 135                 140

Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
145                 150                 155                 160

Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
                165                 170                 175

Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
            180                 185                 190

Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
        195                 200                 205

Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg
    210                 215                 220

Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
225                 230                 235                 240

Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
                245                 250                 255

Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
            260                 265                 270
```

```
Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile
        275                 280                 285

Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
    290                 295                 300

Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
305                 310                 315                 320

Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
                325                 330                 335

Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
            340                 345                 350

Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp
        355                 360                 365

Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
    370                 375                 380

Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
385                 390                 395                 400

Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
                405                 410                 415

Gln
```

<210> 202
<211> 416
<212> PRT
<213> Artificial Sequence

<220>

<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-13)-IL7R(316-459)-IL12Rb2(775-825)

<400> 202

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Gly Leu Ser
    130                 135                 140


Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
145                 150                 155                 160


Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
                165                 170                 175
```

```
Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
            180                 185                 190

Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
        195                 200                 205

Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp
    210                 215                 220

Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
225                 230                 235                 240

Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
                245                 250                 255

Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
            260                 265                 270

Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
        275                 280                 285

Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
    290                 295                 300

His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
305                 310                 315                 320

Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
                325                 330                 335

Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
            340                 345                 350

Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro
        355                 360                 365
```

Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
370 375 380

Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
385 390 395 400

Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
405 410 415

<210> 203
<211> 415
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-14)-IL7R(316-459)-IL12Rb2(775-825)

<400> 203

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

```
Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Ser Ala
    130                 135                 140

Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
145                 150                 155                 160

Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
                165                 170                 175

Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
            180                 185                 190

Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
        195                 200                 205

Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu
    210                 215                 220

Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
225                 230                 235                 240

Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
                245                 250                 255

Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
            260                 265                 270

Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser
        275                 280                 285

Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
    290                 295                 300
```

```
Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
305                 310                 315                 320


Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
                325                 330                 335


Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
            340                 345                 350


Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys
        355                 360                 365


Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
    370                 375                 380


Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
385                 390                 395                 400


His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
                405                 410                 415


<210>  204
<211>  414
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-15)-IL7R(316-459)-IL12Rb2(775-825)

<400>  204

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30
```

```
Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ser Ala Val
    130                 135                 140

Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
145                 150                 155                 160

Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
                165                 170                 175

Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
            180                 185                 190

Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
        195                 200                 205

Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val
    210                 215                 220
```

```
Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
225                 230                 235                 240


Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
                245                 250                 255


Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
            260                 265                 270


Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
        275                 280                 285


Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
    290                 295                 300


Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
305                 310                 315                 320


Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
                325                 330                 335


Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
            340                 345                 350


Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro
        355                 360                 365


Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
    370                 375                 380


Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
385                 390                 395                 400


Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
                405                 410
```

<210> 205
<211> 413
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-16)-IL7R(316-459)-IL12Rb2(775-825)

<400> 205

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Val Leu
    130                 135                 140


Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
145                 150                 155                 160
```

```
Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
                165                 170                 175

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
            180                 185                 190

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
        195                 200                 205

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
    210                 215                 220

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
225                 230                 235                 240

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
                245                 250                 255

Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
            260                 265                 270

Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
        275                 280                 285

Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
    290                 295                 300

Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
305                 310                 315                 320

Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
                325                 330                 335

Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
            340                 345                 350
```

```
Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu
        355                 360                 365


Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
    370                 375                 380


His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
385                 390                 395                 400


Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
                405                 410


<210>  206
<211>  412
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-17)-IL7R(316-459)-IL12Rb2(775-825)

<400>  206

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80
```

```
Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Val Leu Gly
    130                 135                 140

Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
145                 150                 155                 160

His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
                165                 170                 175

Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
            180                 185                 190

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
        195                 200                 205

Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly
    210                 215                 220

Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
225                 230                 235                 240

Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
                245                 250                 255

Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
            260                 265                 270
```

```
Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
        275                 280                 285


Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
    290                 295                 300


Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
305                 310                 315                 320


Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
                325                 330                 335


Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
            340                 345                 350


Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn
        355                 360                 365


Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
    370                 375                 380


Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
385                 390                 395                 400


Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
                405                 410


<210>  207
<211>  411
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N-18)-IL7R(316-459)-IL12Rb2(775-825)

<400>  207

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15
```

```
His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Leu Gly Leu
    130                 135                 140

Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
145                 150                 155                 160

Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
                165                 170                 175

Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
            180                 185                 190

Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
        195                 200                 205
```

```
Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe
    210                 215                 220

Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
225                 230                 235                 240

Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
                245                 250                 255

Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala
            260                 265                 270

Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
        275                 280                 285

Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
    290                 295                 300

Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
305                 310                 315                 320

Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
                325                 330                 335

Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
            340                 345                 350

Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro
        355                 360                 365

Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
    370                 375                 380

Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
385                 390                 395                 400
```

Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
405 410

<210> 208
<211> 430
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+1)-IL7R(316-459)-IL12Rb2(775-825)

<400> 208

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

```
Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu
    130                 135                 140

Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val
145                 150                 155                 160

Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
                165                 170                 175

Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
            180                 185                 190

Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
        195                 200                 205

Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
    210                 215                 220

Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val
225                 230                 235                 240

Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
                245                 250                 255

Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
            260                 265                 270

Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
        275                 280                 285

Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
    290                 295                 300

Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
305                 310                 315                 320
```

Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
325 330 335

Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
340 345 350

Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
355 360 365

Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro
370 375 380

Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
385 390 395 400

Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
405 410 415

Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
420 425 430

<210> 209
<211> 431
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+2)-IL7R(316-459)-IL12Rb2(775-825)

<400> 209

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

```
Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val
    130                 135                 140

Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala
145                 150                 155                 160

Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
                165                 170                 175

Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
            180                 185                 190

Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
        195                 200                 205

Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
    210                 215                 220

Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu
225                 230                 235                 240
```

```
Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
                245                 250                 255

Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
            260                 265                 270

Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
        275                 280                 285

Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser
    290                 295                 300

Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
305                 310                 315                 320

Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
                325                 330                 335

Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
            340                 345                 350

Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
        355                 360                 365

Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys
    370                 375                 380

Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
385                 390                 395                 400

Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
                405                 410                 415

His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
            420                 425                 430
```

<210> 210
<211> 432
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+3)-IL7R(316-459)-IL12Rb2(775-825)

<400> 210

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu
130 135 140

```
Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser
145                 150                 155                 160

Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
                165                 170                 175

Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
            180                 185                 190

Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
        195                 200                 205

Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
    210                 215                 220

Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp
225                 230                 235                 240

Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
                245                 250                 255

Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
            260                 265                 270

Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
        275                 280                 285

Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
    290                 295                 300

Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
305                 310                 315                 320

His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
                325                 330                 335
```

Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
340 345 350

Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
355 360 365

Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro
370 375 380

Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
385 390 395 400

Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
405 410 415

Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
420 425 430

<210> 211
<211> 433
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+4)-IL7R(316-459)-IL12Rb2(775-825)

<400> 211

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

```
Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile
    130                 135                 140

Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu
145                 150                 155                 160

Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
                165                 170                 175

Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
            180                 185                 190

Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
        195                 200                 205

Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
    210                 215                 220

Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg
225                 230                 235                 240

Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
                245                 250                 255
```

```
Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
            260                 265                 270

Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
        275                 280                 285

Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile
    290                 295                 300

Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
305                 310                 315                 320

Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
                325                 330                 335

Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
            340                 345                 350

Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
        355                 360                 365

Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp
    370                 375                 380

Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
385                 390                 395                 400

Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
                405                 410                 415

Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
            420                 425                 430

Gln
```

<210> 212
<211> 434
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+5)-IL7R(316-459)-IL12Rb2(775-825)

<400> 212

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                  10                  15


His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30


Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45


Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60


Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80


Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95


Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110


Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125


Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu
    130                 135                 140
```

```
Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly
145                 150                 155                 160


Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
                165                 170                 175


His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
            180                 185                 190


His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
        195                 200                 205


Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
    210                 215                 220


Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala
225                 230                 235                 240


Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu
                245                 250                 255


Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn
            260                 265                 270


Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp
        275                 280                 285


Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro
    290                 295                 300


Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn
305                 310                 315                 320


Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn
                325                 330                 335
```

Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu
340 345 350

Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn
355 360 365

Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser
370 375 380

Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
385 390 395 400

Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
405 410 415

Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu
420 425 430

Pro Gln

<210> 213
<211> 435
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+6)-IL7R(316-459)-IL12Rb2(775-825)

<400> 213

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

```
Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu
    130                 135                 140

Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu
145                 150                 155                 160

Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
                165                 170                 175

Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
            180                 185                 190

Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
        195                 200                 205

Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
    210                 215                 220

Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
225                 230                 235                 240
```

```
Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
                245                 250                 255

Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
            260                 265                 270

Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
        275                 280                 285

Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
    290                 295                 300

Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
305                 310                 315                 320

Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
                325                 330                 335

Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
            340                 345                 350

Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
        355                 360                 365

Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
    370                 375                 380

Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
385                 390                 395                 400

Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
                405                 410                 415

Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
            420                 425                 430
```

Glu Pro Gln
435

<210> 214
<211> 436
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)

<400> 214

Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
20 25 30

Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
35 40 45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
50 55 60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65 70 75 80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
85 90 95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
100 105 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
115 120 125

```
Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val
    130                 135                 140

Leu Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val
145                 150                 155                 160

Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
                165                 170                 175

Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
            180                 185                 190

Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
        195                 200                 205

Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
    210                 215                 220

Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
225                 230                 235                 240

Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln
                245                 250                 255

Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser
            260                 265                 270

Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly
        275                 280                 285

Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
    290                 295                 300

Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
305                 310                 315                 320
```

```
Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
                325                 330                 335

Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
            340                 345                 350

Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
        355                 360                 365

Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
    370                 375                 380

Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
385                 390                 395                 400

Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
                405                 410                 415

Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
            420                 425                 430

Leu Glu Pro Gln
        435
```

<210> 215
<211> 437
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 SS-FKBP(F36V)-TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)

<400> 215

```
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15

His Ala Ala Arg Pro Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly
            20                  25                  30
```

```
Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr
        35                  40                  45

Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg
    50                  55                  60

Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly
65                  70                  75                  80

Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu
                85                  90                  95

Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile
            100                 105                 110

Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu
        115                 120                 125

Glu Ser Asp Pro Thr Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu
    130                 135                 140

Val Leu Leu Ile Leu Val Leu Ile Ser Leu Val Thr Ala Leu His Leu
145                 150                 155                 160

Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
                165                 170                 175

Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
            180                 185                 190

Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
        195                 200                 205

Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
    210                 215                 220
```

```
Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
225                 230                 235                 240

Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
                245                 250                 255

Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
            260                 265                 270

Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
        275                 280                 285

Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
    290                 295                 300

Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
305                 310                 315                 320

Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
                325                 330                 335

Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
            340                 345                 350

Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
        355                 360                 365

Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
    370                 375                 380

Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
385                 390                 395                 400

Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
                405                 410                 415
```

```
Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
            420                 425                 430


Glu Leu Glu Pro Gln
        435


<210>  216
<211>  53
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  dimerization domain

<400>  216

Met Leu Gln Met Ala Gly Gln Cys Ser Gln Asn Glu Tyr Phe Asp Ser
1               5                   10                  15


Leu Leu His Ala Cys Ile Pro Cys Gln Leu Arg Cys Ser Ser Asn Thr
            20                  25                  30


Pro Pro Leu Thr Cys Gln Arg Tyr Cys Asn Ala Ser Val Thr Asn Ser
        35                  40                  45


Val Lys Gly Thr Asn
    50


<210>  217
<211>  170
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  dimerization domain

<400>  217

Met Gln Ile Pro Gln Ala Pro Trp Pro Val Val Trp Ala Val Leu Gln
1               5                   10                  15
```

```
Leu Gly Trp Arg Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp
            20                  25                  30

Asn Pro Pro Thr Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp
        35                  40                  45

Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val
    50                  55                  60

Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala
65                  70                  75                  80

Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg
                85                  90                  95

Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg
            100                 105                 110

Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu
        115                 120                 125

Ala Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val
    130                 135                 140

Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro
145                 150                 155                 160

Arg Pro Ala Gly Gln Phe Gln Thr Leu Val
                165                 170
```

<210> 218
<211> 108
<212> PRT
<213> Artificial Sequence

<220>

<223> dimerization domain

<400> 218

Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro
1 5 10 15

Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
20 25 30

Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
35 40 45

Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
50 55 60

Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
65 70 75 80

Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
85 90 95

Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser
100 105

<210> 219
<211> 102
<212> PRT
<213> Artificial Sequence

<220>
<223> exemplary tyrosine kinase activating domain

<400> 219

Ser Glu Pro Val Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile
1 5 10 15

Leu Thr Leu Ser Leu Ile Leu Val Val Ile Leu Val Leu Leu Thr Val
20 25 30

```
Leu Ala Leu Leu Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro
        35                  40                  45


Gly Ile Pro Ser Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His
    50                  55                  60


Lys Gly Asn Phe Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp
65                  70                  75                  80


Trp Ser Pro Cys Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu
                85                  90                  95


Val Leu Ser Glu Arg Cys
            100


<210>  220
<211>  348
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  exemplary tyrosine kinase activating domain

<400>  220

Gly Leu Glu Gly Cys Pro Thr Asn Gly Pro Lys Ile Pro Ser Ile Ala
1               5                   10                  15


Thr Gly Met Val Gly Ala Leu Leu Leu Leu Leu Val Val Ala Leu Gly
            20                  25                  30


Ile Gly Leu Phe Met Arg Arg Arg His Ile Val Arg Lys Arg Thr Leu
        35                  40                  45


Arg Arg Leu Leu Gln Glu Arg Glu Leu Val Glu Pro Leu Thr Pro Ser
    50                  55                  60
```

```
Gly Glu Ala Pro Asn Gln Ala Leu Leu Arg Ile Leu Lys Glu Thr Glu
65                  70                  75                  80

Phe Lys Lys Ile Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr
                85                  90                  95

Lys Gly Leu Trp Ile Pro Glu Gly Glu Lys Val Lys Ile Pro Val Ala
            100                 105                 110

Ile Lys Glu Leu Arg Glu Ala Thr Ser Pro Lys Ala Asn Lys Glu Ile
        115                 120                 125

Leu Asp Glu Ala Tyr Val Met Ala Ser Val Asp Asn Pro His Val Cys
    130                 135                 140

Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Ile Thr Gln
145                 150                 155                 160

Leu Met Pro Phe Gly Cys Leu Leu Asp Tyr Val Arg Glu His Lys Asp
                165                 170                 175

Asn Ile Gly Ser Gln Tyr Leu Leu Asn Trp Cys Val Gln Ile Ala Lys
            180                 185                 190

Gly Met Asn Tyr Leu Glu Asp Arg Arg Leu Val His Arg Asp Leu Ala
        195                 200                 205

Ala Arg Asn Val Leu Val Lys Thr Pro Gln His Val Lys Ile Thr Asp
    210                 215                 220

Phe Gly Leu Ala Lys Leu Leu Gly Ala Glu Glu Lys Glu Tyr His Ala
225                 230                 235                 240

Glu Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu
                245                 250                 255
```

```
His Arg Ile Tyr Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr
            260                 265                 270


Val Trp Glu Leu Met Thr Phe Gly Ser Lys Pro Tyr Asp Gly Ile Pro
        275                 280                 285


Ala Ser Glu Ile Ser Ser Ile Leu Glu Lys Gly Glu Arg Leu Pro Gln
    290                 295                 300


Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp
305                 310                 315                 320


Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Arg Glu Leu Ile Ile Glu
                325                 330                 335


Phe Ser Lys Met Ala Arg Asp Pro Gln Arg Tyr Leu
            340                 345


<210>  221
<211>  219
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  exemplary tyrosine effector domain

<400>  221

Val Thr Gln Leu Leu Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser
1               5                   10                  15


Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr
            20                  25                  30


Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Val
        35                  40                  45


Tyr Phe Thr Tyr Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu Gly Val
    50                  55                  60
```

```
Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser
65                  70                  75                  80

Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu
                85                  90                  95

Leu Phe Ser Pro Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser Thr Ala
            100                 105                 110

Pro Gly Gly Ser Gly Ala Gly Glu Glu Arg Met Pro Pro Ser Leu Gln
        115                 120                 125

Glu Arg Val Pro Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro Pro Thr
    130                 135                 140

Pro Gly Val Pro Asp Leu Val Asp Phe Gln Pro Pro Pro Glu Leu Val
145                 150                 155                 160

Leu Arg Glu Ala Gly Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly
                165                 170                 175

Val Ser Phe Pro Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala
            180                 185                 190

Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln
        195                 200                 205

Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
    210                 215
```

<210> 222
<211> 231
<212> PRT
<213> Artificial Sequence

<220>

<223> exemplary tyrosine effector domain

<400> 222

```
Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr Asp Ser
1               5                  10                  15


Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp Val Val
            20                  25                  30


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


Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala Thr Ser Asn
    50                  55                  60


Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser Cys Pro
65                  70                  75                  80


Ile Lys Glu Asp Ser Phe Leu Gln Arg Tyr Ser Ser Asp Pro Thr Gly
                85                  90                  95


Ala Leu Thr Glu Asp Ser Ile Asp Asp Thr Phe Leu Pro Val Pro Glu
            100                 105                 110


Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser Val Gln Asn
        115                 120                 125


Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser Arg Asp Pro
    130                 135                 140


His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro Glu Tyr Leu
145                 150                 155                 160


Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp Ser Pro Ala
                165                 170                 175
```

His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro Asp
180 185 190

Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile Phe
195 200 205

Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro Gln
210 215 220

Ser Ser Glu Phe Ile Gly Ala
225 230

<210> 223
<211> 156
<212> PRT
<213> Artificial Sequence

<220>
<223> exemplary tyrosine effector domain

<400> 223

Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp Asp Phe
1 5 10 15

Asp Ser Asp Tyr Glu Asn Pro Asp Glu His Ser Asp Ser Glu Met Tyr
20 25 30

Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro Pro Pro
35 40 45

Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe Ala Arg
50 55 60

Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro Pro Phe
65 70 75 80

Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys Ala Arg
85 90 95

```
Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro Gln Val
            100                 105                 110


Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr Val Val
        115                 120                 125


Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu Ser Ser
    130                 135                 140


Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
145                 150                 155


<210>  224
<211>  15
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  peptide linker

<400>  224

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1               5                   10                  15


<210>  225
<211>  380
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V)-EpoR(237-508;L241G,L242P)

<400>  225

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30
```

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
    210                 215                 220
```

```
Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
225                 230                 235                 240


Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
                245                 250                 255


Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
            260                 265                 270


Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
        275                 280                 285


Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
    290                 295                 300


Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
305                 310                 315                 320


Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
                325                 330                 335


Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
            340                 345                 350


Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala
        355                 360                 365


Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser
    370                 375                 380


<210>  226
<211>  450
<212>  PRT
<213>  Artificial Sequence

<220
```

<223> EpoR(273-508)-FKBP(F36V)-FKBP(F36V)

<400> 226

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
1               5                  10                  15


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
            20                  25                  30


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
        35                  40                  45


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
    50                  55                  60


Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
65                  70                  75                  80


Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
                85                  90                  95


Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
            100                 105                 110


Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
        115                 120                 125


Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
    130                 135                 140


Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
145                 150                 155                 160


Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
                165                 170                 175
```

```
Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
            180                 185                 190


Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
        195                 200                 205


Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala
    210                 215                 220


Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser Met Gly Val Gln
225                 230                 235                 240


Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly
                245                 250                 255


Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp Gly Lys Lys
            260                 265                 270


Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly
        275                 280                 285


Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser
    290                 295                 300


Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly
305                 310                 315                 320


Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe
                325                 330                 335


Asp Val Glu Leu Leu Lys Leu Gly Val Gln Val Glu Thr Ile Ser Pro
            340                 345                 350


Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His
        355                 360                 365
```

```
Tyr Thr Gly Met Leu Glu Asp Gly Lys Lys Val Asp Ser Ser Arg Asp
    370                 375                 380

Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg
385                 390                 395                 400

Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Arg Ala Lys
                405                 410                 415

Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly
            420                 425                 430

Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Lys
        435                 440                 445

Leu Glu
    450
```

<210> 227
<211> 450
<212> PRT
<213> Artificial Sequence

<220
<223> EpoR(273-508)-FKBP(E31G,36V,R71G,K105E)-FKBP(E31G,36V,R71G,K105E)

<400> 227

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
1               5                   10                  15

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
            20                  25                  30

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
        35                  40                  45

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
    50                  55                  60
```

```
Arg Cys Trp Gly Thr Met Gln Ala Val Glu Pro Gly Thr Asp Asp Glu
65                  70                  75                  80

Gly Pro Leu Leu Glu Pro Val Gly Ser Glu His Ala Gln Asp Thr Tyr
                85                  90                  95

Leu Val Leu Asp Lys Trp Leu Leu Pro Arg Asn Pro Pro Ser Glu Asp
            100                 105                 110

Leu Pro Gly Pro Gly Gly Ser Val Asp Ile Val Ala Met Asp Glu Gly
        115                 120                 125

Ser Glu Ala Ser Ser Cys Ser Ser Ala Leu Ala Ser Lys Pro Ser Pro
    130                 135                 140

Glu Gly Ala Ser Ala Ala Ser Phe Glu Tyr Thr Ile Leu Asp Pro Ser
145                 150                 155                 160

Ser Gln Leu Leu Arg Pro Trp Thr Leu Cys Pro Glu Leu Pro Pro Thr
                165                 170                 175

Pro Pro His Leu Lys Tyr Leu Tyr Leu Val Val Ser Asp Ser Gly Ile
            180                 185                 190

Ser Thr Asp Tyr Ser Ser Gly Asp Ser Gln Gly Ala Gln Gly Gly Leu
        195                 200                 205

Ser Asp Gly Pro Tyr Ser Asn Pro Tyr Glu Asn Ser Leu Ile Pro Ala
    210                 215                 220

Ala Glu Pro Leu Pro Pro Ser Tyr Val Ala Cys Ser Met Gly Val Gln
225                 230                 235                 240

Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly
                245                 250                 255
```

```
Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Gly Asp Gly Lys Lys
            260                 265                 270

Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe Met Leu Gly
        275                 280                 285

Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala Gln Met Ser
    290                 295                 300

Val Gly Gln Gly Ala Lys Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly
305                 310                 315                 320

Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr Leu Val Phe
                325                 330                 335

Asp Val Glu Leu Leu Glu Leu Gly Val Gln Val Glu Thr Ile Ser Pro
            340                 345                 350

Gly Asp Gly Arg Thr Phe Pro Lys Arg Gly Gln Thr Cys Val Val His
        355                 360                 365

Tyr Thr Gly Met Leu Gly Asp Gly Lys Lys Val Asp Ser Ser Arg Asp
    370                 375                 380

Arg Asn Lys Pro Phe Lys Phe Met Leu Gly Lys Gln Glu Val Ile Arg
385                 390                 395                 400

Gly Trp Glu Glu Gly Val Ala Gln Met Ser Val Gly Gln Gly Ala Lys
                405                 410                 415

Leu Thr Ile Ser Pro Asp Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly
            420                 425                 430

Ile Ile Pro Pro His Ala Thr Leu Val Phe Asp Val Glu Leu Leu Glu
        435                 440                 445
```

Leu Glu
450

<210> 228
<211> 496
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-EpoR(237-338;L241G,L242P)-GHR(353-638)

<400> 228

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
115 120 125

```
Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Pro Asp Glu Lys Thr Glu Glu Ser Asp Thr Asp Arg Leu Leu
    210                 215                 220

Ser Ser Asp His Glu Lys Ser His Ser Asn Leu Gly Val Lys Asp Gly
225                 230                 235                 240

Asp Ser Gly Arg Thr Ser Cys Cys Glu Pro Asp Ile Leu Glu Thr Asp
                245                 250                 255

Phe Asn Ala Asn Asp Ile His Glu Gly Thr Ser Glu Val Ala Gln Pro
            260                 265                 270

Gln Arg Leu Lys Gly Glu Ala Asp Leu Leu Cys Leu Asp Gln Lys Asn
        275                 280                 285

Gln Asn Asn Ser Pro Tyr His Asp Ala Cys Pro Ala Thr Gln Gln Pro
    290                 295                 300

Ser Val Ile Gln Ala Glu Lys Asn Lys Pro Gln Pro Leu Pro Thr Glu
305                 310                 315                 320
```

```
Gly Ala Glu Ser Thr His Gln Ala Ala His Ile Gln Leu Ser Asn Pro
                325                 330                 335

Ser Ser Leu Ser Asn Ile Asp Phe Tyr Ala Gln Val Ser Asp Ile Thr
            340                 345                 350

Pro Ala Gly Ser Val Val Leu Ser Pro Gly Gln Lys Asn Lys Ala Gly
        355                 360                 365

Met Ser Gln Cys Asp Met His Pro Glu Met Val Ser Leu Cys Gln Glu
    370                 375                 380

Asn Phe Leu Met Asp Asn Ala Tyr Phe Cys Glu Ala Asp Ala Lys Lys
385                 390                 395                 400

Cys Ile Pro Val Ala Pro His Ile Lys Val Glu Ser His Ile Gln Pro
                405                 410                 415

Ser Leu Asn Gln Glu Asp Ile Tyr Ile Thr Thr Glu Ser Leu Thr Thr
            420                 425                 430

Ala Ala Gly Arg Pro Gly Thr Gly Glu His Val Pro Gly Ser Glu Met
        435                 440                 445

Pro Val Pro Asp Tyr Thr Ser Ile His Ile Val Gln Ser Pro Gln Gly
    450                 455                 460

Leu Ile Leu Asn Ala Thr Ala Leu Pro Leu Pro Asp Lys Glu Phe Leu
465                 470                 475                 480

Ser Ser Cys Gly Tyr Val Ser Thr Asp Gln Leu Asn Lys Ile Met Pro
                485                 490                 495
```

<210> 229
<211> 429
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL2Rb(333-551)

<400> 229

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110


Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175
```

```
Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Val Thr Gln Leu Leu Leu Gln Gln Asp Lys Val Pro Glu Pro
    210                 215                 220

Ala Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln
225                 230                 235                 240

Gly Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys
                245                 250                 255

Gln Val Tyr Phe Thr Tyr Asp Pro Tyr Ser Glu Glu Asp Pro Asp Glu
            260                 265                 270

Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro
        275                 280                 285

Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp
    290                 295                 300

Leu Leu Leu Phe Ser Pro Ser Leu Leu Gly Gly Pro Ser Pro Pro Ser
305                 310                 315                 320

Thr Ala Pro Gly Gly Ser Gly Ala Gly Glu Glu Arg Met Pro Pro Ser
                325                 330                 335

Leu Gln Glu Arg Val Pro Arg Asp Trp Asp Pro Gln Pro Leu Gly Pro
            340                 345                 350

Pro Thr Pro Gly Val Pro Asp Leu Val Asp Phe Gln Pro Pro Pro Glu
        355                 360                 365
```

```
Leu Val Leu Arg Glu Ala Gly Glu Glu Val Pro Asp Ala Gly Pro Arg
    370                 375                 380

Glu Gly Val Ser Phe Pro Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe
385                 390                 395                 400

Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser
                405                 410                 415

Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
            420                 425
```

<210> 230
<211> 354
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)

<400> 230

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80
```

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
    210                 215                 220

Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
225                 230                 235                 240

Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
                245                 250                 255

Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
            260                 265                 270
```

```
Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
        275                 280                 285


Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
    290                 295                 300


Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
305                 310                 315                 320


Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
                325                 330                 335


Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
            340                 345                 350


Asn Gln



<210>  231
<211>  359
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(714-862)

<400>  231

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60
```

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Val Thr Pro Val Phe Arg His Pro Pro Cys Ser Asn Trp Pro
    210                 215                 220

Gln Arg Glu Lys Gly Ile Gln Gly His Gln Ala Ser Glu Lys Asp Met
225                 230                 235                 240

Met His Ser Ala Ser Ser Pro Pro Pro Pro Arg Ala Leu Gln Ala Glu
                245                 250                 255
```

```
Ser Arg Gln Leu Val Asp Leu Tyr Lys Val Leu Glu Ser Arg Gly Ser
            260                 265                 270


Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
        275                 280                 285


Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
    290                 295                 300


Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu
305                 310                 315                 320


Pro Gln His Ile Ser Leu Ser Val Phe Pro Ser Ser Ser Leu His Pro
                325                 330                 335


Leu Thr Phe Ser Cys Gly Asp Lys Leu Thr Leu Asp Gln Leu Lys Met
            340                 345                 350


Arg Cys Asp Ser Leu Met Leu
        355


<210>  232
<211>  261
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL12Rb2(775-825)

<400>  232

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30
```

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
    210                 215                 220
```

Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
225 230 235 240

Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
245 250 255

Glu Leu Glu Pro Gln
260

<210> 233
<211> 427
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL21R(322-538)

<400> 233

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

```
Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr Glu Leu Gln
    210                 215                 220

Glu Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys Pro Ser Phe
225                 230                 235                 240

Trp Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser Glu Glu Arg
                245                 250                 255

Asp Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr Val Leu Asp
            260                 265                 270

Ala Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp Asp Gly Tyr
        275                 280                 285

Pro Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro Gly Leu Glu
    290                 295                 300
```

```
Asp Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys Gly Cys Val
305                 310                 315                 320


Ser Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser Leu Leu Asp
                325                 330                 335


Arg Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala Gly Gly Leu
            340                 345                 350


Pro Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser Glu Ala Gly
        355                 360                 365


Ser Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser Gly Phe Val
    370                 375                 380


Gly Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr Ser Pro Gly
385                 390                 395                 400


Asp Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Ile Pro
                405                 410                 415


Pro Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser
            420                 425


<210>  234
<211>  416
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR2(310-515)

<400>  234

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15
```

```
Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205
```

```
Arg Cys Lys Lys Lys Val Trp Asp Tyr Asn Tyr Asp Asp Glu Ser Asp
    210                 215                 220

Ser Asp Thr Glu Ala Ala Pro Arg Thr Ser Gly Gly Gly Tyr Thr Met
225                 230                 235                 240

His Gly Leu Thr Val Arg Pro Leu Gly Gln Ala Ser Ala Thr Ser Thr
                245                 250                 255

Glu Ser Gln Leu Ile Asp Pro Glu Ser Glu Glu Glu Pro Asp Leu Pro
            260                 265                 270

Glu Val Asp Val Glu Leu Pro Thr Met Pro Lys Asp Ser Pro Gln Gln
        275                 280                 285

Leu Glu Leu Leu Ser Gly Pro Cys Glu Arg Arg Lys Ser Pro Leu Gln
    290                 295                 300

Asp Pro Phe Pro Glu Glu Asp Tyr Ser Ser Thr Glu Gly Ser Gly Gly
305                 310                 315                 320

Arg Ile Thr Phe Asn Val Asp Leu Asn Ser Val Phe Leu Arg Val Leu
                325                 330                 335

Asp Asp Glu Asp Ser Asp Asp Leu Glu Ala Pro Leu Met Leu Ser Ser
            340                 345                 350

His Leu Glu Glu Met Val Asp Pro Glu Asp Pro Asp Asn Val Gln Ser
        355                 360                 365

Asn His Leu Leu Ala Ser Gly Glu Gly Thr Gln Pro Thr Phe Pro Ser
    370                 375                 380

Pro Ser Ser Glu Gly Leu Trp Ser Glu Asp Ala Pro Ser Asp Gln Ser
385                 390                 395                 400
```

Asp Thr Ser Glu Ser Asp Val Asp Leu Gly Asp Gly Tyr Ile Met Arg
405 410 415

<210> 235
<211> 431
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-EpoR(237-338;L241G,L242P)-IFNAR1(300-520)

<400> 235

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
115 120 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
130 135 140

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Arg Gly Val Arg Pro Thr Pro Arg Val Arg Ala Pro Ala Thr
    210                 215                 220

Gln Gln Thr Arg Trp Lys Lys Asp Leu Ala Glu Asp Glu Glu Glu Glu
225                 230                 235                 240

Asp Glu Glu Asp Thr Glu Asp Gly Val Ser Phe Gln Pro Tyr Ile Glu
                245                 250                 255

Pro Pro Ser Phe Leu Gly Gln Glu His Gln Ala Pro Gly His Ser Glu
            260                 265                 270

Ala Gly Gly Val Asp Ser Gly Arg Pro Arg Ala Pro Leu Val Pro Ser
        275                 280                 285

Glu Gly Ser Ser Ala Trp Asp Ser Ser Asp Arg Ser Trp Ala Ser Thr
    290                 295                 300

Val Asp Ser Ser Trp Asp Arg Ala Gly Ser Ser Gly Tyr Leu Ala Glu
305                 310                 315                 320

Lys Gly Pro Gly Gln Gly Pro Gly Gly Asp Gly His Gln Glu Ser Leu
                325                 330                 335
```

```
Pro Pro Pro Glu Phe Ser Lys Asp Ser Gly Phe Leu Glu Glu Leu Pro
            340                 345                 350

Glu Asp Asn Leu Ser Ser Trp Ala Thr Trp Gly Thr Leu Pro Pro Glu
        355                 360                 365

Pro Asn Leu Val Pro Gly Gly Pro Pro Val Ser Leu Gln Thr Leu Thr
    370                 375                 380

Phe Cys Trp Glu Ser Ser Pro Glu Glu Glu Glu Glu Ala Arg Glu Ser
385                 390                 395                 400

Glu Ile Glu Asp Ser Asp Ala Gly Ser Trp Gly Ala Glu Ser Thr Gln
                405                 410                 415

Arg Thr Glu Asp Arg Gly Arg Thr Leu Gly His Tyr Met Ala Arg
            420                 425                 430


<210>  236
<211>  413
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)-muEpoR(236-337;L264G,L265P)-muIL2Rb(337-539)

<400>  236

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45
```

```
Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Ala
            100                 105                 110

Ser Leu Leu Thr Ala Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Leu Ile Ser Leu Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Thr Leu Gln Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Leu Gln Arg Asp Gly Cys Leu Trp Trp Ser Pro Gly
            180                 185                 190

Ser Ser Phe Pro Glu Asp Pro Pro Ala His Leu Glu Val Leu Ser Glu
        195                 200                 205

Pro Arg Ala Val Gln Leu Leu Leu Leu Gln Lys Asp Ser Ala Pro Leu
    210                 215                 220

Pro Ser Pro Ser Gly His Ser Gln Ala Ser Cys Phe Thr Asn Gln Gly
225                 230                 235                 240
```

```
Tyr Phe Phe Phe His Leu Pro Asn Ala Leu Glu Ile Glu Ser Cys Gln
                245                 250                 255

Val Tyr Phe Thr Tyr Asp Pro Cys Val Glu Glu Glu Val Glu Glu Asp
            260                 265                 270

Gly Ser Arg Leu Pro Glu Gly Ser Pro His Pro Pro Leu Leu Pro Leu
        275                 280                 285

Ala Gly Glu Gln Asp Asp Tyr Cys Ala Phe Pro Pro Arg Asp Asp Leu
    290                 295                 300

Leu Leu Phe Ser Pro Ser Leu Ser Thr Pro Asn Thr Ala Tyr Gly Gly
305                 310                 315                 320

Ser Arg Ala Pro Glu Glu Arg Ser Pro Leu Ser Leu His Glu Gly Leu
                325                 330                 335

Pro Ser Leu Ala Ser Arg Asp Leu Met Gly Leu Gln Arg Pro Leu Glu
            340                 345                 350

Arg Met Pro Glu Gly Asp Gly Glu Gly Leu Ser Ala Asn Ser Ser Gly
        355                 360                 365

Glu Gln Ala Ser Val Pro Glu Gly Asn Leu His Gly Gln Asp Gln Asp
    370                 375                 380

Arg Gly Gln Gly Pro Ile Leu Thr Leu Asn Thr Asp Ala Tyr Leu Ser
385                 390                 395                 400

Leu Gln Glu Leu Gln Ala Gln Asp Ser Val His Leu Ile
                405                 410
```

<210> 237
<211> 354
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-muEpoR(236-337;L264G,L265P)-muIL7R(316-459)

<400> 237

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Ala
            100                 105                 110


Ser Leu Leu Thr Ala Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Leu Ile Ser Leu Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Thr Leu Gln Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175
```

```
Gln Leu Trp Leu Leu Gln Arg Asp Gly Cys Leu Trp Trp Ser Pro Gly
            180                 185                 190

Ser Ser Phe Pro Glu Asp Pro Pro Ala His Leu Glu Val Leu Ser Glu
        195                 200                 205

Pro Arg Ala Arg Asp Glu Val Glu Ser Phe Leu Pro Asn Asp Leu Pro
    210                 215                 220

Ala Gln Pro Glu Glu Leu Glu Thr Gln Gly His Arg Ala Ala Val His
225                 230                 235                 240

Ser Ala Asn Arg Ser Pro Glu Thr Ser Val Ser Pro Pro Glu Thr Val
                245                 250                 255

Arg Arg Glu Ser Pro Leu Arg Cys Leu Ala Arg Asn Leu Ser Thr Cys
            260                 265                 270

Asn Ala Pro Pro Leu Leu Ser Ser Arg Ser Pro Asp Tyr Arg Asp Gly
        275                 280                 285

Asp Arg Asn Arg Pro Pro Val Tyr Gln Asp Leu Leu Pro Asn Ser Gly
    290                 295                 300

Asn Thr Asn Val Pro Val Pro Val Pro Gln Pro Leu Pro Phe Gln Ser
305                 310                 315                 320

Gly Ile Leu Ile Pro Val Ser Gln Arg Gln Pro Ile Ser Thr Ser Ser
                325                 330                 335

Val Leu Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
            340                 345                 350

Asn Lys
```

<210> 238
<211> 405
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-EpoR(237-338;L241G,L242P)-IL7R(316-459)-IL12Rb2(775-825)

<400> 238

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
115 120 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
130 135 140

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
    210                 215                 220


Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
225                 230                 235                 240


Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
                245                 250                 255


Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
            260                 265                 270


Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
        275                 280                 285


Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
    290                 295                 300


Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
305                 310                 315                 320


Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
                325                 330                 335
```

Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
340 345 350

Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
355 360 365

Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
370 375 380

Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
385 390 395 400

Glu Leu Glu Pro Gln
405

<210> 239
<211> 395
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-GP130(609-700)-IL7R(316-459)-IL12Rb2(775-825)

<400> 239

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Thr Thr Pro Lys
            100                 105                 110

Phe Ala Gln Gly Glu Ile Glu Ala Ile Val Val Pro Val Cys Leu Ala
        115                 120                 125

Phe Leu Leu Thr Thr Leu Leu Gly Val Leu Phe Cys Phe Asn Lys Arg
    130                 135                 140

Asp Leu Ile Lys Lys His Ile Trp Pro Asn Val Pro Asp Pro Ser Lys
145                 150                 155                 160

Ser His Ile Ala Gln Trp Ser Pro His Thr Pro Pro Arg His Asn Phe
                165                 170                 175

Asn Ser Lys Asp Gln Met Tyr Ser Asp Gly Asn Phe Thr Asp Val Ser
            180                 185                 190

Val Val Glu Ile Glu Ala Asn Asp Ala Arg Asp Glu Val Glu Gly Phe
        195                 200                 205

Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
    210                 215                 220

Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
225                 230                 235                 240

Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala
                245                 250                 255

Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
            260                 265                 270
```

```
Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
        275                 280                 285


Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
    290                 295                 300


Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
305                 310                 315                 320


Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
                325                 330                 335


Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro
            340                 345                 350


Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
        355                 360                 365


Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
    370                 375                 380


Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385                 390                 395


<210>  240
<211>  402
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)-PrlR(221-319)-IL7R(316-459)-IL12Rb2(775-825)

<400>  240

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15
```

```
Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ala Thr Phe Ile
            100                 105                 110

Gln Ile Pro Ser Asp Phe Thr Met Asn Asp Thr Thr Val Trp Ile Ser
        115                 120                 125

Val Ala Val Leu Ser Ala Val Ile Cys Leu Ile Ile Val Trp Ala Val
    130                 135                 140

Ala Leu Lys Gly Tyr Ser Met Val Thr Cys Ile Phe Pro Pro Val Pro
145                 150                 155                 160

Gly Pro Lys Ile Lys Gly Phe Asp Ala His Leu Leu Glu Lys Gly Lys
                165                 170                 175

Ser Glu Glu Leu Leu Ser Ala Leu Gly Cys Gln Asp Phe Pro Pro Thr
            180                 185                 190

Ser Asp Tyr Glu Asp Leu Leu Val Glu Tyr Leu Glu Val Asp Asp Ala
        195                 200                 205
```

```
Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu
    210                 215                 220

Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn
225                 230                 235                 240

Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp
                245                 250                 255

Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro
            260                 265                 270

Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn
        275                 280                 285

Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn
    290                 295                 300

Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu
305                 310                 315                 320

Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn
                325                 330                 335

Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser
            340                 345                 350

Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
        355                 360                 365

Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
    370                 375                 380

Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu
385                 390                 395                 400
```

Pro Gln

<210> 241
<211> 405
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-GHR(251-352)-IL7R(316-459)-IL12Rb2(775-825)

<400> 241

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Leu Pro Gln Met
            100                 105                 110


Ser Gln Phe Thr Cys Glu Glu Asp Phe Tyr Phe Pro Trp Leu Leu Ile
        115                 120                 125


Ile Ile Phe Gly Ile Phe Gly Leu Thr Val Met Leu Phe Val Phe Leu
    130                 135                 140
```

```
Phe Ser Lys Gln Gln Arg Ile Lys Met Leu Ile Leu Pro Pro Val Pro
145                 150                 155                 160

Val Pro Lys Ile Lys Gly Ile Asp Pro Asp Leu Leu Lys Glu Gly Lys
                165                 170                 175

Leu Glu Glu Val Asn Thr Ile Leu Ala Ile His Asp Ser Tyr Lys Pro
            180                 185                 190

Glu Phe His Ser Asp Asp Ser Trp Val Glu Phe Ile Glu Leu Asp Ile
        195                 200                 205

Asp Glu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
    210                 215                 220

Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
225                 230                 235                 240

Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
                245                 250                 255

Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
            260                 265                 270

Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
        275                 280                 285

Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
    290                 295                 300

Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
305                 310                 315                 320

Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
                325                 330                 335
```

```
Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
            340                 345                 350


Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
        355                 360                 365


Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
    370                 375                 380


Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
385                 390                 395                 400


Glu Leu Glu Pro Gln
                405


<210>  242
<211>  400
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)-GCSFR(614-710)-IL7R(316-459)-IL12Rb2(775-825)

<400>  242

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60
```

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Leu Thr Leu Met
            100                 105                 110

Thr Leu Thr Pro Glu Gly Ser Glu Leu His Ile Ile Leu Gly Leu Phe
        115                 120                 125

Gly Leu Leu Leu Leu Leu Thr Cys Leu Cys Gly Thr Ala Trp Leu Cys
    130                 135                 140

Cys Ser Pro Asn Arg Lys Asn Pro Leu Trp Pro Ser Val Pro Asp Pro
145                 150                 155                 160

Ala His Ser Ser Leu Gly Ser Trp Val Pro Thr Ile Met Glu Glu Asp
                165                 170                 175

Ala Phe Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile Thr Lys Leu Thr
            180                 185                 190

Val Leu Glu Glu Asp Glu Lys Lys Pro Val Pro Trp Glu Ala Arg Asp
        195                 200                 205

Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
    210                 215                 220

Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
225                 230                 235                 240

Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
                245                 250                 255
```

```
Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
            260                 265                 270


Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
        275                 280                 285


His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
    290                 295                 300


Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
305                 310                 315                 320


Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
                325                 330                 335


Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro
            340                 345                 350


Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
        355                 360                 365


Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
    370                 375                 380


Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385                 390                 395                 400


<210>  243
<211>  408
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)-TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)

<400>  243

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15
```

```
Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205
```

```
Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320

Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            340                 345                 350

Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
        355                 360                 365

Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
    370                 375                 380

Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
385                 390                 395                 400
```

Ser Leu Glu Glu Leu Glu Pro Gln
405

<210> 244
<211> 251
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(376-416)

<400> 244

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
115 120 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
130 135 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145 150 155 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
165 170 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
180 185 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
195 200 205

Arg Cys Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
210 215 220

Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
225 230 235 240

Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
245 250

<210> 245
<211> 246
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(424-459)

<400> 245

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
    210                 215                 220
```

```
Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
225                 230                 235                 240


Ser Phe Tyr Gln Asn Gln
                245


<210>  246
<211>  278
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459)

<400>  246

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110
```

```
Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
    210                 215                 220


Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
225                 230                 235                 240


Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile
                245                 250                 255


Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
            260                 265                 270


Ser Phe Tyr Gln Asn Gln
        275


<210>  247
<211>  246
<212>  PRT
<213>  Artificial Sequence
```

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(424-459;Y456F)

<400> 247

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110


Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175
```

```
Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
    210                 215                 220


Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
225                 230                 235                 240


Ser Phe Phe Gln Asn Gln
                245


<210>  248
<211>  278
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL7R(376-416,424-459;Y456F)

<400>  248

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60
```

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
    210                 215                 220

Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
225                 230                 235                 240

Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Gln Gly Gln Pro Ile
                245                 250                 255
```

Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
260 265 270

Ser Phe Phe Gln Asn Gln
275

<210> 249
<211> 251
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(393-433)

<400> 249

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
115 120 125

```
Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln
    210                 215                 220

Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro
225                 230                 235                 240

Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser
                245                 250
```

<210> 250
<211> 244
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(518-551)

<400> 250

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15
```

```
Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205
```

Arg Cys Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu
210 215 220

Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro
225 230 235 240

Thr His Leu Val

<210> 251
<211> 292
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433)

<400> 251

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

```
Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn
    210                 215                 220

His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His
225                 230                 235                 240

Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala
                245                 250                 255

Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly
            260                 265                 270

Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu
        275                 280                 285

Phe Ser Pro Ser
    290
```

<210> 252
<211> 285
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(339-379,518-551)

<400> 252

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
115 120 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
130 135 140

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn
    210                 215                 220


His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His
225                 230                 235                 240


Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Gly Gln Gly Glu Phe
                245                 250                 255


Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser
            260                 265                 270


Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
        275                 280                 285


<210>  253
<211>  285
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(393-433,518-551)

<400>  253

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15
```

```
Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205
```

```
Arg Cys Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln
    210                 215                 220

Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro
225                 230                 235                 240

Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe
                245                 250                 255

Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser
            260                 265                 270

Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
        275                 280                 285
```

<210> 254
<211> 326
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-IL2Rb(339-379,393-433,518-551)

<400> 254

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60
```

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn
    210                 215                 220

His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe Phe His
225                 230                 235                 240

Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala
                245                 250                 255
```

```
Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly
            260                 265                 270


Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu
        275                 280                 285


Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu
    290                 295                 300


Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln
305                 310                 315                 320


Asp Pro Thr His Leu Val
                325


<210>  255
<211>  441
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(955-1186)

<400>  255

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80
```

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr
    210                 215                 220

Asp Ser Asn Phe Tyr Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp
225                 230                 235                 240

Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser
                245                 250                 255

Ser Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala Thr
            260                 265                 270
```

```
Ser Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser
        275                 280                 285

Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Tyr Ser Ser Asp Pro
    290                 295                 300

Thr Gly Ala Leu Thr Glu Asp Ser Ile Asp Asp Thr Phe Leu Pro Val
305                 310                 315                 320

Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly Ser Val
                325                 330                 335

Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro Ser Arg
            340                 345                 350

Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly Asn Pro Glu
        355                 360                 365

Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr Phe Asp Ser
    370                 375                 380

Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn
385                 390                 395                 400

Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly
                405                 410                 415

Ile Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala
            420                 425                 430

Pro Gln Ser Ser Glu Phe Ile Gly Ala
        435                 440
```

<210> 256
<211> 428

<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(955-1044,1058-1186;Y974F)

<400> 256

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110


Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160
```

```
Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr
    210                 215                 220

Asp Ser Asn Phe Phe Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp
225                 230                 235                 240

Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser
                245                 250                 255

Ser Pro Ser Thr Ser Arg Thr Pro Leu Leu Ser Ser Leu Ser Ala Thr
            260                 265                 270

Ser Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln Ser
        275                 280                 285

Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe
    290                 295                 300

Leu Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro Ala
305                 310                 315                 320

Gly Ser Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala
                325                 330                 335

Pro Ser Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly
            340                 345                 350
```

```
Asn Pro Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser Thr
        355                 360                 365


Phe Asp Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile Ser
    370                 375                 380


Leu Asp Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys
385                 390                 395                 400


Pro Asn Gly Ile Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu
                405                 410                 415


Arg Val Ala Pro Gln Ser Ser Glu Phe Ile Gly Ala
            420                 425


<210>  257
<211>  264
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(955-1009;Y974F)

<400>  257

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80
```

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Val Ile Gln Gly Asp Glu Arg Met His Leu Pro Ser Pro Thr
    210                 215                 220

Asp Ser Asn Phe Phe Arg Ala Leu Met Asp Glu Glu Asp Met Asp Asp
225                 230                 235                 240

Val Val Asp Ala Asp Glu Tyr Leu Ile Pro Gln Gln Gly Phe Phe Ser
                245                 250                 255

Ser Pro Ser Thr Ser Arg Thr Pro
            260
```

<210> 258
<211> 264
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1019-1085)

<400> 258

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
100 105 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
115 120 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
130 135 140

```
Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Asn Asn Ser Thr Val Ala Cys Ile Asp Arg Asn Gly Leu Gln
    210                 215                 220


Ser Cys Pro Ile Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr
225                 230                 235                 240


Phe Leu Pro Val Pro Glu Tyr Ile Asn Gln Ser Val Pro Lys Arg Pro
                245                 250                 255


Ala Gly Ser Val Gln Asn Pro Val
            260


<210>  259
<211>  264
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1037-1044,1058-1103;Y1068/1101F)

<400>  259

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30
```

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Lys Glu Asp Ser Phe Leu Gln Arg Ile Asp Asp Thr Phe Leu
    210                 215                 220
```

```
Pro Val Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala Gly
225                 230                 235                 240


Ser Val Gln Asn Pro Val Tyr His Asn Gln Pro Leu Asn Pro Ala Pro
                245                 250                 255


Ser Arg Asp Pro His Phe Gln Asp
            260


<210>  260
<211>  264
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1066-1118;Y1068/1086F)

<400>  260

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95
```

```
Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110


Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Val Pro Glu Phe Ile Asn Gln Ser Val Pro Lys Arg Pro Ala
    210                 215                 220


Gly Ser Val Gln Asn Pro Val Phe His Asn Gln Pro Leu Asn Pro Ala
225                 230                 235                 240


Pro Ser Arg Asp Pro His Tyr Gln Asp Pro His Ser Thr Ala Val Gly
                245                 250                 255


Asn Pro Glu Tyr Leu Asn Thr Val
            260
```

<210> 261
<211> 264
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1122-1165)

<400> 261

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110


Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175
```

```
Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Pro Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys Val Asn Ser
    210                 215                 220


Thr Phe Asp Ser Pro Ala His Trp Ala Gln Lys Gly Ser His Gln Ile
225                 230                 235                 240


Ser Leu Asp Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro Lys Glu Ala
                245                 250                 255


Lys Pro Asn Gly Ile Phe Lys Gly
            260


<210>  262
<211>  264
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-EGFR(1133-1186;Y1148F)

<400>  262

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45
```

```
Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Trp Ala Gln Lys Gly Ser His Gln Ile Ser Leu Asp Asn Pro
    210                 215                 220

Asp Phe Gln Gln Asp Phe Phe Pro Lys Glu Ala Lys Pro Asn Gly Ile
225                 230                 235                 240
```

```
Phe Lys Gly Ser Thr Ala Glu Asn Ala Glu Tyr Leu Arg Val Ala Pro
                245                 250                 255


Gln Ser Ser Glu Phe Ile Gly Ala
            260


<210>  263
<211>  366
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- EpoR(237-338;L241G,L242P)-BLNK(53-208)

<400>  263

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110


Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125
```

```
Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp
    210                 215                 220

Asp Phe Asp Ser Asp Tyr Glu Asn Pro Asp Glu His Ser Asp Ser Glu
225                 230                 235                 240

Met Tyr Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro
                245                 250                 255

Pro Pro Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe
            260                 265                 270

Ala Arg Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro
        275                 280                 285

Pro Phe Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys
    290                 295                 300

Ala Arg Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro
305                 310                 315                 320
```

Gln Val Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr
325 330 335

Val Val Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu
340 345 350

Ser Ser Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
355 360 365

<210> 264
<211> 366
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F)

<400> 264

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

```
Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110


Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125


Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140


Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160


Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175


Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190


Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205


Arg Cys Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp
    210                 215                 220


Asp Phe Asp Ser Asp Phe Glu Asn Pro Asp Glu His Ser Asp Ser Glu
225                 230                 235                 240


Met Tyr Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Tyr Glu Pro
                245                 250                 255


Pro Pro Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe
            260                 265                 270


Ala Arg Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro
        275                 280                 285
```

```
Pro Phe Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys
    290                 295                 300

Ala Arg Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro
305                 310                 315                 320

Gln Val Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr
                325                 330                 335

Val Val Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu
            340                 345                 350

Ser Ser Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
        355                 360                 365
```

<210> 265
<211> 366
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- EpoR(237-338;L241G,L242P)-BLNK(53-208;Y72F,Y96F)

<400> 265

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80
```

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Glu Pro Val
            100                 105                 110

Ser Gly Pro Thr Pro Ser Asp Leu Asp Pro Leu Ile Leu Thr Leu Ser
        115                 120                 125

Leu Ile Leu Val Val Ile Leu Val Gly Pro Thr Val Leu Ala Leu Leu
    130                 135                 140

Ser His Arg Arg Ala Leu Lys Gln Lys Ile Trp Pro Gly Ile Pro Ser
145                 150                 155                 160

Pro Glu Ser Glu Phe Glu Gly Leu Phe Thr Thr His Lys Gly Asn Phe
                165                 170                 175

Gln Leu Trp Leu Tyr Gln Asn Asp Gly Cys Leu Trp Trp Ser Pro Cys
            180                 185                 190

Thr Pro Phe Thr Glu Asp Pro Pro Ala Ser Leu Glu Val Leu Ser Glu
        195                 200                 205

Arg Cys Ala Ser Glu Ser Pro Ala Asp Glu Glu Glu Gln Trp Ser Asp
    210                 215                 220

Asp Phe Asp Ser Asp Phe Glu Asn Pro Asp Glu His Ser Asp Ser Glu
225                 230                 235                 240

Met Tyr Val Met Pro Ala Glu Glu Asn Ala Asp Asp Ser Phe Glu Pro
                245                 250                 255

Pro Pro Val Glu Gln Glu Thr Arg Pro Val His Pro Ala Leu Pro Phe
            260                 265                 270
```

```
Ala Arg Gly Glu Tyr Ile Asp Asn Arg Ser Ser Gln Arg His Ser Pro
        275                 280                 285

Pro Phe Ser Lys Thr Leu Pro Ser Lys Pro Ser Trp Pro Ser Glu Lys
    290                 295                 300

Ala Arg Leu Thr Ser Thr Leu Pro Ala Leu Thr Ala Leu Gln Lys Pro
305                 310                 315                 320

Gln Val Pro Pro Lys Pro Lys Gly Leu Leu Glu Asp Glu Ala Asp Tyr
                325                 330                 335

Val Val Pro Val Glu Asp Asn Asp Glu Asn Tyr Ile His Pro Thr Glu
            340                 345                 350

Ser Ser Ser Pro Pro Pro Glu Lys Ala Pro Met Val Asn Arg
        355                 360                 365


<210>  266
<211>  357
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)

<400>  266

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45
```

```
Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240
```

```
Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255


Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270


Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285


Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300


Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320


Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335


Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            340                 345                 350


Phe Tyr Gln Asn Gln
        355


<210>  267
<211>  432
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rb(333-551)

<400>  267

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30
```

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Val Thr Gln Leu Leu Leu Gln Gln Asp Lys Val
    210                 215                 220
```

```
Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser Leu Thr Ser Cys Phe
225                 230                 235                 240

Thr Asn Gln Gly Tyr Phe Phe Phe His Leu Pro Asp Ala Leu Glu Ile
                245                 250                 255

Glu Ala Cys Gln Val Tyr Phe Thr Tyr Asp Pro Tyr Ser Glu Glu Asp
            260                 265                 270

Pro Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro
        275                 280                 285

Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser
    290                 295                 300

Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Leu Leu Gly Gly Pro Ser
305                 310                 315                 320

Pro Pro Ser Thr Ala Pro Gly Gly Ser Gly Ala Gly Glu Glu Arg Met
                325                 330                 335

Pro Pro Ser Leu Gln Glu Arg Val Pro Arg Asp Trp Asp Pro Gln Pro
            340                 345                 350

Leu Gly Pro Pro Thr Pro Gly Val Pro Asp Leu Val Asp Phe Gln Pro
        355                 360                 365

Pro Pro Glu Leu Val Leu Arg Glu Ala Gly Glu Glu Val Pro Asp Ala
    370                 375                 380

Gly Pro Arg Glu Gly Val Ser Phe Pro Trp Ser Arg Pro Pro Gly Gln
385                 390                 395                 400

Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala
                405                 410                 415
```

```
Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
            420                 425                 430


<210>  268
<211>  288
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)

<400>  268

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125
```

```
Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser
    210                 215                 220

Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys
225                 230                 235                 240

Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln
                245                 250                 255

Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala
            260                 265                 270

Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
        275                 280                 285
```

<210> 269
<211> 329
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)

<400> 269

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190
```

```
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu
    210                 215                 220

Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe
225                 230                 235                 240

Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu
                245                 250                 255

Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro
            260                 265                 270

Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp
        275                 280                 285

Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn
    290                 295                 300

Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu
305                 310                 315                 320

Gln Gly Gln Asp Pro Thr His Leu Val
                325
```

<210> 270
<211> 408
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)

<400> 270

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190
```

```
Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320

Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            340                 345                 350

Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
        355                 360                 365

Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
    370                 375                 380
```

Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
385 390 395 400

Ser Leu Glu Glu Leu Glu Pro Gln
405

<210> 271
<211> 574
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-IL21R(322-538)

<400> 271

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
115 120 125

```
Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320
```

```
Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            340                 345                 350

Phe Tyr Gln Asn Gln Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr
        355                 360                 365

Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys
    370                 375                 380

Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser
385                 390                 395                 400

Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr
                405                 410                 415

Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp
            420                 425                 430

Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro
        435                 440                 445

Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys
    450                 455                 460

Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser
465                 470                 475                 480

Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala
                485                 490                 495

Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser
            500                 505                 510
```

```
Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser
        515                 520                 525


Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr
    530                 535                 540


Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val
545                 550                 555                 560


Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser
                565                 570


<210>  272
<211>  574
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)- IL21R(322-538)-IL7R(316-459)

<400>  272

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80
```

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr
    210                 215                 220

Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys
225                 230                 235                 240

Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser
                245                 250                 255

Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr
            260                 265                 270
```

```
Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp
        275                 280                 285

Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro
    290                 295                 300

Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys
305                 310                 315                 320

Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser
                325                 330                 335

Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala
            340                 345                 350

Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser
        355                 360                 365

Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser
    370                 375                 380

Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr
385                 390                 395                 400

Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val
                405                 410                 415

Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser Ala Arg
            420                 425                 430

Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
        435                 440                 445

Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
    450                 455                 460
```

```
Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
465                 470                 475                 480


Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile
                485                 490                 495


Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
            500                 505                 510


Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
        515                 520                 525


Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
    530                 535                 540


Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
545                 550                 555                 560


Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
                565                 570


<210>  273
<211>  505
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)-IL21R(322-538)

<400>  273

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45
```

```
Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser
    210                 215                 220

Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys
225                 230                 235                 240
```

```
Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln
                245                 250                 255

Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala
            260                 265                 270

Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
        275                 280                 285

Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr Glu Leu Gln Glu Pro
    290                 295                 300

Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys Pro Ser Phe Trp Pro
305                 310                 315                 320

Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser Glu Glu Arg Asp Arg
                325                 330                 335

Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr Val Leu Asp Ala Glu
            340                 345                 350

Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp Asp Gly Tyr Pro Ala
        355                 360                 365

Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro Gly Leu Glu Asp Pro
    370                 375                 380

Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys Gly Cys Val Ser Ala
385                 390                 395                 400

Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser Leu Leu Asp Arg Leu
                405                 410                 415

Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala Gly Gly Leu Pro Trp
            420                 425                 430
```

```
Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser Glu Ala Gly Ser Pro
        435                 440                 445


Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser Gly Phe Val Gly Ser
    450                 455                 460


Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr Ser Pro Gly Asp Glu
465                 470                 475                 480


Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Ile Pro Pro Pro
                485                 490                 495


Leu Ser Ser Pro Gly Pro Gln Ala Ser
            500                 505


<210>  274
<211>  505
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)- IL21R(322-538)-IL2Rbsmall(393-433,518-551)

<400>  274

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60
```

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr
    210                 215                 220

Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys
225                 230                 235                 240

Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser
                245                 250                 255
```

```
Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr
            260                 265                 270

Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp
        275                 280                 285

Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro
    290                 295                 300

Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys
305                 310                 315                 320

Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser
                325                 330                 335

Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala
            340                 345                 350

Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser
        355                 360                 365

Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser
    370                 375                 380

Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr
385                 390                 395                 400

Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val
                405                 410                 415

Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser Asp Glu
            420                 425                 430

Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro
        435                 440                 445
```

Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp
450 455 460

Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn
465 470 475 480

Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu
485 490 495

Gln Gly Gln Asp Pro Thr His Leu Val
500 505

<210> 275
<211> 546
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-
TPOR/MPLR(478-582)-IL2Rbsmall(339-379,393-433,518-551)-IL21R(322-538)

<400> 275

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala

```
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu
    210                 215                 220

Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe
225                 230                 235                 240

Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu
                245                 250                 255

Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro
            260                 265                 270

Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp
```

275 280 285

Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn
290 295 300

Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu
305 310 315 320

Gln Gly Gln Asp Pro Thr His Leu Val Pro Arg Ser Pro Ala Lys Arg
325 330 335

Leu Gln Leu Thr Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser Asp
340 345 350

Gly Val Pro Lys Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly Gly
355 360 365

Ser Ala Tyr Ser Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser Ile
370 375 380

Asp Thr Val Thr Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro Cys
385 390 395 400

Ser Cys Glu Asp Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly Leu
405 410 415

Glu Pro Ser Pro Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr Thr
420 425 430

Val Leu Ser Cys Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly Gly
435 440 445

Pro Leu Gly Ser Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp Gly
450 455 460

Glu Asp Trp Ala Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly Gly

465 470 475 480

Val Ser Glu Ser Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met Asp
485 490 495

Thr Phe Asp Ser Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val Glu
500 505 510

Cys Asp Phe Thr Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr Leu
515 520 525

Arg Gln Trp Val Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro Gln
530 535 540

Ala Ser
545

<210> 276
<211> 546
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582)-
IL21R(322-538)-IL2Rbsmall(339-379,393-433,518-551)

<400> 276

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Pro Arg Ser Pro Ala Lys Arg Leu Gln Leu Thr
    210                 215                 220

Glu Leu Gln Glu Pro Ala Glu Leu Val Glu Ser Asp Gly Val Pro Lys
225                 230                 235                 240

Pro Ser Phe Trp Pro Thr Ala Gln Asn Ser Gly Gly Ser Ala Tyr Ser
                245                 250                 255
```

```
Glu Glu Arg Asp Arg Pro Tyr Gly Leu Val Ser Ile Asp Thr Val Thr
            260                 265                 270

Val Leu Asp Ala Glu Gly Pro Cys Thr Trp Pro Cys Ser Cys Glu Asp
        275                 280                 285

Asp Gly Tyr Pro Ala Leu Asp Leu Asp Ala Gly Leu Glu Pro Ser Pro
    290                 295                 300

Gly Leu Glu Asp Pro Leu Leu Asp Ala Gly Thr Thr Val Leu Ser Cys
305                 310                 315                 320

Gly Cys Val Ser Ala Gly Ser Pro Gly Leu Gly Gly Pro Leu Gly Ser
                325                 330                 335

Leu Leu Asp Arg Leu Lys Pro Pro Leu Ala Asp Gly Glu Asp Trp Ala
            340                 345                 350

Gly Gly Leu Pro Trp Gly Gly Arg Ser Pro Gly Gly Val Ser Glu Ser
        355                 360                 365

Glu Ala Gly Ser Pro Leu Ala Gly Leu Asp Met Asp Thr Phe Asp Ser
    370                 375                 380

Gly Phe Val Gly Ser Asp Cys Ser Ser Pro Val Glu Cys Asp Phe Thr
385                 390                 395                 400

Ser Pro Gly Asp Glu Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val
                405                 410                 415

Val Ile Pro Pro Pro Leu Ser Ser Pro Gly Pro Gln Ala Ser Gln Gln
            420                 425                 430

Asp Lys Val Pro Glu Pro Ala Ser Leu Ser Ser Asn His Ser Leu Thr
        435                 440                 445
```

```
Ser Cys Phe Thr Asn Gln Gly Tyr Phe Phe His Leu Pro Asp Ala
    450                 455                 460


Leu Glu Ile Glu Ala Cys Gln Asp Glu Gly Val Ala Gly Ala Pro Thr
465                 470                 475                 480


Gly Ser Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala
                485                 490                 495


Tyr Cys Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser
            500                 505                 510


Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr
        515                 520                 525


Asp Ala Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His
    530                 535                 540


Leu Val
545


<210>  277
<211>  432
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-IL2Rbsmall(393-433,518-551)-IL7R(316-459)

<400>  277

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30
```

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser
    210                 215                 220
```

```
Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys
225                 230                 235                 240


Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln
                245                 250                 255


Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala
            260                 265                 270


Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
        275                 280                 285


Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
    290                 295                 300


Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
305                 310                 315                 320


Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
                325                 330                 335


Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
            340                 345                 350


Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
        355                 360                 365


Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
    370                 375                 380


Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
385                 390                 395                 400


Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
                405                 410                 415
```

Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
            420   425   430

<210> 278
<211> 432
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-IL2Rbsmall(393-433,518-551)

<400> 278

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1   5   10   15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20   25   30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35   40   45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50   55   60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65   70   75   80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85   90   95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100   105   110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115   120   125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130   135   140

```
Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320

Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335
```

```
Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            340                 345                 350


Phe Tyr Gln Asn Gln Asp Glu Gly Val Ala Gly Ala Pro Thr Gly Ser
        355                 360                 365


Ser Pro Gln Pro Leu Gln Pro Leu Ser Gly Glu Asp Asp Ala Tyr Cys
    370                 375                 380


Thr Phe Pro Ser Arg Asp Asp Leu Leu Leu Phe Ser Pro Ser Gly Gln
385                 390                 395                 400


Gly Glu Phe Arg Ala Leu Asn Ala Arg Leu Pro Leu Asn Thr Asp Ala
                405                 410                 415


Tyr Leu Ser Leu Gln Glu Leu Gln Gly Gln Asp Pro Thr His Leu Val
            420                 425                 430


<210>  279
<211>  473
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-
IL2Rbsmall(339-379,393-433,518-551)-IL7R(316-459)

<400>  279

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45
```

```
Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu
    210                 215                 220

Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe
225                 230                 235                 240
```

```
Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu
                245                 250                 255

Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro
            260                 265                 270

Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp
        275                 280                 285

Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn
    290                 295                 300

Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu
305                 310                 315                 320

Gln Gly Gln Asp Pro Thr His Leu Val Ala Arg Asp Glu Val Glu Gly
                325                 330                 335

Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
            340                 345                 350

Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
        355                 360                 365

Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
    370                 375                 380

Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
385                 390                 395                 400

Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
                405                 410                 415

Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
            420                 425                 430
```

```
Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
        435                 440                 445


Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
    450                 455                 460


Thr Met Ser Ser Phe Tyr Gln Asn Gln
465                 470


<210>  280
<211>  473
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-
IL2Rbsmall(339-379,393-433,518-551)

<400>  280

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95
```

```
Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125


Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140


Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160


Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175


Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190


Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205


Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220


Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240


Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255


Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270


Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285
```

```
Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300


Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320


Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335


Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            340                 345                 350


Phe Tyr Gln Asn Gln Gln Gln Asp Lys Val Pro Glu Pro Ala Ser Leu
        355                 360                 365


Ser Ser Asn His Ser Leu Thr Ser Cys Phe Thr Asn Gln Gly Tyr Phe
    370                 375                 380


Phe Phe His Leu Pro Asp Ala Leu Glu Ile Glu Ala Cys Gln Asp Glu
385                 390                 395                 400


Gly Val Ala Gly Ala Pro Thr Gly Ser Ser Pro Gln Pro Leu Gln Pro
                405                 410                 415


Leu Ser Gly Glu Asp Asp Ala Tyr Cys Thr Phe Pro Ser Arg Asp Asp
            420                 425                 430


Leu Leu Leu Phe Ser Pro Ser Gly Gln Gly Glu Phe Arg Ala Leu Asn
        435                 440                 445


Ala Arg Leu Pro Leu Asn Thr Asp Ala Tyr Leu Ser Leu Gln Glu Leu
    450                 455                 460


Gln Gly Gln Asp Pro Thr His Leu Val
465                 470
```

<210> 281
<211> 408
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)-PD1(156-191)-TPOR/MPLR (514-582)-IL7R(316-459)-IL12Rb2(775-825)

<400> 281

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Pro Ser Pro Ser
            100                 105                 110


Pro Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Val Gly Val Val Gly
        115                 120                 125


Gly Leu Leu Gly Ser Leu Val Leu Leu Val Trp Val Leu Ala Val Ile
    130                 135                 140


Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160
```

```
Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320

Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
            340                 345                 350
```

```
Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
        355                 360                 365


Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
    370                 375                 380


Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
385                 390                 395                 400


Ser Leu Glu Glu Leu Glu Pro Gln
                405


<210>  282
<211>  267
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582)-EGFR(1122-1165)

<400>  282

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80
```

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
        115                 120                 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
    130                 135                 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Pro Glu Tyr Leu Asn Thr Val Gln Pro Thr Cys
    210                 215                 220

Val Asn Ser Thr Phe Asp Ser Pro Ala His Trp Ala Gln Lys Gly Ser
225                 230                 235                 240

His Gln Ile Ser Leu Asp Asn Pro Asp Tyr Gln Gln Asp Phe Phe Pro
                245                 250                 255

Lys Glu Ala Lys Pro Asn Gly Ile Phe Lys Gly
            260                 265
```

<210> 283
<211> 408
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582)-IL7R(316-459)-IL12Rb2(775-825)FKBP switch containing wildtype TpoR TM sequence

<400> 283

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Ser Leu Val Thr Ala
115 120 125

Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu
130 135 140

Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp

```
145                 150                 155                 160

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
                165                 170                 175

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
            180                 185                 190

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
        195                 200                 205

Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
    210                 215                 220

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
225                 230                 235                 240

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
                245                 250                 255

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
            260                 265                 270

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
        275                 280                 285

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
    290                 295                 300

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
305                 310                 315                 320

Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
                325                 330                 335

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
```

340 345 350

Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
355 360 365

Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
370 375 380

Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
385 390 395 400

Ser Leu Glu Glu Leu Glu Pro Gln
405

<210> 284
<211> 407
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-1)-IL7R(316-459)-IL12Rb2(775-825)

<400> 284

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Trp Ile Ser Leu Val Thr Ala Leu
        115                 120                 125


His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
    130                 135                 140


Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
145                 150                 155                 160


Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
                165                 170                 175


Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
            180                 185                 190


Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
        195                 200                 205


Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
    210                 215                 220


Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
225                 230                 235                 240


Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
                245                 250                 255


Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
            260                 265                 270
```

```
Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
        275                 280                 285


Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
    290                 295                 300


Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
305                 310                 315                 320


Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
                325                 330                 335


Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
            340                 345                 350


Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
        355                 360                 365


Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
    370                 375                 380


Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
385                 390                 395                 400


Leu Glu Glu Leu Glu Pro Gln
                405


<210>  285
<211>  406
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582;N-2)-IL7R(316-459)-IL12Rb2(775-825)

<400>  285

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
```

```
1               5                   10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ile Ser Leu Val Thr Ala Leu His
        115                 120                 125

Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp
    130                 135                 140

Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
145                 150                 155                 160

Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
                165                 170                 175

Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
            180                 185                 190

Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
```

```
        195                 200                 205

Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
    210                 215                 220

Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val
225                 230                 235                 240

Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser
                245                 250                 255

Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala
            260                 265                 270

Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu
        275                 280                 285

Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu
    290                 295                 300

Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly
305                 310                 315                 320

Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser
                325                 330                 335

Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
            340                 345                 350

Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr
        355                 360                 365

Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser
    370                 375                 380

Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu
```

385 390 395 400

Glu Glu Leu Glu Pro Gln
405

<210> 286
<211> 407
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-2+1)-IL7R(316-459)-IL12Rb2(775-825)

<400> 286

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

Arg Val Glu Thr Ala Thr Glu Thr Leu Ile Ser Leu Val Thr Ala Leu
115 120 125

```
His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg
    130                 135                 140

Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
145                 150                 155                 160

Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
                165                 170                 175

Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
            180                 185                 190

Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
        195                 200                 205

Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
    210                 215                 220

Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
225                 230                 235                 240

Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
                245                 250                 255

Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
            260                 265                 270

Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
        275                 280                 285

Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
    290                 295                 300

Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
305                 310                 315                 320
```

```
Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
                325                 330                 335


Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
            340                 345                 350


Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
        355                 360                 365


Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
    370                 375                 380


Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
385                 390                 395                 400


Leu Glu Glu Leu Glu Pro Gln
                405


<210>  287
<211>  405
<212>  PRT
<213>  Artificial Sequence

<220
<223>  FKBP(F36V)- TPOR/MPLR(478-582;N-3)-IL7R(316-459)-IL12Rb2(775-825)

<400>  287

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
```

```
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ser Leu Val Thr Ala Leu His Leu
        115                 120                 125

Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
    130                 135                 140

Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
145                 150                 155                 160

Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
                165                 170                 175

Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
            180                 185                 190

Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
        195                 200                 205

Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
    210                 215                 220

Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
225                 230                 235                 240

Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
```

245 250 255

Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
260 265 270

Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
275 280 285

Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
290 295 300

Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
305 310 315 320

Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
325 330 335

Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
340 345 350

Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
355 360 365

Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
370 375 380

Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
385 390 395 400

Glu Leu Glu Pro Gln
405

<210> 288
<211> 404
<212> PRT
<213> Artificial Sequence

<220

<223> FKBP(F36V)- TPOR/MPLR(478-582;N-4)-IL7R(316-459)-IL12Rb2(775-825)

<400> 288

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Leu Val Thr Ala Leu His Leu Val
        115                 120                 125

Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe
    130                 135                 140

Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro
145                 150                 155                 160

Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu
                165                 170                 175
```

```
Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro
            180                 185                 190


Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro
        195                 200                 205


Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln
    210                 215                 220


Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser
225                 230                 235                 240


Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly
                245                 250                 255


Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp
            260                 265                 270


Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly
        275                 280                 285


Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr
    290                 295                 300


Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu
305                 310                 315                 320


Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly
                325                 330                 335


Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn
            340                 345                 350


Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu
        355                 360                 365
```

Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile
370 375 380

Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu
385 390 395 400

Leu Glu Pro Gln

<210> 289
<211> 405
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-4+1)-IL7R(316-459)-IL12Rb2(775-825)

<400> 289

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr

```
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ile Leu Val Thr Ala Leu His Leu
        115                 120                 125

Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln
    130                 135                 140

Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu
145                 150                 155                 160

Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala
                165                 170                 175

Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu
            180                 185                 190

Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu
        195                 200                 205

Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro
    210                 215                 220

Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln
225                 230                 235                 240

Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe
                245                 250                 255

Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys
            260                 265                 270

Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser
        275                 280                 285

Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly
```

290 295 300

Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile
305 310 315 320

Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu
325 330 335

Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln
340 345 350

Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val
355 360 365

Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn
370 375 380

Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu
385 390 395 400

Glu Leu Glu Pro Gln
405

<210> 290
<211> 403
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-5)-IL7R(316-459)-IL12Rb2(775-825)

<400> 290

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Val Thr Ala Leu His Leu Val Leu
        115                 120                 125

Gly Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro
    130                 135                 140

Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp
145                 150                 155                 160

Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser
                165                 170                 175

Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser
            180                 185                 190

Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu
        195                 200                 205

Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln
    210                 215                 220
```

```
Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro
225                 230                 235                 240


Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg
                245                 250                 255


Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala
            260                 265                 270


Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys
        275                 280                 285


Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr
    290                 295                 300


Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr
305                 310                 315                 320


Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser
                325                 330                 335


Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln
            340                 345                 350


Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro
        355                 360                 365


Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp
    370                 375                 380


Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu
385                 390                 395                 400


Glu Pro Gln
```

<210> 291
<211> 402
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-6)-IL7R(316-459)-IL12Rb2(775-825)

<400> 291

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Thr Ala Leu His Leu Val Leu Gly
        115                 120                 125


Leu Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala
    130                 135                 140


His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu
```

```
145                 150                 155                 160

His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro
                165                 170                 175

Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu
            180                 185                 190

Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala
        195                 200                 205

Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu
    210                 215                 220

Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn
225                 230                 235                 240

Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp
                245                 250                 255

Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro
            260                 265                 270

Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn
        275                 280                 285

Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn
    290                 295                 300

Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu
305                 310                 315                 320

Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn
                325                 330                 335

Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser
```

340 345 350

Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala
355 360 365

Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp
370 375 380

Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu
385 390 395 400

Pro Gln

<210> 292
<211> 401
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-7)-IL7R(316-459)-IL12Rb2(775-825)

<400> 292

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Leu His Leu Val Leu Gly Leu
        115                 120                 125

Ser Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His
    130                 135                 140

Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His
145                 150                 155                 160

Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro
                165                 170                 175

Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu
            180                 185                 190

Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg
        195                 200                 205

Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu
    210                 215                 220

Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys
225                 230                 235                 240

Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser
                245                 250                 255

Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile
            260                 265                 270
```

```
Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly
        275                 280                 285


Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser
    290                 295                 300


Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn
305                 310                 315                 320


Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln
                325                 330                 335


Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp
            340                 345                 350


Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly
        355                 360                 365


Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu
    370                 375                 380


Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro
385                 390                 395                 400


Gln
```

<210> 293
<211> 400
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-8)-IL7R(316-459)-IL12Rb2(775-825)

<400> 293

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
```

```
1               5                   10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Leu His Leu Val Leu Gly Leu Ser
        115                 120                 125

Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
    130                 135                 140

Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
145                 150                 155                 160

Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
                165                 170                 175

Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
            180                 185                 190

Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp
```

```
        195                 200                 205

Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
    210                 215                 220

Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
225                 230                 235                 240

Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
                245                 250                 255

Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
            260                 265                 270

Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
        275                 280                 285

His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
    290                 295                 300

Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
305                 310                 315                 320

Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
                325                 330                 335

Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro
            340                 345                 350

Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
        355                 360                 365

Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
    370                 375                 380

Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
```

385 390 395 400

<210> 294
<211> 399
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-9)-IL7R(316-459)-IL12Rb2(775-825)

<400> 294

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

Arg Val Glu Thr Ala Thr Glu Thr His Leu Val Leu Gly Leu Ser Ala
115 120 125

Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
130 135 140

```
Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
145                 150                 155                 160


Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
                165                 170                 175


Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
            180                 185                 190


Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu
        195                 200                 205


Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
    210                 215                 220


Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
225                 230                 235                 240


Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
                245                 250                 255


Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser
            260                 265                 270


Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
        275                 280                 285


Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
    290                 295                 300


Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
305                 310                 315                 320


Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
                325                 330                 335
```

Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys
340 345 350

Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
355 360 365

Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
370 375 380

His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385 390 395

<210> 295
<211> 398
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-10)-IL7R(316-459)-IL12Rb2(775-825)

<400> 295

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala

```
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Leu Val Leu Gly Leu Ser Ala Val
        115                 120                 125

Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
    130                 135                 140

Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
145                 150                 155                 160

Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
                165                 170                 175

Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
            180                 185                 190

Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val
        195                 200                 205

Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
    210                 215                 220

Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
225                 230                 235                 240

Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
                245                 250                 255

Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
            260                 265                 270

Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
```

275 280 285

Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
290 295 300

Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
305 310 315 320

Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
325 330 335

Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro
340 345 350

Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
355 360 365

Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
370 375 380

Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385 390 395

<210> 296
<211> 397
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-11)-IL7R(316-459)-IL12Rb2(775-825)

<400> 296

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

```
Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Val Leu Gly Leu Ser Ala Val Leu
        115                 120                 125

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
    130                 135                 140

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
145                 150                 155                 160

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
                165                 170                 175

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
            180                 185                 190

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
        195                 200                 205

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
    210                 215                 220
```

```
Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
225                 230                 235                 240


Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
                245                 250                 255


Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
            260                 265                 270


Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
        275                 280                 285


Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
    290                 295                 300


Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
305                 310                 315                 320


Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
                325                 330                 335


Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu
            340                 345                 350


Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
        355                 360                 365


His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
    370                 375                 380


Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385                 390                 395


<210>  297
<211>  396
<212>  PRT
```

<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-12)-IL7R(316-459)-IL12Rb2(775-825)

<400> 297

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Ser Ala Val Leu Gly
        115                 120                 125


Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
    130                 135                 140


His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
145                 150                 155                 160


Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
```

165 170 175

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
180 185 190

Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly
195 200 205

Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
210 215 220

Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
225 230 235 240

Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
245 250 255

Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
260 265 270

Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
275 280 285

Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
290 295 300

Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
305 310 315 320

Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
325 330 335

Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn
340 345 350

Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His

355 360 365

Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
370 375 380

Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385 390 395

<210> 298
<211> 395
<212> PRT
<213> Artificial Sequence

<220
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-13)-IL7R(316-459)-IL12Rb2(775-825)

<400> 298

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

```
Arg Val Glu Thr Ala Thr Glu Thr Gly Leu Ser Ala Val Leu Gly Leu
        115                 120                 125


Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
    130                 135                 140


Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
145                 150                 155                 160


Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
                165                 170                 175


Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
            180                 185                 190


Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe
        195                 200                 205


Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
    210                 215                 220


Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
225                 230                 235                 240


Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala
                245                 250                 255


Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
            260                 265                 270


Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
        275                 280                 285


Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
    290                 295                 300
```

```
Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
305                 310                 315                 320


Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
                325                 330                 335


Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro
            340                 345                 350


Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
        355                 360                 365


Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
    370                 375                 380


Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385                 390                 395


<210>  299
<211>  394
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V)- TPOR/MPLR(478-582;N-14)-IL7R(316-459)-IL12Rb2(775-825)

<400>  299

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
```

```
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Leu Ser Ala Val Leu Gly Leu Leu
        115                 120                 125

Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
    130                 135                 140

Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
145                 150                 155                 160

Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
                165                 170                 175

Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
            180                 185                 190

Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu
        195                 200                 205

Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu
    210                 215                 220

Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile
225                 230                 235                 240

Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly
```

245 250 255

Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu
260 265 270

Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu
275 280 285

Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser
290 295 300

Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
305 310 315 320

Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
325 330 335

Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala
340 345 350

Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
355 360 365

Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
370 375 380

Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
385 390

<210> 300
<211> 393
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-15)-IL7R(316-459)-IL12Rb2(775-825)

<400> 300

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ser Ala Val Leu Gly Leu Leu Leu
        115                 120                 125

Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
    130                 135                 140

Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
145                 150                 155                 160

Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
                165                 170                 175

Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
            180                 185                 190
```

```
Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
        195                 200                 205

Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
    210                 215                 220

Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
225                 230                 235                 240

Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
                245                 250                 255

Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
            260                 265                 270

Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
        275                 280                 285

Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
    290                 295                 300

Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
305                 310                 315                 320

Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
                325                 330                 335

Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
            340                 345                 350

Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
        355                 360                 365

Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
    370                 375                 380
```

```
Asp Ser Leu Glu Glu Leu Glu Pro Gln
385                 390


<210>  301
<211>  392
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V)- TPOR/MPLR(478-582;N-16)-IL7R(316-459)-IL12Rb2(775-825)

<400>  301

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Ala Val Leu Gly Leu Leu Leu Leu
        115                 120                 125


Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp
```

```
    130                 135                 140

Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp
145                 150                 155                 160

Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu
                165                 170                 175

Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg
            180                 185                 190

Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp
        195                 200                 205

Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly
    210                 215                 220

Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro
225                 230                 235                 240

Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val
                245                 250                 255

Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys
            260                 265                 270

Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu
        275                 280                 285

Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln
    290                 295                 300

Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu
305                 310                 315                 320

Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser
```

325 330 335

Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro
340 345 350

Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu
355 360 365

Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp
370 375 380

Ser Leu Glu Glu Leu Glu Pro Gln
385 390

<210> 302
<211> 391
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N-17)-IL7R(316-459)-IL12Rb2(775-825)

<400> 302

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

```
Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Val Leu Gly Leu Leu Leu Leu Arg
        115                 120                 125


Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro
    130                 135                 140


Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr
145                 150                 155                 160


Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu
                165                 170                 175


Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr
            180                 185                 190


Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr
        195                 200                 205


Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp
    210                 215                 220


Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu
225                 230                 235                 240


Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser
                245                 250                 255


Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg
            260                 265                 270
```

```
Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser
        275                 280                 285


Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser
    290                 295                 300


Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr
305                 310                 315                 320


Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe
                325                 330                 335


Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp
            340                 345                 350


Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro
        355                 360                 365


Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser
    370                 375                 380


Leu Glu Glu Leu Glu Pro Gln
385                 390


<210>  303
<211>  390
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V)- TPOR/MPLR(478-582;N-18)-IL7R(316-459)-IL12Rb2(775-825)

<400>  303

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
```

```
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Leu Gly Leu Leu Leu Leu Arg Trp
        115                 120                 125

Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu Trp Pro Ser
    130                 135                 140

Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala
145                 150                 155                 160

Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys Glu Glu Val
                165                 170                 175

Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro
            180                 185                 190

Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln Asp Thr Phe
        195                 200                 205

Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly Gly Asp Val
```

```
    210                 215                 220

Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr Pro Glu Ser
225                 230                 235                 240

Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn Val Ser Ala
                245                 250                 255

Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu
            260                 265                 270

Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu Leu Ser Leu
        275                 280                 285

Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly
    290                 295                 300

Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile Leu Thr Ser
305                 310                 315                 320

Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr
                325                 330                 335

Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr
            340                 345                 350

Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr Leu Pro Ser
        355                 360                 365

Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala Asp Ser Leu
    370                 375                 380

Glu Glu Leu Glu Pro Gln
385                 390
```

<210> 304

<211> 409
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N+1)-IL7R(316-459)-IL12Rb2(775-825)

<400> 304

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45


Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60


Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80


Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95


Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110


Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile Ser Leu Val Thr
        115                 120                 125


Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu Leu
    130                 135                 140


Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala Leu
145                 150                 155                 160
```

```
Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu Arg
                165                 170                 175


Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr Cys
            180                 185                 190


Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser Glu
        195                 200                 205


Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu Gln
    210                 215                 220


Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu Gly
225                 230                 235                 240


Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile Thr
                245                 250                 255


Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly Asn
            260                 265                 270


Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu Asp
        275                 280                 285


Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu Leu
    290                 295                 300


Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser Leu
305                 310                 315                 320


Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro Ile
                325                 330                 335


Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met Ser
            340                 345                 350
```

Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala Cys
355 360 365

Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly Tyr
370 375 380

Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu Ala
385 390 395 400

Asp Ser Leu Glu Glu Leu Glu Pro Gln
405

<210> 305
<211> 410
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N+2)-IL7R(316-459)-IL12Rb2(775-825)

<400> 305

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala

85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu Ile Ser Leu Val
115 120 125

Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu Leu
130 135 140

Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His Ala
145 150 155 160

Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr Leu
165 170 175

Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp Thr
180 185 190

Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser Ser
195 200 205

Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe Leu
210 215 220

Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg Leu
225 230 235 240

Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val Ile
245 250 255

Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala Gly
260 265 270

Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser Leu

275 280 285

Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp Leu
290 295 300

Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe Ser
305 310 315 320

Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln Pro
325 330 335

Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr Met
340 345 350

Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro Ala
355 360 365

Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp Gly
370 375 380

Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro Leu
385 390 395 400

Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
405 410

<210> 306
<211> 411
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N+3)-IL7R(316-459)-IL12Rb2(775-825)

<400> 306

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

```
Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val Leu Ile Ser Leu
        115                 120                 125

Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly Leu
    130                 135                 140

Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg His
145                 150                 155                 160

Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln Tyr
                165                 170                 175

Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser Asp
            180                 185                 190

Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys Ser
        195                 200                 205
```

```
Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly Phe
    210                 215                 220

Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln Arg
225                 230                 235                 240

Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val Val
                245                 250                 255

Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu Ala
            260                 265                 270

Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg Ser
        275                 280                 285

Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln Asp
    290                 295                 300

Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro Phe
305                 310                 315                 320

Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly Gln
                325                 330                 335

Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val Thr
            340                 345                 350

Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn Pro
        355                 360                 365

Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His Asp
    370                 375                 380

Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala Pro
385                 390                 395                 400
```

Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
405 410

<210> 307
<211> 412
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N+4)-IL7R(316-459)-IL12Rb2(775-825)

<400> 307

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Ile Leu Val Leu Ile Ser
115 120 125

Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu Gly

```
    130                 135                 140

Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu Arg
145                 150                 155                 160

His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly Gln
                165                 170                 175

Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val Ser
            180                 185                 190

Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro Lys
        195                 200                 205

Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu Gly
    210                 215                 220

Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys Gln
225                 230                 235                 240

Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp Val
                245                 250                 255

Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys Leu
            260                 265                 270

Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser Arg
        275                 280                 285

Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr Gln
    290                 295                 300

Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro Pro
305                 310                 315                 320

Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln Gly
```

325 330 335

Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr Val
340 345 350

Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu Asn
355 360 365

Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr His
370 375 380

Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu Ala
385 390 395 400

Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
405 410

<210> 308
<211> 413
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N+5)-IL7R(316-459)-IL12Rb2(775-825)

<400> 308

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

```
Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Ile Leu Val Leu Ile
        115                 120                 125

Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val Leu
    130                 135                 140

Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg Leu
145                 150                 155                 160

Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu Gly
                165                 170                 175

Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr Val
            180                 185                 190

Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu Pro
        195                 200                 205

Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val Glu
    210                 215                 220

Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu Lys
225                 230                 235                 240

Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu Asp
                245                 250                 255
```

```
Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr Cys
            260                 265                 270


Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser Ser
        275                 280                 285


Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val Tyr
    290                 295                 300


Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro Pro
305                 310                 315                 320


Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala Gln
                325                 330                 335


Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala Tyr
            340                 345                 350


Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro Glu
        355                 360                 365


Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro Thr
    370                 375                 380


His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His Glu
385                 390                 395                 400


Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
                405                 410


<210>  309
<211>  414
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V)- TPOR/MPLR(478-582;N+6)-IL7R(316-459)-IL12Rb2(775-825)
```

<400> 309

```
Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                  10                  15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Leu Ile Leu Val Leu
        115                 120                 125

Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala Val
    130                 135                 140

Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg Arg
145                 150                 155                 160

Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val Leu
                165                 170                 175

Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala Thr
```

```
            180                 185                 190

Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile Leu
        195                 200                 205

Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu Val
    210                 215                 220

Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser Glu
225                 230                 235                 240

Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser Glu
                245                 250                 255

Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu Thr
            260                 265                 270

Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser Ser
        275                 280                 285

Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His Val
    290                 295                 300

Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu Pro
305                 310                 315                 320

Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val Ala
                325                 330                 335

Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu Ala
            340                 345                 350

Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys Pro
        355                 360                 365

Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu Pro
```

370 375 380

Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser His
385 390 395 400

Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
405 410

<210> 310
<211> 415
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP(F36V)- TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)

<400> 310

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1 5 10 15

Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
20 25 30

Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
35 40 45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
50 55 60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65 70 75 80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
85 90 95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
100 105 110

```
Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Val Leu Leu Ile Leu Val
        115                 120                 125


Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser Ala
    130                 135                 140


Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr Arg
145                 150                 155                 160


Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg Val
                165                 170                 175


Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys Ala
            180                 185                 190


Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu Ile
        195                 200                 205


Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp Glu
    210                 215                 220


Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu Ser
225                 230                 235                 240


Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro Ser
                245                 250                 255


Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser Leu
            260                 265                 270


Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu Ser
        275                 280                 285


Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro His
    290                 295                 300
```

```
Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr Leu
305                 310                 315                 320


Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro Val
                325                 330                 335


Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu Glu
            340                 345                 350


Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro Lys
        355                 360                 365


Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp Leu
    370                 375                 380


Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro Ser
385                 390                 395                 400


His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
                405                 410                 415


<210>  311
<211>  416
<212>  PRT
<213>  Artificial Sequence

<220>
<223>  FKBP(F36V)- TPOR/MPLR(478-582;N+7)-IL7R(316-459)-IL12Rb2(775-825)

<400>  311

Met Gly Val Gln Val Glu Thr Ile Ser Pro Gly Asp Gly Arg Thr Phe
1               5                   10                  15


Pro Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu
            20                  25                  30


Asp Gly Lys Lys Val Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys
```

```
        35                  40                  45

Phe Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val
    50                  55                  60

Ala Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp
65                  70                  75                  80

Tyr Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala
                85                  90                  95

Thr Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu Ser Asp Pro Thr
            100                 105                 110

Arg Val Glu Thr Ala Thr Glu Thr Ala Trp Leu Val Leu Leu Ile Leu
        115                 120                 125

Val Leu Ile Ser Leu Val Thr Ala Leu His Leu Val Leu Gly Leu Ser
    130                 135                 140

Ala Val Leu Gly Leu Leu Leu Leu Arg Trp Gln Phe Pro Ala His Tyr
145                 150                 155                 160

Arg Arg Leu Arg His Ala Leu Trp Pro Ser Leu Pro Asp Leu His Arg
                165                 170                 175

Val Leu Gly Gln Tyr Leu Arg Asp Thr Ala Ala Leu Ser Pro Pro Lys
            180                 185                 190

Ala Thr Val Ser Asp Thr Cys Glu Glu Val Glu Pro Ser Leu Leu Glu
        195                 200                 205

Ile Leu Pro Lys Ser Ser Glu Arg Thr Pro Leu Pro Leu Ala Arg Asp
    210                 215                 220

Glu Val Glu Gly Phe Leu Gln Asp Thr Phe Pro Gln Gln Leu Glu Glu
```

```
225                 230                 235                 240

Ser Glu Lys Gln Arg Leu Gly Gly Asp Val Gln Ser Pro Asn Cys Pro
                245                 250                 255

Ser Glu Asp Val Val Ile Thr Pro Glu Ser Phe Gly Arg Asp Ser Ser
            260                 265                 270

Leu Thr Cys Leu Ala Gly Asn Val Ser Ala Cys Asp Ala Pro Ile Leu
        275                 280                 285

Ser Ser Ser Arg Ser Leu Asp Cys Arg Glu Ser Gly Lys Asn Gly Pro
    290                 295                 300

His Val Tyr Gln Asp Leu Leu Leu Ser Leu Gly Thr Thr Asn Ser Thr
305                 310                 315                 320

Leu Pro Pro Pro Phe Ser Leu Gln Ser Gly Ile Leu Thr Leu Asn Pro
                325                 330                 335

Val Ala Gln Gly Gln Pro Ile Leu Thr Ser Leu Gly Ser Asn Gln Glu
            340                 345                 350

Glu Ala Tyr Val Thr Met Ser Ser Phe Tyr Gln Asn Gln Ser Asp Pro
        355                 360                 365

Lys Pro Glu Asn Pro Ala Cys Pro Trp Thr Val Leu Pro Ala Gly Asp
    370                 375                 380

Leu Pro Thr His Asp Gly Tyr Leu Pro Ser Asn Ile Asp Asp Leu Pro
385                 390                 395                 400

Ser His Glu Ala Pro Leu Ala Asp Ser Leu Glu Glu Leu Glu Pro Gln
                405                 410                 415
```